THE CONTRIBUTION OF POSTURAL ADJUSTMENTS TO BODY BALANCE AND MOTOR PERFORMANCE: VOLUME II

EDITED BY: Eric Yiou, Teddy Caderby, Paolo Cavallari and Martin Descarreaux
PUBLISHED IN: Frontiers in Human Neuroscience, Frontiers in Neurology and Frontiers in Bioengineering and Biotechnology

frontiers Research Topics

ISSN 1664-8714
ISBN 978-2-83250-336-2
DOI 10.3389/978-2-83250-336-2

About Frontiers

Frontiers is more than just an open-access publisher of scholarly articles: it is a pioneering approach to the world of academia, radically improving the way scholarly research is managed. The grand vision of Frontiers is a world where all people have an equal opportunity to seek, share and generate knowledge. Frontiers provides immediate and permanent online open access to all its publications, but this alone is not enough to realize our grand goals.

Frontiers Journal Series

The Frontiers Journal Series is a multi-tier and interdisciplinary set of open-access, online journals, promising a paradigm shift from the current review, selection and dissemination processes in academic publishing. All Frontiers journals are driven by researchers for researchers; therefore, they constitute a service to the scholarly community. At the same time, the Frontiers Journal Series operates on a revolutionary invention, the tiered publishing system, initially addressing specific communities of scholars, and gradually climbing up to broader public understanding, thus serving the interests of the lay society, too.

Dedication to Quality

Each Frontiers article is a landmark of the highest quality, thanks to genuinely collaborative interactions between authors and review editors, who include some of the world's best academicians. Research must be certified by peers before entering a stream of knowledge that may eventually reach the public - and shape society; therefore, Frontiers only applies the most rigorous and unbiased reviews.
Frontiers revolutionizes research publishing by freely delivering the most outstanding research, evaluated with no bias from both the academic and social point of view. By applying the most advanced information technologies, Frontiers is catapulting scholarly publishing into a new generation.

What are Frontiers Research Topics?

Frontiers Research Topics are very popular trademarks of the Frontiers Journals Series: they are collections of at least ten articles, all centered on a particular subject. With their unique mix of varied contributions from Original Research to Review Articles, Frontiers Research Topics unify the most influential researchers, the latest key findings and historical advances in a hot research area! Find out more on how to host your own Frontiers Research Topic or contribute to one as an author by contacting the Frontiers Editorial Office: frontiersin.org/about/contact

THE CONTRIBUTION OF POSTURAL ADJUSTMENTS TO BODY BALANCE AND MOTOR PERFORMANCE: VOLUME II

Topic Editors:
Eric Yiou, Université Paris-Saclay, France
Teddy Caderby, Université de la Réunion, France
Paolo Cavallari, University of Milan, Italy
Martin Descarreaux, Université du Québec à Trois-Rivières, Canada

Citation: Yiou, E., Caderby, T., Cavallari, P., Descarreaux, M., eds. (2022). The Contribution of Postural Adjustments to Body Balance and Motor Performance: Volume II. Lausanne: Frontiers Media SA.
doi: 10.3389/978-2-83250-336-2

Table of Contents

05 ***Editorial: The Contribution of Postural Adjustments to Body Balance and Motor Performance: Volume II***
Teddy Caderby, Paolo Cavallari, Martin Descarreaux and Eric Yiou

08 ***Computerized Dual-Task Testing of Gait Visuomotor and Cognitive Functions in Parkinson's Disease: Test-Retest Reliability and Validity***
Mayank Bhatt, Bhuvan Mahana, Ji Hyun Ko, Tiffany A. Kolesar, Anuprita Kanitkar and Tony Szturm

20 ***In Patients With Parkinson's Disease in an OFF-Medication State, Does Bilateral Electrostimulation of Tibialis Anterior Improve Anticipatory Postural Adjustments During Gait Initiation?***
Arnaud Delafontaine, Paul Fourcade, Ahmed Zemouri, D. G. Diakhaté, Gabriel Saiydoun and Eric Yiou

27 ***Motor Responses of Lumbar Erector Spinae Induced by Electrical Vestibular Stimulation in Seated Participants***
Amélie Desgagnés, Mikaël Desmons, Jean-Philippe Cyr, Martin Simoneau and Hugo Massé-Alarie

40 ***Proof-of-Concept of the Virtual Reality Comprehensive Balance Assessment and Training for Sensory Organization of Dynamic Postural Control***
Sanghee Moon, Chun-Kai Huang, Maryam Sadeghi, Abiodun E. Akinwuntan and Hannes Devos

50 ***Physical and Psychological Factors Associated With Walking Capacity in Patients With Lumbar Spinal Stenosis With Neurogenic Claudication: A Systematic Scoping Review***
Marième Houle, Jean-Daniel Bonneau, Andrée-Anne Marchand and Martin Descarreaux

62 ***Effect of Seat Backrest Inclination on the Muscular Pattern and Biomechanical Parameters of the Sit-to-Stand***
Nadège Tebbache and Alain Hamaoui

75 ***Vibration of the Whole Foot Soles Surface Using an Inexpensive Portable Device to Investigate Age-Related Alterations of Postural Control***
Lydiane Lauzier, Mohamed Abdelhafid Kadri, Emilie Bouchard, Kevin Bouchard, Sébastien Gaboury, Jean-Michel Gagnon, Marie-Pier Girard, Andréanne Larouche, Roxane Robert, Patrick Lapointe, Rubens A. da Silva and Louis-David Beaulieu

82 ***Effects of Robot-Aided Rehabilitation on the Ankle Joint Properties and Balance Function in Stroke Survivors: A Randomized Controlled Trial***
Xiaoxue Zhai, Qiong Wu, Xin Li, Quan Xu, Yanlin Zhang, Senchao Fan, Li-Qun Zhang and Yu Pan

95 ***Age-Related Changes of the Anticipatory Postural Adjustments During Gait Initiation Preceded by Vibration of Lower Leg Muscles***
Jana Kimijanová, Diana Bzdúšková, Zuzana Hirjaková and František Hlavačka

103 ***Normative Data for the NeuroCom® Sensory Organization Test in Subjects Aged 80–89 Years***
Laura Perucca, Antonio Robecchi Majnardi, Silvia Frau and Stefano Scarano

111 ***Specific Posture-Stabilising Effects of Vision and Touch Are Revealed by Distinct Changes of Body Oscillation Frequencies***
Stefania Sozzi, Antonio Nardone and Marco Schieppati

136 ***Kinematic Changes in the Uninjured Limb After a Traumatic Brachial Plexus Injury***
Lidiane Souza, Luiggi Lustosa, Ana Elisa Lemos Silva, José Vicente Martins, Thierry Pozzo and Claudia D. Vargas

147 ***Gait Adaptation to a Phase-Specific Nociceptive Electrical Stimulation Applied at the Ankle: A Model to Study Musculoskeletal-Like Pain***
Michaël Bertrand-Charette, Renaud Jeffrey-Gauthier, Jean-Sébastien Roy and Laurent J. Bouyer

158 ***Tai Chi Training as a Primary Daily Care Plan for Better Balance Ability in People With Parkinson's Disease: An Opinion and Positioning Article***
Ting Zhang, Zhenyu Lv and Song Gao

163 ***Startle Increases the Incidence of Anticipatory Muscle Activations but Does Not Change the Task-Specific Muscle Onset for Patients After Subacute Stroke***
Nan Xia, Chang He, Yang-An Li, Minghui Gu, Zejian Chen, Xiupan Wei, Jiang Xu and Xiaolin Huang

176 ***Impaired Lower Limb Proprioception in Spinocerebellar Ataxia Type 3 and Its Affected Factors***
Xia-Hua Liu, Zhi-Yong Wang, Ying Li, Hao-Ling Xu, Arif Sikandar, Jun Ni and Shi-Rui Gan

182 ***Visual Perturbation Suggests Increased Effort to Maintain Balance in Early Stages of Parkinson's to be an Effect of Age Rather Than Disease***
Justus Student, David Engel, Lars Timmermann, Frank Bremmer and Josefine Waldthaler

195 ***Altered Muscle Contributions are Required to Support the Stance Limb During Voluntary Toe-Walking***
Enrico De Pieri, Jacqueline Romkes, Christian Wyss, Reinald Brunner and Elke Viehweger

frontiers | Frontiers in Human Neuroscience

EDITORIAL
published: 24 May 2022
doi: 10.3389/fnhum.2022.910540

Editorial: The Contribution of Postural Adjustments to Body Balance and Motor Performance: Volume II

Teddy Caderby[1], *Paolo Cavallari*[2], *Martin Descarreaux*[3] *and Eric Yiou*[4,5]*

[1] Laboratoire IRISSE, UFR des Sciences de l'Homme et l'Environnement, Université de la Réunion, Le Tampon, France, [2] Human Physiology Section of the Department of Pathophysiology and Transplantation, Università Degli Studi di Milano, Milan, Italy, [3] Department of Human Kinetics, Université du Québec à Trois-Rivières, Trois-Rivières, QC, Canada, [4] EA 4532 Complexité, Innovation, Activités Motrices et Sportives, Université Paris-Saclay, Orsay, France, [5] Laboratoire Complexité, Innovation et Activités Motrices et Sportives, Université d'Orléans, Orléans, France

Keywords: postural control, rehabilitation, innovative tools, gait, multisensory integration, motor control, human

Editorial on the Research Topic

The Contribution of Postural Adjustments to Body Balance and Motor Performance: Volume II

Edited and reviewed by:
Julie Duque, Catholic University of Louvain, Belgium

***Correspondence:**
Eric Yiou
eric.yiou@universite-paris-saclay.fr

Specialty section:
This article was submitted to Motor Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *01 April 2022*
Accepted: *13 May 2022*
Published: *24 May 2022*

Citation:
Caderby T, Cavallari P, Descarreaux M and Yiou E (2022) Editorial: The Contribution of Postural Adjustments to Body Balance and Motor Performance: Volume II. Front. Hum. Neurosci. 16:910540. doi: 10.3389/fnhum.2022.910540

This second volume of the Research Topic provides an up-to-date picture on how humans control balance and body motion during daily motor tasks, with a special focus on the relationship between postural adjustments, body balance and motor performance in healthy adults and individuals with various health conditions. It includes 18 contributions separated into four sections, each of them focusing on a specific aspect of balance and body motion control. In the first section, the focus is on multisensory integration in balance control during standing, sitting and gait initiation. The second section reports results of studies investigating the adaptability of gait and balance control under specific and controlled conditions in healthy individuals. The third section reports results of studies focusing on gait and balance disorders in specific clinical populations. Finally, in the last section, results of studies focusing on the development of innovative tools and methods to assess and improve gait, balance and cognitive functions in neurological patients are reported.

MULTISENSORY INTEGRATION IN BALANCE CONTROL

Balance control is a complex motor skill which involves the integration of many types of sensory information (sight, vestibular system and proprioception) and can be modified by sensory input alterations consequent to a pathology or aging processes.

Postural instability during stance with eyes closed was investigated by Sozzi et al. by using spectral analysis of center-of-pressure (COP) oscillations and different sensory conditions. While standing on foam, vision did not reduce low-frequency oscillations, while touch diminished the entire spectrum, except for the medium-high frequencies, as if sway reduction by touch would rely on rapid balance corrections.

Desgagnés et al. showed that surface anodal stimulation over the right mastoid in seated participants induced an ipsilateral body sway. Current intensity and duration affected amplitude and occurrence of the inhibitory short-latency and the excitatory medium-latency responses in lumbar erector spinae muscles; responses were amplified by right, but not left, head rotation. Vision did not influence the responses, suggesting its minimal contribution to vestibulomotor control during sitting. The lack of response reversal in the sagittal plane may reflect the biomechanical role of lumbar erector spinae to tune the lumbar lordosis during an induced body sway.

Relative contribution of sensory and motor components on postural control in young and old participants was investigated both by Lauzier et al. and Kimijanová et al. According to the Canadian group, feet soles vibration and standing on foam increased COP parameters, but foam was more effective than vibration in both groups. Conversely to foam, changes in COP parameters after vibration were no longer different between groups when correcting for the baseline levels; thus aging seems to differently affect "motor" and "sensory" components, the latter being relatively unaltered. The Slovak group showed instead that young people significantly modified anticipatory postural adjustments (APAs) during gait initiation when a previous vibratory perturbation was delivered to lower leg muscles. Sensitively scaled APAs according to the actual position of the body verticality, an effect which is absent in old participants. Significant age-related declines in APAs were observed regardless of altered proprioception. This seems to indicate that at the transition from standing to walking they probably require higher reliance on the visual input.

Since aging is known to increase the falling risk, the Sensory Organization Test (SOT) applied to old people appears to be a useful tool for assessing postural stability, risk of falling, and balance improvement during rehabilitation. Perucca et al. presented normative data of SOT for 80–84 and 85–89 years groups and concluded that the vestibular balance tended to be affected by aging more than vision and proprioception-based systems. However, Moon et al. stressed that SOT has limitations (high cost, lack of portability etc.) that hinder its use in clinical practice. Thus they developed an innovative system, called VR-ComBAT (for "Virtual Reality Comprehensive Balance Assessment and Training"), that provides a safe, feasible, and cost-effective virtual reality environment allowing the investigation of multisensory integration in balance control.

ADAPTABILITY OF GAIT AND POSTURAL CONTROL

Investigating gait and postural control adaptations under specific and controlled conditions in healthy individuals can be a relevant approach to identify solutions for the assessment and improvement of these functions in people with balance and mobility impairments. Bertrand-Charrette et al. pointed out that pain experimentally induced by electrical stimulation caused robust gait pattern adaptations in healthy participants and thus provided a valid model to study musculoskeletal pain-induced gait adaptations under controlled conditions.

During toe walking De Pieri et al. showed that healthy adults generate a larger support moment during the stance phase to maintain the knee stable compared to normal walking. These results suggest that the support moment can be an insightful parameter for assessing the muscle demand associated with gait in patients affected by toe walking, such as patients with cerebral palsy or idiopathic toe walking.

Tebbache and Hamaoui showed that during a sit-to-stand task, an increase in backrest inclination resulted in an increase in the activity level of the neck and trunk flexor muscles during the postural phase (prior to seat-off), but a decreased level activity of some lower limb muscles during the rising phase. These results, which reveal a change in muscle demand as a function of backrest inclination, may be particularly useful in developing solutions to improve sit-to-stand performance in people with muscle weakness.

GAIT AND BALANCE DISORDERS IN SPECIFIC CLINICAL POPULATIONS

Several musculoskeletal and neurological conditions can affect gait and postural control often leading to increased disability and significant reduction in quality of life and life expectancy. Consequently, much attention has been given to the investigation of both gait and postural control in patients with various neuromusculoskeletal conditions, either to establish baseline comparisons with healthy individuals, track natural history of diseases or assess clinical improvement following clinical interventions. As illustrated by the following studies, translational research including basic sciences, applied research and pragmatic clinical studies significantly contributes to the development of tailored rehabilitation strategies targeting gait and balance disorder.

Student et al. compared mean sway amplitude and mean velocity of both the COP and COM in patients with early-to-mid stage Parkinson's disease (PD), aged-matched healthy individuals and young healthy adults. Using a moving room paradigm, the authors showed that the net effect of a visual perturbation on mean COP velocity was significantly higher in patients with early-to-mid stage PD and aged-matched healthy individuals suggesting that such changes are mostly an effect of aging rather than a specific effect of early PD.

In a study investigating the task specificities of anticipatory muscle activations throughout various hand activities in subacute stroke survivors, Xia et al. showed several differences between stroke patients and healthy participants. Among the several between group differences observed, the authors reported changes in anticipatory muscle activations in the extensor carpi radialis muscle as well as changes in APAs.

Walking capacity is a critical health outcome in several patient populations with musculoskeletal or neurological diseases. Through a scoping review, Houle et al. summarized the best currently available scientific evidence regarding walking capacity in patients with lumbar spinal stenosis and associated neurogenic

claudication. Their review showed on one side that several physical and psychological factors are associated with walking capacity in patients with lumbar spinal stenosis, and on the other side that assessment of walking capacity and associated physical and psychological factors lacks standardization therefore limiting stronger conclusions on the topic.

Spinocerebellar ataxia type 3 is a neurodegenerative disorder characterized by progressive ataxia, external progressive ophthalmoplegia, and other neurological manifestations. Liu et al. evaluated lower limb proprioception in 80 patients to assess the association between proprioception and clinical features of spinocerebellar ataxia type 3. Their results showed that lower limb proprioception was significantly impaired in patients with spinocerebellar ataxia type 3 and that increased impairment was associated with increasing age at onset and increasing disease duration.

Finally, Souza et al. compared the index finger kinematics during a free-endpoint whole-body reaching task and a cup-to-mouth task in participants with traumatic brachial plexus injury (uninjured limb) and healthy matched controls. Significant differences in movement parameters led the author to suggest that traumatic brachial plexus injuries lead to increased motor planning cost for the movement of the uninjured limb and that this cost is higher in tasks that require greater postural balance.

GAIT, BALANCE AND COGNITIVE REHABILITATION IN PATIENTS WITH PARKINSON'S DISEASE AND STROKE

The development of innovative tools and methods directed to assess and improve gait, balance and cognitive functions in PD patients and stroke are important for rehabilitation interventions.

Bhatt et al. developed a computer game-based rehabilitation treadmill platform for dual-task (DT) assessment and training in PD. Authors showed that this platform has the ability to repeatedly record reliable DT interference effects over time and track PD progression. The platform is directly applicable to other diseases than PD that affect gait and cognition.

Functional electrical stimulation (FES) and robot-aided stretching device are two other promising tools that may improve balance and gait function in neurological patients. Delafontaine et al. reported that bilateral applications of FES to the *tibialis anterior* muscles (ankle dorsi-flexor) may improve the capacity of PD to generate the APAs associated with gait initiation. Future studies are required before considering that this tool is valuable to optimize the effects of L-DOPA medication on gait initiation.

Zhai et al. stressed that stroke survivors with impaired control of the ankle due to stiff plantar-flexors often experience abnormal postural control, which affects balance and gait. These authors reported that robot-aided and manual ankle stretching training provided similar improvements in the ankle properties and balance post-stroke. However, only the robot-aided stretching training improved spasticity and stiffness of dorsiflexion significantly. Authors thus suggested that robot-aided rehabilitation may optimize current rehabilitation programs in stroke survivors.

Beside the use of innovative tools, physical activity is important for the rehabilitation and promotion of healthy aging. Zhang et al. defended the point-of-view that the practice of tai chi, a traditional Chinese martial art, can improve balance ability and reduce the risk of falls in people with mild to moderate PD.

In conclusion, this collection contributes to a better understanding of the basic mechanisms underlying the control of body balance and body motion during daily motor tasks. The collection also promotes the development of innovative tools and methods to assess and train gait and balance, with relevant applications in the fields of neurodegenerative conditions and rehabilitation.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Human Neuroscience

ORIGINAL RESEARCH
published: 15 July 2021
doi: 10.3389/fnhum.2021.706230

Computerized Dual-Task Testing of Gait Visuomotor and Cognitive Functions in Parkinson's Disease: Test-Retest Reliability and Validity

*Mayank Bhatt[1], Bhuvan Mahana[1], Ji Hyun Ko[2], Tiffany A. Kolesar[2], Anuprita Kanitkar[1] and Tony Szturm[1]**

[1] College of Rehabilitation Sciences, University of Manitoba, Winnipeg, MB, Canada, [2] Department of Human Anatomy and Cell Science, University of Manitoba, Winnipeg, MB, Canada

OPEN ACCESS

Edited by:
Martin Descarreaux,
Université du Québec à Trois-Rivières, Canada

Reviewed by:
Yi-Ning Wu,
University of Massachusetts Lowell, United States
Stefano Filippo Castiglia,
Sapienza University of Rome, Italy

***Correspondence:**
Tony Szturm
Tony.Szturm@umanitoba.ca

Specialty section:
This article was submitted to Motor Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: 07 May 2021
Accepted: 15 June 2021
Published: 15 July 2021

Citation:
Bhatt M, Mahana B, Ko JH, Kolesar TA, Kanitkar A and Szturm T (2021) Computerized Dual-Task Testing of Gait Visuomotor and Cognitive Functions in Parkinson's Disease: Test-Retest Reliability and Validity. Front. Hum. Neurosci. 15:706230. doi: 10.3389/fnhum.2021.706230

Background: Mobility and cognitive impairments in Parkinson's disease (PD) often coexist and are prognostic of adverse health events. Consequently, assessment and training that simultaneously address both gait function and cognition are important to consider in rehabilitation and promotion of healthy aging. For this purpose, a computer game-based rehabilitation treadmill platform (GRP) was developed for dual-task (DT) assessment and training.

Objective: The first objective was to establish the test-retest reliability of the GRP assessment protocol for DT gait, visuomotor and executive cognitive function in PD patients. The second objective was to examine the effect of task condition [single task (ST) vs. DT] and disease severity (stage 2 vs. stage 3) on gait, visuomotor and cognitive function.

Methods: Thirty individuals aged 55 to 70 years, diagnosed with PD; 15 each at Hoehn and Yahr scale stage 2 (PD-2) and 3 (PD-3) performed a series of computerized visuomotor and cognitive game tasks while sitting (ST) and during treadmill walking (DT). A treadmill instrumented with a pressure mat was used to record center of foot pressure and compute the average and coefficient of variation (COV) of step time, step length, and drift during 1-min, speed-controlled intervals. Visuomotor and cognitive game performance measures were quantified using custom software. Testing was conducted on two occasions, 1 week apart.

Results: With few exceptions, the assessment protocol showed moderate to high intraclass correlation coefficient (ICC) values under both ST and DT conditions for the spatio-temporal gait measures (average and COV), as well as the visuomotor tracking and cognitive game performance measures. A significant decline in gait, visuomotor, and cognitive game performance measures was observed

during DT compared to ST conditions, and in the PD-3 compared to PD-2 groups.

Conclusion: The high to moderate ICC values along with the lack of systematic errors in the measures indicate that this tool has the ability to repeatedly record reliable DT interference (DTI) effects over time. The use of interactive digital media provides a flexible method to produce and evaluate DTI for a wide range of executive cognitive activities. This also proves to be a sensitive tool for tracking disease progression.

Clinical Trial Registration: www.ClinicalTrials.gov, identifier NCT03232996.

Keywords: treadmill walking, spatiotemporal gait variables, cognitive performance, dual-task performance, Parkinson's disease, intra-class correlation coefficient

INTRODUCTION

Safe, independent community walking requires both mobility skills and cognitive flexibility to manage complex terrains, for navigation in busy environments, to identify and track relevant visual targets, reading, and for processing of what is being seen. Mobility limitations (balance and gait impairments; Rochester et al., 2004; Kang et al., 2005) and decline in executive cognitive function (Olchik et al., 2017; Roheger et al., 2018) common to Parkinson's disease (PD) often coexist (Plotnik et al., 2011; Schneider et al., 2015) and are prognostic of adverse health events, including falls (Mak et al., 2014; Paul et al., 2014). Over 60% of individuals with PD fall each year and a significant portion of those who fall will experience multiple falls (Pickering et al., 2007; Lord et al., 2017; Creaby and Cole, 2018). The consequences of falls are often severe, leading to disability, loss of independence, and social isolation.

The concept of motor automaticity has an important implication in the pathophysiology of PD related to mobility limitations and increased fall risk (Wu et al., 2015; Gilat et al., 2017). One model of executive cognitive functions presents the supervisory attentional system, which distinguishes between processing of non-routine, attentionally demanding activities vs. routine, automated tasks (Dirnberger and Jahanshahi, 2013). The role of the striatum has been equated with that of routine tasks, such as locomotion, that are usually performed automatically (Gilat et al., 2017). The information processing demands of community ambulation are presumed to affect the already limited locomotor control of PD patients (Rochester et al., 2004; Kang et al., 2005), and this may result in greater gait instability and a higher risk of falls (Heinzel et al., 2016; Penko et al., 2018). Consequently, dual-task (DT) assessment and training programs that address both mobility and cognition are important to consider in the prevention and rehabilitation of mobility and cognitive decline.

Impairments in gait (Rosenberg-Katz et al., 2015; Wu et al., 2015; Gilat et al., 2017), and in executive functions (Monchi et al., 2001, 2004) are associated with disruption of frontostriatal circuits in PD. This is consistent with findings of studies which have evaluated frontal lobe activity during DT-walking using functional near infrared spectroscopy (fNIRS). Several fNIRS studies have reported increased activation levels of the prefrontal cortex (PFC) during DT-walking as compared to walk-only trials in healthy able-bodied adults (Fraser et al., 2016; Maidan et al., 2016). Similar fNIRS studies evaluating PD patients have reported no difference in PFC activation levels for DT-walking trials as compared to walk-only trials (Holtzer et al., 2015; Maidan et al., 2016; Liu et al., 2021). A recent positron emission tomography pilot study of DT-walking evaluated brain glucose metabolism in PD (Hoehn and Yahr stages 2 and 3) in ten patients who rested and five who conducted a DT treadmill/cognitive video game task during the uptake period (Szturm et al., 2020). DT interference (DTI) was consistently shown for gait and cognitive game performance measures for the DT-walking group. As expected, glucose metabolism was significantly increased in several brain regions of the patients in the DT group, compared to the resting group, including the primary visual/sensorimotor areas, thalamus, superior colliculus, and cerebellum. Within the DT group, the three patients in the earlier stage of PD (Hoehn and Yahr stage 2) showed increased glucose uptake in the PFC during DT treadmill walking compared to the resting group, while the two patients at Hoehn and Yahr stage 3 did not. These behavioral and neuroimaging results suggest that simultaneous tasks may be accomplished via different mechanisms as neurodegeneration progresses in PD. A clinically valid and reliable treatment to assess and improve DT performance may translate to improved or slowed decline of cognitive performance and mobility.

Most DT gait studies are performed overground and all overground studies report a significant decrease in gait speed during the DT-walking condition as compared to walk only trials (Al-Yahya et al., 2011; Rochester et al., 2014; Stegemöller et al., 2014; Salazar et al., 2017; Raffegeau et al., 2019). Besides gait speed, many DT gait studies examine how cognitive demand affects gait rhythm and stability (i.e., recording spatiotemporal gait variables; Frenkel-Toledo et al., 2005; Montero-Odasso et al., 2012; Nankar et al., 2017). However, gait speed is a confounding variable as spatiotemporal and other kinematic gait variables are sensitive to changes in gait speed (Jordan et al., 2007; Chung and Wang, 2010; Keene et al., 2016; Cole et al., 2017). Most of the overground DT-walking studies use an instrumented walkway, which records only 4–6 consecutive steps (Bruijn et al., 2009; Hollman et al., 2010). It has been shown that using a continuous walking protocol instead of short intermittent walks, and collecting more than 30 consecutive steps

improved reliability, in particular for measures of gait variability (Bruijn et al., 2009; Hollman et al., 2010; Galna et al., 2013). Furthermore, there is a limited choice of executive cognitive tasks that can be completed during overground walking, and for the short time period to walk a few meters. For example, common cognitive tasks used during overground walking include recall of names/words, serial subtraction, or auditory Stroop tests (Al-Yahya et al., 2011; Raffegeau et al., 2019). Walking outdoors requires visual attention, search, and processing of what is being seen (i.e., relevant visual information). Cortical areas devoted to visuospatial processing of behaviorally significant information, such as the PFC may be particularly susceptible to the neurodegenerative process in PD (Klencklen et al., 2012; Battisto et al., 2018; Lally et al., 2020). To overcome these limitations, Szturm et al. (2017, 2020) developed a computer game-based rehabilitation treadmill platform (GRP; Mahana et al., 2021) which provides an integrated approach to assess and treat the decline in balance, gait, visuomotor, and executive cognitive functions. The GRP consists of a standard treadmill instrumented with a pressure mapping system used to compute spatiotemporal gait variables and gait stability measures (Szturm et al., 2017; Ahmadi et al., 2018, 2019) and a computer display placed at the front of the treadmill for participants to view and interact with computer-generated activities while walking. The GRP includes an interactive computer game application for DT which allows for recording and analyzing participant's actions and choices while walking and playing targeted cognitive games. Therefore, gait and cognitive performance can be measured synchronously during continuous, speed-controlled, steady state gait trials, lasting minutes.

In a previous study (Szturm et al., 2017), reliability of the GRP assessment tool has been established in older adults with fall histories. The present study aims to establish the reliability of the GRP assessment protocol in individuals with PD, and to examine the influence that visuospatial cognitive tasks have on gait performance in Hoehn and Yahr stage 2 (PD-2) vs. stage 3 (PD-3) patients. The first objective of the present study was to establish test-retest reliability and the minimal detectable change (MDC) of spatio-temporal gait variables, as well as visuomotor and cognitive performance measures examined during single task (ST; i.e., walking only or playing video games while sitting) and DT (i.e., walking while playing video games) conditions. The second objective was to examine the effects of task condition (ST vs. DT conditions) and disease severity (stage 2 vs. 3) on gait, visuomotor and cognitive performance measures. This objective addressed three hypotheses, which are as follows: (1) increased visuospatial cognitive loads (ST-walking vs. DT-walking) will have a significant effect on gait performance measures in both PD-2 and PD-3 patients, and *vice versa*: increased physical demands (sitting vs. walking) will have a significant effect on visuomotor and cognitive performance measures (ST-gaming vs. DT-gaming); (2) increased cognitive loads (ST-walking vs. DT-walking) have a greater influence in gait performance measures in PD-3 patients as compared to PD-2 patients; and (3) increased physical demands (sitting vs. walking) will have a greater influence on visuomotor and cognitive performance measures in PD-3 patients as compared to PD-2 patients.

MATERIALS AND METHODS

Participants

Thirty PD patients were recruited for this study. The inclusion criteria included: (a) 50–75 years of age, (b) clinical diagnosis of PD (Hoehn and Yahr stages 2 and 3) made by a movement disorders specialist based upon the United Kingdom PD Society Brain Bank diagnostic criteria (Hughes et al., 1992), (c) treated with antiparkinsonian medications, (d) able to walk at least 50 m without any assistance, and (e) adequate hearing and vision to perform the computer game task, i.e., while viewing an 80 cm monitor at a distance of 1 m. The exclusion criterions included (a) any significant cognitive impairment [Montreal cognitive assessment scores (MoCA; Nasreddine et al., 2005) <25], (b) any other neurological disorder except PD, (c) with any musculoskeletal impairment or uncontrolled cardio-vascular condition that might prevent participants from walking on a treadmill for 2–4 min. The Human Research Ethics Board at the University of Manitoba approved the study, and the study is registered at ClinicalTrials.gov. The Protocol Registration System number is NCT03232996. All participants provided informed consent. The participants were tested on two separate days, 1 week apart, and at the same time of day, during the ON medication phase. The Unified Parkinson's Disease Rating Scale (UPDRS; Fahn et al., 1987) was completed in the first test session. Participants were instructed to take their medications at the same time prior to testing.

Instrumentation and Test Protocol

Figure 1 presents the components of the treadmill platform. Participants stood on a treadmill at a viewing distance of 100 cm from an 80 cm computer monitor. The treadmill is instrumented with a pressure mat (Vista Medical, Ca) which was used to record vertical foot contact forces and to compute spatiotemporal gait variables (Rochester et al., 2014). A miniature, wireless inertial-based (IB) mouse Scoop Pointer Remote (Model: RXR1000-0302E; Hillcrest labs) was used to control and interact with two computer applications described below. The IB mouse contains a 2-axis gyroscope and 2-axis accelerometer and firmware that provides an instantaneous angular position signal, and emulates a plug-n-play standard optical computer mouse. Velcro was used to secure the wireless motion mouse to a sports cap or plastic head band allowing head rotation to be used to point the device to control the position and motion of a computer cursor or game sprite. Therefore, a hands-free computer game controller was used to interact with various computer applications (cognitive activities) while treadmill walking. Head pointing movements are among the most natural and can easily be performed with minimal instruction.

Two computer applications were developed for DT balance assessment. Details of the applications and protocols can be found in Szturm et al. (2017). First, visuomotor tracking (VMT), as shown in **Figures 1B,E**, involves tracking a visual target that moves horizontally left and right on a computer display for several cycles. Two cursors of different shapes appear on the monitor. The target was a circle, its motion was computer

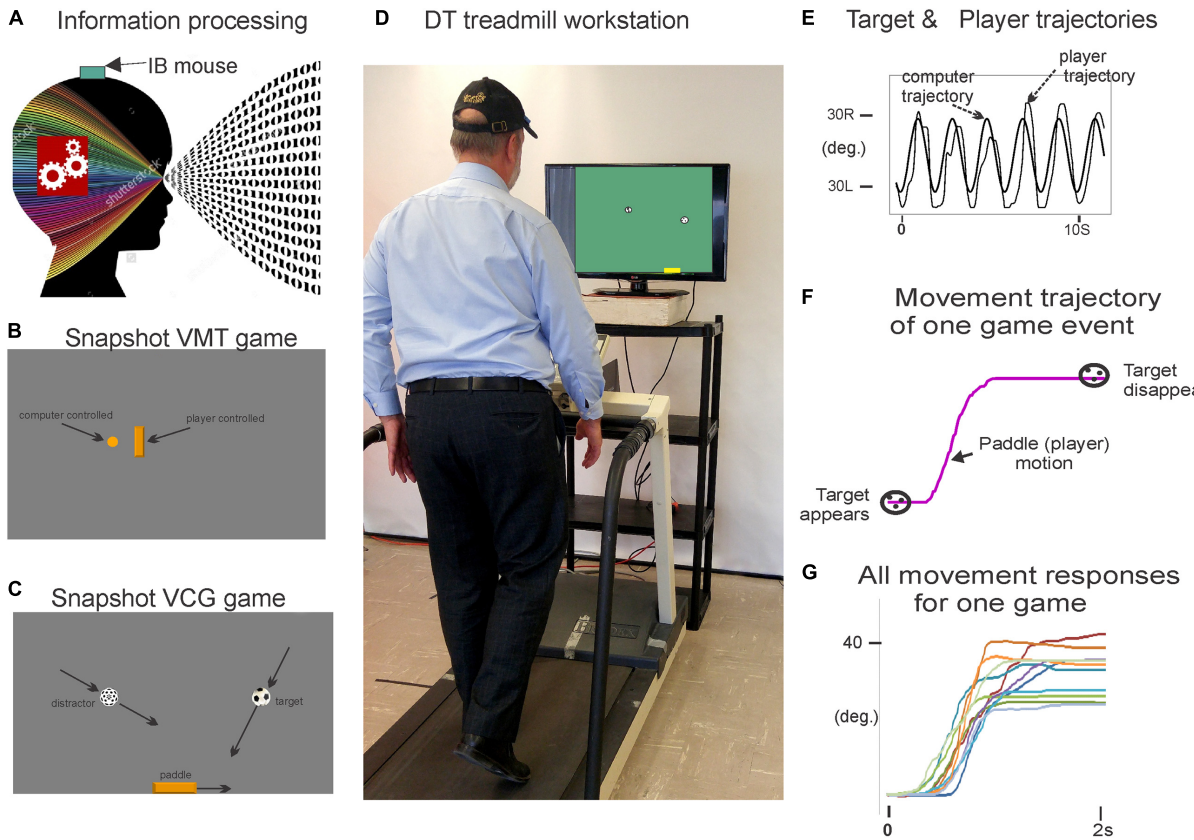

FIGURE 1 | Illustration of the treadmill platform and experimental set-up; **(A)** the motion mouse is shown attached to the head via a baseball cap. **(D)** Participant is walking on the instrumented treadmill while viewing a computer monitor. Head rotation (via motion mouse) is used to interact with the visuospatial cognitive task. **(B,C)** present snap shots of the VMT and VCG. **(E)** Presents synchronous plots of the target cursor motion and user movement trajectories (head rotation) for a typical VMT task. Maxima are the left most position and minima the right most position. **(F)** Presents the trajectory for one game movement response from target appearance to target disappearance. **(G)** Presents overlay trajectories of all game movement responses for one game session. Parts of Figure 1 have previously been published in Szturm et al. (2017, 2021).

controlled and moved at a predetermined frequency of 0.5 Hz with an amplitude of 80% of the monitor width. The second cursor, a rectangle, was slaved to head rotation via the IB mouse. Participants were instructed to move and overlap the rectangle head-controlled cursor with the target circle for several cycles. The second computer application involved a visuomotor cognitive game (VCG), as shown in **Figures 1C,F,G**. The goal of this task is to move a game paddle (via head rotation) horizontally to interact with the moving game objects. The game objects are categorized as designated targets or designated distractors. The game objects appear at random locations at the top of the display every 2 s and move to the bottom of the display. The game objects move in a diagonal path from top to bottom. In response to each game event, participants produced a head rotation (i.e., rotation of the IB mouse) to move the game paddle to catch the target objects while avoiding the distractors. A logged data file is generated that synchronously records (100 Hz sampling rate) the coordinates of the game paddle and the game objects (tracking cursor, target, and distractor objects).

These tasks were performed while walking on a treadmill at 0.9 m/s for 1 min. This speed was well tolerated by the PD-3 group in pilot-testing, allowing these patients to walk without falling or needing to lean on the treadmill supports. Four conditions were included: (a) walk only ST condition (WO), (b) DT-walk while performing a VMT task, (c) DT-walk while performing a VCG task, and (d) a ST gaming condition while seated (VMT and VCG games). Participants were not allowed to lean on the treadmill structure during testing. Prior to testing, the participants were allowed to play the games while seated for a few minutes to become familiar with each task.

Data Analysis

The following outcome measures were computed from the recorded pressure mat data; (a) average and coefficient of variation (COV) were computed over 30 consecutive steps, for right and left step length (SL) and swing time (SwT; 44), and (b) the location of all heel contacts in the mediolateral (ML) axis during each walk trial were determined, and the dispersion of heel contact locations were computed as the COV, and reported as ML-drift (Ahmadi et al., 2018). Since the statistical analysis showed no significant difference in means of right and left gait variables, only the right gait variables are presented.

VMT Performance Measures

Figure 1E presents synchronous plots of the computer-controlled target motion (circle cursor) and participants head rotation (rectangle cursor) for a typical VMT task. The total residual error (TRE) was determined by computing the difference between the trajectories of the target and head cursor motions for each sample period (Szturm et al., 2017). The first two cycles of the VMT tasks were excluded to allow the participants time to acquire the moving target and begin tracking.

VCG Performance Measures

Figure 1F presents the trajectory of an individual game movement response. The duration of each VCG trial was 60 s and each game event was 2 s. Therefore, 30 game movement responses were made, half in each direction. Based on the time indexes of each target appearance and disappearance, the software segments each individual game movement response and sorts them by direction. **Figure 1G** presents overlay plots of all game movement responses in one direction (Szturm et al., 2017). The following variables were determined from the game movement responses: (a) average response time (Avg. RT), i.e., the time from target appearance to the start of the game paddle (head rotation), (b) success rate (SR) determined as the percentage of target objects that were caught, and (c) movement variance (MV). The individual movement traces for each direction in one game session were averaged and the standard deviation (SD) computed for each sampled data point. The total SD over all sampled data points was taken as movement variation.

Statistical Analysis

The sample size for this study was computed using **Table 1**, of Zou (2012). Thirty participants were required for an intraclass correlation coefficient (ICC) value of 0.8, assurance of 70%, and class interval half-width of 0.15. Normal distribution of the data was assessed using the Shapiro–Wilk test, and Mauchly's test of sphericity was used to test the equality of variance for comparison between different task conditions and stages of PD. The gait, VMT and VCG performance measures satisfied the assumptions of normality and equal variance.

Relative reliability was assessed using a two-way random model ICC. The ICC scores were considered to be high when equal to or greater than 0.70, moderate between 0.50 and 0.69, and low when less than 0.50 (Lexell and Downham, 2005). MDC was computed according to a published guideline (Lexell and Downham, 2005). Absolute reliability was analyzed using MDC (Messick, 1995; Haley and Fragala-Pinkham, 2006). Systematic errors between the test periods were evaluated using a paired *t*-test.

A repeated measures ANOVA was used to evaluate the effect of task condition (ST vs. DT), disease severity (Hoehn and Yahr stage 2 vs. 3) and the interaction of task and disease stage. The significance level was α set at $p < 0.05$. Effect size was calculated (Cohen's *d*); values less than 0.20 were considered negligible, values between 0.20 and 0.50 were considered small, between 0.50 and 0.80 were medium, and greater than 0.80 was considered large (Schäfer and Schwarz, 2019). All statistical analysis was conducted using SPSS (v.22, SPSS Science, Chicago, IL, United States, RRID:SCR_019096).

TABLE 1 | Demographic and clinical data by Hoehn and Yahr stage (stage 2: PD-2; stage 3: PD-3).

	PD-2	PD-3	*p-value* (PD-2 vs. PD-3)
Total participants	15	15	
Age (mean ± SD) years	63.2 ± 5.5	66.6 ± 5.6	0.105
Male/Female	9/6	10/5	0.705
Time since diagnosis (years)	4.4 ± 4.1	6.7 ± 4.4	0.150
UPDRS Total (mean ± SD)	28.6 ± 9.9	43.6 ± 9.6	<0.001
UPDRS Motor (mean ± SD)	20.9 ± 7.7	30.8 ± 6.6	<0.001
MoCA (mean ± SD)	29.0 ± 1.0	28.7 ± 1.0	0.418

RESULTS

Table 1 presents the demographic and clinical data for PD-2 and PD-3 participants. The male to female ratios were similar in the two PD groups. There was a slight age difference between the two groups but this was not statistically different [$t(28) = 1.678$, $p = 0.105$]. Test scores for the MoCA were similar between groups ($p > 0.7$). The UPDRS scores (Total and Motor) were significantly greater in the PD-3 group as compared to the PD-2 group ($p < 0.001$).

Table 2 presents group means and SD for tests 1 and 2, ICC values, and MDC values for gait variables (average and COV for SL and SwT and ML-drift). High test-retest reliability (ICC values of 0.76–0.98) were observed for average SL and SwT during the three-walking conditions: ST-walking only (WO), VMT-walking and VCG-walking. MDC as a percentage of the group mean (MDC%) ranged from 15–20% for Avg-SL and Avg-SwT. Moderate to high test-retest reliability (ICC values of 0.58–0.96) was observed for COV-SL and COV-SwT during the three walking conditions. The MDC% values for COV were higher than for average gait values; values ranged from 52–74%. Lower ICC values were observed for the ML-drift measures; range 0.43–0.88. The MDC% values for ML-drift were high, ranging 67–75%. Paired student *t*-tests revealed no significant difference between test 1 and test 2 for any of the gait variables (average, COV, or ML-drift, $p > 0.2$).

Table 3 presents the ICC values and MDC values, along with group means and SD for both the VMT (TRE) and VCG (movement onset time, success rate, and movement variation) outcome measures. Moderate to high test-retest reliability (ICC values ranging from 0.48 to 0.95) were observed for TRE. The MDC% values for TRE were 19% for sitting and 21% for VMT-walking. Moderate to high test-retest reliability was observed (ICC values ranging from 0.41 to 0.95) for movement onset time, success rate, and movement variation. The MDC% values for movement onset time and success rate ranged from 11 to 20%, and for movement variation MDC% was 20% in sitting and 19% during walking. Paired student *t*-tests revealed no significant differences between test 1 and test 2 for any of the VMT or VCG outcome measures ($p > 0.3$).

TABLE 2 | Test-retest reliability results for spatial and temporal gait outcome measures (average and COV).

Condition	Test 1 mean (SD)	Test 2 mean (SD)	ICC Value (95% CI)	MDC (MDC%)
Average SL (cm)				
WO	45.9 (13.6)	44.7 (14.1)	0.92 (0.84–0.96)	9.1 (20)
VCG	43.3 (16.8)	41.6 (16.4)	0.97 (0.93–0.98)	7.9 (18)
VMT	42.1 (13.8)	46.3 (14.7)	0.91 (0.81–0.96)	8.3 (19)
Average SwT (s)				
WO	0.72 (0.1)	0.70 (0.1)	0.91 (0.81–0.96)	0.12 (16.7)
VCG	0.65 (0.1)	0.65 (0.1)	0.90 (0.76–0.95)	0.10 (15.4)
VMT	0.66 (0.1)	0.67 (0.1)	0.90 (0.76–0.95)	0.11 (16.7)
COV SL (%)				
WO	26.2 (14.3)	24.6 (13.1)	0.81 (0.58–0.91)	18.2 (70)
VCG	36.5 (21.5)	35.8 (21.1)	0.90 (0.77–0.95)	18.8 (52)
VMT	36.1 (16.5)	34.0 (14.4)	0.87 (0.71–0.94)	23.1 (64)
COV SwT (%)				
WO	10.9 (6.1)	11.1 (5.6)	0.89 (0.76–0.95)	7.5 (69)
VCG	12.5 (6.7)	12.7 (7.3)	0.84 (0.64–0.92)	8.8 (70)
VMT	13.1 (9.1)	13.1 (9.1)	0.91 (0.80–0.96)	9.5 (74)
ML-Drift (%)				
WO	13.9 (7.7)	13.4 (6.8)	0.63 (0.43–0.83)	9.2 (67)
VCG	18.6 (9.4)	17.1 (10.4)	0.74 (0.55–0.88)	14.1 (75)
VMT	16.3 (7.5)	17.7 (8.1)	0.67 (0.45–0.85)	11.8 (73)

Presented are the group mean (standard deviation, SD) for test 1 and test 2 (occurring 1 week later), intraclass correlation coefficient (ICC) values (95% confidence interval, CI), and minimal detectable change (MDC% as a percentage of the group mean). The values are for single-task walking only (WO), dual-task visuomotor cognitive game (VCG), and dual-task visuomotor tracking (VMT) tasks.

TABLE 3 | Test-retest reliability for visuomotor tracking (VMT) and visuomotor cognitive game (VCG) task performance during ST-sitting and DT-walking on the treadmill.

Condition	Test 1 mean (SD)	Test 2 mean (SD)	ICC Value (95% CI)	MDC (MDC%)
Visuomotor tracking performance				
Total residual error				
Sitting	11.3 (2.2)	10.9 (2.6)	0.88 (0.74–0.95)	2.2 (19)
Walking	14.6 (3.2)	13.3 (3.1)	0.76 (0.48–0.89)	3.1 (21)
Visuomotor cognitive game performance				
Movement onset time				
Sitting	0.6 (0.1)	0.6 (0.1)	0.85 (0.68–0.93)	0.07 (11)
Walking	0.7 (0.1)	0.6 (0.1)	0.55 (0.41–0.71)	0.14 (20)
Success rate				
Sitting	82.9 (15.4)	86.7 (14.2)	0.85 (0.65–0.93)	16.5 (20)
Walking	73.4 (15.9)	72.5 (19.2)	0.89 (0.77–0.95)	14.4 (19)
Movement variation				
Sitting	18.1 (2.2)	18.8 (3.1)	0.60 (0.45–0.72)	3.7 (20)
Walking	21.9 (3.8)	22.1 (3.5)	0.85 (0.67–0.93)	4.1 (19)

This table demonstrates the mean (standard deviation, SD) for test 1 and test 2, intraclass correlation coefficient (ICC) values (95% confidence interval, CI), and minimal detectable change (MDC% as a percentage of the group mean).

Validity

Statistical results of the effect of task condition (WO vs. VMT/VCG), disease stage (PD-2 vs. PD-3), and task × stage interaction on the gait variables are presented in **Table 4**. There was a significant main effect of task condition on all gait performance measures ($p < 0.05$) except for ML-drift between WO and VMT conditions ($p = 0.1$). There was a significant main effect of disease stage on all gait outcome measures ($p < 0.05$) except for Avg-SwT ($p = 0.1$). With one exception (COV of SwT for the VCG task, $p = 0.008$), there was no interaction effect (task × stage) on any of the gait outcome measures ($p > 0.1$).

Group means and SD of the spatiotemporal gait variables by task condition and disease stage are presented in **Figure 2**. As compared to the WO condition, the addition of the VMT and VCG tasks resulted in (a) a significant decrease in Avg-SwT and Avg-SL, and (b) a significant increase in COV-SL, COV-SwT, and ML-drift. As compared to the PD-2 group, the PD-3 group had significantly shorter Avg-SwT, larger COV values, and greater ML-drift. This was the case for WO, VMT, and VCG walk trials. Effect sizes for task condition and disease stage were similar, ranging from small to medium (0.20 to 0.52).

The magnitude of DTI (i.e., effects of task condition) of cognitive demands on gait performance measures was similar in both PD-2 and PD-3 groups. The one exception was a greater magnitude of DTI on COV-SwT for the PD-3 group as compared to the PD-2 group. Effect sizes for task × stage interaction were negligible, less than 0.20.

Statistical results of the effect of task condition and disease stage on VMT and VCG performance measures are presented in **Table 5**. There was a significant effect due to task condition and disease stage on TRE ($p < 0.001$), but there was no significant task × stage interaction effect for TRE ($p = 0.2$). As evident in **Figure 3**, TRE was significantly greater during DT-walking as compared to sitting, and was significantly greater in the PD-3 group compared to the PD-2 group. This was the case when tested in sitting and during DT-walking.

There was a significant effect due to VCG task condition on movement onset time, success rate, and movement variation (**Table 5**). There was a significant effect due to disease stage on success rate but not on movement onset time or movement variation. There was no significant task × stage interaction effect on any of the three VCG outcome measures. As evident in **Figure 3**, there was a significant decrease in success rate and a significant increase in movement onset time and movement variation when tested during DT-walking as compared to sitting. Also, success rate was significantly higher in the PD-2 group compared to the PD-3 group when tested in sitting and during DT-walking. Medium effect sizes for TRE ($d = 0.56$), success rate ($d = 0.58$), and movement variation (0.52) were observed for task condition. Small effects sizes for TRE (0.47) and success rate (0.20) were observed for disease stage. Effect sizes for task × stage interaction were negligible, less than 0.20.

DISCUSSION

Overall, with a few exceptions, the computer game-based DT treadmill walking assessment protocol showed moderate to high test-retest reliability for the spatio-temporal gait measures, and VMT and VCG performance measures, under the DT condition.

TABLE 4 | Main effects and effect sizes (Cohen's *d*) of task condition and PD severity on the gait outcome measures.

Gait outcome measures	Task condition			PD stage			Interaction (Task × Stage)		
	F	*p*	*d*	*F*	*p*	*d*	*F*	*p*	*d*
Visuomotor tracking performance									
Avg. SL (cm)	3.8	0.05	0.20	20.5	0.001	0.52	0.3	0.6	0.01
Avg. SwT (s)	8.1	0.01	0.29	0.6	0.5	0.10	0.1	0.8	0.01
COV SL (%)	19.8	0.001	0.51	12.6	0.02	0.34	2.7	0.1	0.11
COV SwT (%)	5.6	0.03	0.25	12.2	0.002	0.36	0.3	0.6	0.12
ML-drift (%)	2.6	0.1	0.19	6.1	0.02	0.27	2.8	0.1	0.16
Visuomotor cognitive game performance									
Avg. SL (cm)	2.4	0.1	0.12	19.7	0.001	0.50	1.2	0.3	0.05
Avg. SwT (s)	6.5	0.02	0.26	0.9	0.3	0.04	0.001	0.9	0.01
COV SL (%)	15.7	0.001	0.46	12.6	0.002	0.36	0.1	0.8	0.01
COV SwT (%)	3.7	0.05	0.20	7.4	0.01	0.31	8.4	0.008	0.12
ML-drift (%)	5.0	0.03	0.28	6.5	0.02	0.26	0.5	0.5	0.02

Avg., average; SL, step length; SwT, swing time; COV, coefficient of variation; and ML-drift, mediolateral drift.

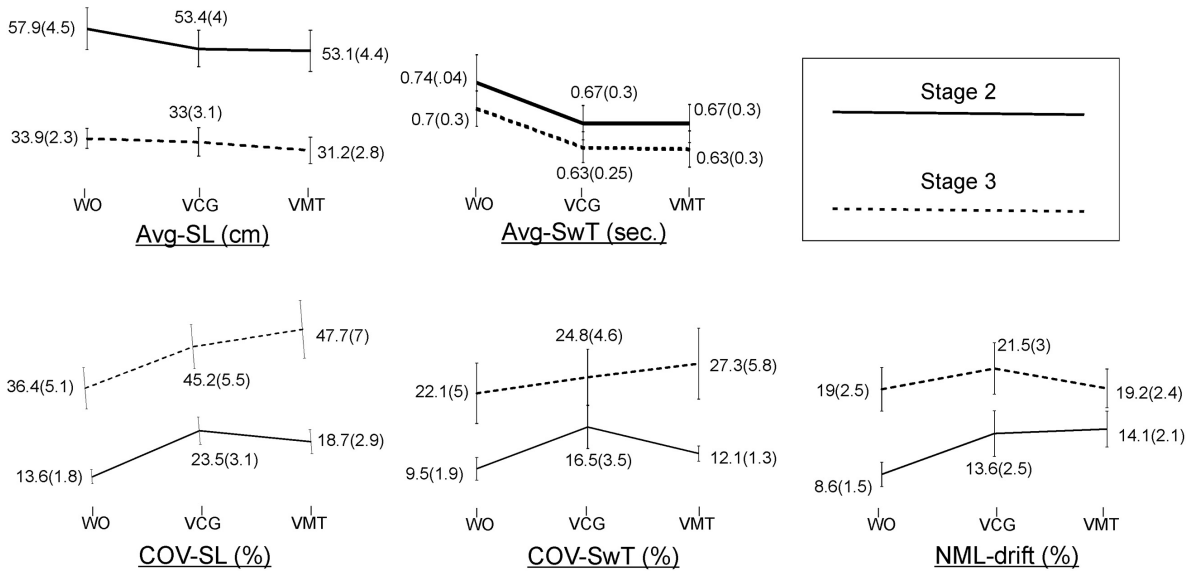

FIGURE 2 | Plots and values of group means and in brackets standard error of mean (SEM) for the gait variables by task condition and disease stage.

TABLE 5 | Main effects and effect sizes (Cohen's *d*) of task condition and PD severity on the visuomotor tracking (VMT) and visuomotor cognitive game (VCG) outcome measures.

Cognitive performance measures	Task condition			PD stage			Interaction (Task × Stage)		
	F	*p*	*d*	*F*	*p*	*d*	*F*	*p*	*d*
Visuomotor tracking performance									
Total residual error	26.4	0.001	0.56	16.8	0.001	0.47	1.6	0.2	0.07
Visuomotor cognitive game performance									
Movement onset time	8.3	0.009	0.32	0.7	0.41	0.03	2.9	0.1	0.10
Success rate	28.8	0.001	0.58	4.2	0.05	0.20	0.03	0.9	0.01
Movement variation	22.2	0.001	0.52	0.7	0.42	0.03	0.06	0.8	0.01

DTI was observed for all outcome measures of gait, VMT, and VCG with one exception: ML drift was not significantly different between WO and VMT trials. The limitation of a treadmill is the relatively narrow belt width, which does limit the degree to which a participant can drift leftward and rightward before stepping off the moving belt and falling. This constraint may

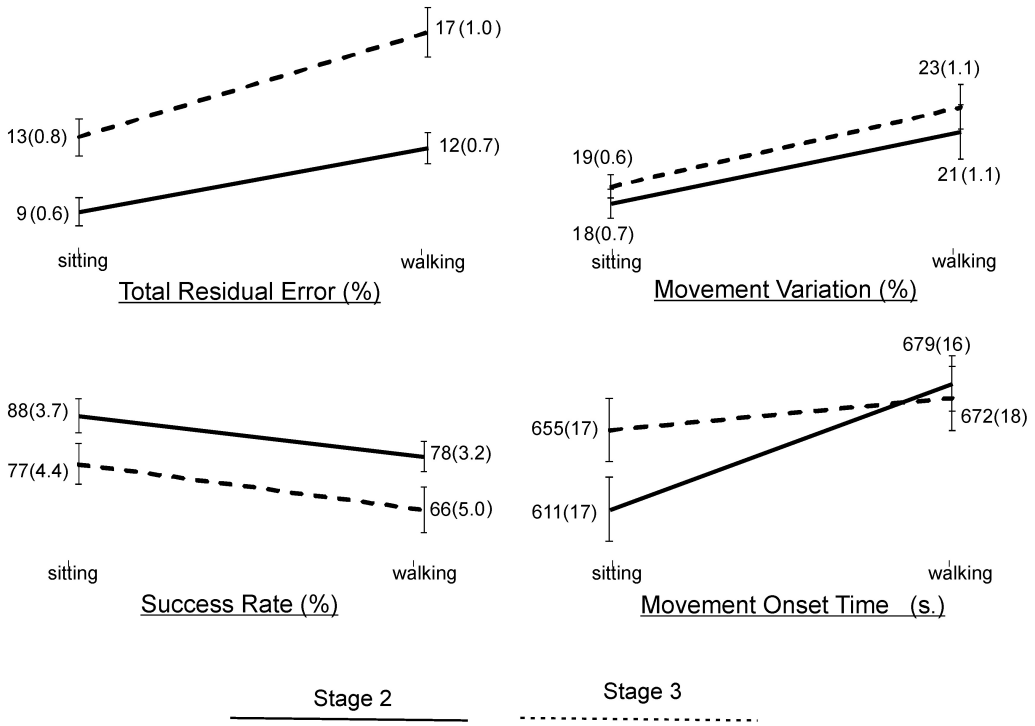

FIGURE 3 | Plots and values of group means and in brackets standard error of mean (SEM) for the VMT and VCG outcome measures by task condition and disease stage.

have influenced the amount of ML drift during the VMT task. However, it is not clear why there was a significant increase in ML drift during the VCG tasks.

The present reliability findings are consistent with the results of Strouwen et al. (2016) who examined test-retest reliability for average SL and average time during overground DT-walking in individuals with PD (Strouwen et al., 2016). Participants walked on a GAITRite instrumented walkway of 4 m while performing backward-digit counting and an auditory Stroop test. Average SL and SwT and the cognitive performance measures (number of errors), demonstrated moderate test-retest reliability during DT-walking. However, it is not known whether gait speed was the same for task conditions and test periods in this study (Strouwen et al., 2016). The present analysis extends these results to include measures of variation: COV-SL, COV-SwT, and ML-drift. In addition, in the present study, participants performed the VMT and VCG tasks for 60 s while walking (DT); the same steady state velocity was used for both DT and ST (walk only) conditions and test periods. Therefore, the present analysis was based on averages and variance of 30 movement cycles (VMT), 30 game movement responses, and on average, 30 consecutive right and left steps. In regard to absolute reliability, MDC% values for the average SL and SwT gait variables for WO, VMT and VCG walking trials were in the range of 15–20%. Values of MDC less than 20% would be considered an acceptable level for use in clinical trials (Koo and Li, 2016). The COV and ML-drift outcome measures had high MDC% values, with a range of 52–75%. When evaluating the effectiveness of treatment programs, outcome measures having high MDC% values would require a greater amount of change from pre- to post-intervention in order to be considered significant. Thus, caution needs to be taken when using gait variability measures to examine change due to some intervention. In this regard, inclusion criteria may need to be restricted (for example to include only Stage 2 or Stage 3 PD patients) as to minimize subject variability.

A significant reduction in average SL, and average SwT was observed when the VMT and VCG tasks were added. This was the case for both PD-2 and PD-3 groups. These findings for average gait variables would indicate a significant effect of visuospatial processing load on locomotor rhythm and pacing. There was also a significant increase in COV of SL, SwT, and ML-drift when the visuospatial processing loads were increased. Gait variability measures are important outcome measures as they reflect gait stability (Frenkel-Toledo et al., 2005; Montero-Odasso et al., 2012, 2018; Ahmadi et al., 2019) and are independent predictors of falls (Callisaya et al., 2011; Heinzel et al., 2016). In addition, previous studies have reported increased ML excursions of the body during treadmill walking when exposed to moving visual scenes (Bauby and Kuo, 2000; O'Connor and Kuo, 2009). Taken together, the present findings for COV-SL/SwT and ML-drift would indicate a main effect of visuospatial processing load on gait stability in PD.

Most studies that examined DT-walking in PD patients have used cognitive tasks such as counting backward tasks, animal/word enumeration tasks, and auditory Stroop tests (Rochester et al., 2014; Stegemöller et al., 2014;

Salazar et al., 2017; Raffegeau et al., 2019). The present study extends these tasks to include VMT and VCG tasks, which require participants to actively rotate their heads in order to track (VMT) and to interact (VCG) with moving target objects and avoid distractor objects. Many different types of similar head pointing movements and gaze fixations occur during our daily activities such as walking and navigating through busy and complex environments, avoiding people and obstacles, shopping and searching for specific items, or during many recreational activities. A significant decline in performance of all visuospatial processing tasks was observed when tested during DT-walking, as compared to sitting. This was the case for both PD-2 and PD-3 groups.

Schlachetzki et al. (2017) showed a significant decrease in gait speed, and SL of stage 3 participants as compared to stage 2. Hass et al. (2012) also reported a significant reduction in average SL, and average SwT of stage 3 participants compared to stage 2. The present study extends these findings and demonstrates a significant decline in gait, VMT and VCG performance measures for the PD-3 group compared to the PD-2 group during both ST and DT treadmill walking conditions. However, there was no significant difference in the magnitude of DTI (task × stage interaction) of cognitive demands on gait performance measures between the PD-2 and PD-3 groups. During the WO trials, SL was significantly less and gait variation and ML-drift were significantly greater in the PD-3 group compared to the PD-2 group. This may indicate that the PD-3 group is near the threshold level (capacity) beyond which a fall or loss of balance would occur, i.e., if the magnitude of DTI was higher in PD-3 patients, they would have fallen. For this reason, a greater increase of DTI in the PD-3 group would not be possible.

Following the principle of neural overlap (Wollesen et al., 2016; Crockett et al., 2017), DTI should be greatest when the cognitive and motor tasks engage the same neural circuits and processing resources, e.g., visual-spatial processing. Walking and maintaining balance on a moving treadmill requires attentional resources for continuous monitoring of rhythm, pacing, spatial orientation relative to borders of the treadmill belt, and to generate timely corrective responses to counter drift. This requires processing and organization of spatial information from multiple sensory systems, including visual spatial information. The VMT and VCG tasks used in the present study require sustained visual attention, visual search, cognitive inhibition and spatial processing of the moving targets, i.e., executive cognitive functions. The increased attentional demands and processing of spatial information to prevent drifting and, more seriously, falling, would compete for resources required to perform the VMT and VCG tasks, and *vice versa*.

LIMITATIONS

One limitation of the present study which is true of all DT studies relates to how individuals spontaneously prioritize their attention between the walking and the tracking/cognitive tasks. It is possible that walking was prioritized and participants did not attend to the tracking/cognitive activities with 100% effort. Alternatively, the information provided during the VMT and VCG tasks was received and processed and the performance was affected due to DTI. Modest performance levels were observed in the present study for both VMT and VCG tasks during walking. This would indicate the participants were attending to and processing the information they saw on the display. However, they may have stopped intermittently for a few seconds and prioritized locomotor processing (i.e., to correct rhythm, pacing and balance). Another limitation is that treadmill and overground are different types of walking tasks. However, treadmill walking involves repetitive stepping and dynamic stability requirements that are comparable to the demands of overground walking, as well the kinematics and kinetics of gait during treadmill and overground walking have very similar patterns and degree of variation (Watt et al., 2010; Hollman et al., 2016; Yao et al., 2019). In the present assessment, treadmill was used to ensure a steady state gait at a controlled speed and within a narrow spatial range (width/length of treadmill walking surface). Also important is that treadmills can be easily equipped with a computer monitor to access digital media. This provides standardized repeatable computer tracking and cognitive game activities and thus presents the same information to all participants on both test days, and for all test conditions (sitting and during walking). In addition, the gait and cognitive outcome measures are quantified not just for a few seconds, but for durations of minutes.

The absence of a healthy age-matched control group is another limitation. This analysis would provide added information as to differences in DTI due to age effects and disease stage. A study is in progress (paused due to COVID-19) to compare the effects of VMT and VCG on gait function (and *vice versa*) between age-matched able-bodied participants and stage 2 and 3 PD participants.

Finally, the VMT and VCG tasks used in the present study involve both head rotation and information processing, and at this point we cannot rule out any intersegmental mechanical effect of the head rotation as a cause of the gait changes observed between the WO and the DT walk trials. Head rotations required for the VCG tasks were relatively small head rotations of between 20–40 degrees, and of 300–500 ms in duration. These small ramp head rotations about the vertical axis would not likely cause any deviation in position of the body center of mass in ML or AP directions, i.e., passive mechanical disturbance to gait. Duysens et al. (2008) examined center of pressure migration during an open-loop tracking task (up to 30 degrees of visual target motion) while treadmill walking. Three tasks were performed: tracking with eye movements only (head stationary), tracking by rotating the head in synchrony with the moving visual target (open-loop tracking task), and tracking while rotating the trunk in synchrony with the moving visual target. The results demonstrated no significant deviation of the center of pressure migration when participants performed the tracking task with eye or head rotation, whereas, trunk rotations led to a doubling of ML-center of pressure deviation. The mechanical effect of head rotation on gait rhythm pacing and variation will receive further investigation.

CONCLUSION

The high to moderate ICC values along with the lack of systematic errors in the measures indicate that this tool has the ability to repeatedly record reliable DTI effects over time. This also proves to be a sensitive tool for tracking disease progression.

A comprehensive analysis of spatial and temporal features of steady state gait has a greater validity to measure gait performance (rhythm, pacing, and stability) as compared to gait speed alone. The use of standardized, interactive computer applications provides a flexible method to produce and evaluate a wide range of executive cognitive activities while performing complex motor behaviors such as walking. Objective evaluation of VMT and VCG computer tasks provide important information about different aspects of information processing.

While the focus of the present work is on assessment of DTI in PD, the GRP platform is directly applicable to other diseases that affect gait and cognition (e.g., cognitive vascular impairment, Alzheimer's disease, and aging). Future studies will examine the type and levels of DTI that are prognostic of falls and adverse health events. A randomized clinical trial is also planned to examine the feasibility and effectiveness of a computer game-based DT training program for PD patients. Many designed cognitive games, as well as many engaging and inexpensive common and modern computer games can be used with the GRP to challenge a broad range of visuomotor and executive cognitive functions (Mahana et al., 2021).

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Human Research Ethics Board at the University of Manitoba. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

MB, BM, and TS: study concept, design, and acquisition. MB, BM, JK, TK, AK, and TS: analysis, interpretation of data, and preparation of the manuscript. All authors contributed to the article and approved the submitted version.

FUNDING

The funding for this study was provided by the University of Manitoba's University Collaborative Research Program (Fund #: 50667), as well as the Weston Brain Institute (Fund #: TR193095), and the Natural Sciences and Engineering Research Council of Canada (NSERC) postdoctoral fellowship (PDF-545615-2020).

ACKNOWLEDGMENTS

The authors would like to thank the funding agencies that helped make this work possible, including the University of Manitoba Collaborative Research Program, the Weston Brain Institute, and the Natural Sciences and Engineering Research Council of Canada.

REFERENCES

Ahmadi, S., Sepehri, N., Wu, C., and Szturm, T. (2019). Comparison of selected measures of gait stability derived from center of pressure displacement signal during single and dual-task treadmill walking. *Med. Eng. Phys.* 74, 49–57. doi: 10.1016/j.medengphy.2019.07.018

Ahmadi, S., Wu, C., Sepehri, N., Kantikar, A., Nankar, M., and Szturm, T. (2018). The effects of aging and dual tasking on human gait complexity during treadmill walking: a comparative study using quantized dynamical entropy and sample entropy. *J. Biomech. Eng.* 140:011006.

Al-Yahya, E., Dawes, H., Smith, L., Dennis, A., Howells, K., and Cockburn, J. (2011). Cognitive motor interference while walking: a systematic review and meta-analysis. *Neurosci. Biobehav. Rev.* 35, 715–728. doi: 10.1016/j.neubiorev.2010.08.008

Battisto, J., Echt, K. V., Wolf, S. L., Weiss, P., and Hackney, M. E. (2018). The body position spatial task, a test of whole-body spatial cognition: comparison between adults with and without Parkinson disease. *Neurorehabil. Neural Repair* 32, 961–975. doi: 10.1177/1545968318804419

Bauby, C. E., and Kuo, A. D. (2000). Active control of lateral balance in human walking. *J. Biomech.* 33, 1433–1440. doi: 10.1016/s0021-9290(00)00101-9

Bruijn, S. M., van Dieen, J. H., Meijer, O. G., and Beek, P. J. (2009). Statistical precision and sensitivity of measures of dynamic gait stability. *J. Neurosci. Methods* 178, 327–333. doi: 10.1016/j.jneumeth.2008.12.015

Callisaya, M. L., Blizzard, L., Schmidt, M. D., Martin, K. L., McGinley, J. L., Sanders, L. M., et al. (2011). Gait, gait variability and the risk of multiple incident falls in older people: a population-based study. *Age Ageing* 40, 481–487. doi: 10.1093/ageing/afr055

Chung, M. J., and Wang, M. J. (2010). The change of gait parameters during walking at different percentage of preferred walking speed for healthy adults aged 20-60 years. *Gait Posture* 31, 131–135. doi: 10.1016/j.gaitpost.2009.09.013

Cole, M. H., Sweeney, M., Conway, Z. J., Blackmore, T., and Silburn, P. A. (2017). Imposed faster and slower walking speeds influence gait stability differently in Parkinson fallers. *Arch. Phys. Med. Rehabil.* 98, 639–648. doi: 10.1016/j.apmr.2016.11.008

Creaby, M. W., and Cole, M. H. (2018). Gait characteristics and falls in Parkinson's disease: a systematic review and meta-analysis. *Parkinsonism Relat. Disord.* 57, 1–8. doi: 10.1016/j.parkreldis.2018.07.008

Crockett, R. A., Hsu, C. L., Best, J. R., and Liu-Ambrose, T. (2017). Resting state default mode network connectivity, dual task performance, gait speed, and postural sway in older adults with mild cognitive impairment. *Front. Aging Neurosci.* 9:423. doi: 10.3389/fnagi.2017.00423

Dirnberger, G., and Jahanshahi, M. (2013). Executive dysfunction in Parkinson's disease: a review. *J. Neuropsychol.* 7, 193–224. doi: 10.1097/wnp.0b013e3181dd4fdb

Duysens, J., Duysens, J. P., Bastiaanse, C. M., van Sprundel, M., Schubert, M., and Smits-Engelsman, B. C. (2008). How trunk turns affect locomotion when you are not looking where you go. *Hum. Mov. Sci.* 27, 759–770. doi: 10.1016/j.humov.2008.04.004

Fahn, S., Elton, R., and Members of the UPDRS Development Committee (1987). "Unified Parkinson's disease rating scale," in *Recent Developments in Parkinson's*

Disease, eds S. Fahn, C. Marsden, M. Goldstein, and D. Calne (Florham Park, NJ: Macmillan Health Care Information), 153–163.

Fraser, S. A., Dupuy, O., Pouliot, P., Lesage, F., and Bherer, L. (2016). Comparable cerebral oxygenation patterns in younger and older adults during dual-task walking with increasing load. *Front. Aging Neurosci.* 8:240. doi: 10.3389/fnagi.2016.00240

Frenkel-Toledo, S., Giladi, N., Peretz, C., Herman, T., Gruendlinger, L., and Hausdorff, J. M. (2005). Effect of gait speed on gait rhythmicity in Parkinson's disease: variability of stride time and swing time respond differently. *J. Neuroeng. Rehabil.* 2:23.

Galna, B., Lord, S., and Rochester, L. (2013). Is gait variability reliable in older adults and Parkinson's disease? Towards an optimal testing protocol. *Gait Posture* 37, 580–585. doi: 10.1016/j.gaitpost.2012.09.025

Gilat, M., Bell, P. T., Ehgoetz Martens, K. A., Georgiades, M. J., Hall, J. M., Walton, C. C., et al. (2017). Dopamine depletion impairs gait automaticity by altering cortico-striatal and cerebellar processing in Parkinson's disease. *Neuroimage* 152, 207–220. doi: 10.1016/j.neuroimage.2017.02.073

Haley, S. M., and Fragala-Pinkham, M. A. (2006). Interpreting change scores of tests and measures used in physical therapy. *Phys. Ther.* 86, 735–743. doi: 10.1093/ptj/86.5.735

Hass, C. J., Malczak, P., Nocera, J., Stegemöller, E. L., Shukala, A., Malaty, I., et al. (2012). Quantitative normative gait data in a large cohort of ambulatory persons with Parkinson's disease. *PLoS One* 7:e42337. doi: 10.1371/journal.pone.0042337

Heinzel, S., Maechtel, M., Hasmann, S. E., Hobert, M. A., Heger, T., Berg, D., et al. (2016). Motor dual-tasking deficits predict falls in Parkinson's disease: a prospective study. *Parkinsonism Relat. Disord.* 26, 73–77. doi: 10.1016/j.parkreldis.2016.03.007

Hollman, J. H., Childs, K. B., McNeil, M. L., Mueller, A. C., Quilter, C. M., and Youdas, J. W. (2010). Number of strides required for reliable measurements of pace, rhythm and variability parameters of gait during normal and dual task walking in older individuals. *Gait Posture* 32, 23–28. doi: 10.1016/j.gaitpost.2010.02.017

Hollman, J. H., Watkins, M. K., Imhoff, A. C., Braun, C. E., Akervik, K. A., and Ness, D. K. (2016). A comparison of variability in spatiotemporal gait parameters between treadmill and overground walking conditions. *Gait Posture* 43, 204–209. doi: 10.1016/j.gaitpost.2015.09.024

Holtzer, R., Mahoney, J. R., Izzetoglu, M., Wang, C., England, S., and Verghese, J. (2015). Online fronto-cortical control of simple and attention-demanding locomotion in humans. *Neuroimage* 112, 152–159. doi: 10.1016/j.neuroimage.2015.03.002

Hughes, A. J., Daniel, S. E., Kilford, L., and Lees, A. J. (1992). Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *J. Neurol. Neurosurg. Psychiatry* 55, 181–184. doi: 10.1136/jnnp.55.3.181

Jordan, K., Challis, J. H., and Newell, K. M. (2007). Walking speed influences on gait cycle variability. *Gait Posture* 26, 128–134. doi: 10.1016/j.gaitpost.2006.08.010

Kang, G. A., Bronstein, J. M., Masterman, D. L., Redelings, M., Crum, J. A., and Ritz, B. (2005). Clinical characteristics in early Parkinson's disease in a central California population-based study. *Mov. Disord.* 20, 1133–1142. doi: 10.1002/mds.20513

Keene, D. J., Moe-Nilssen, R., and Lamb, S. E. (2016). The application of multilevel modelling to account for the influence of walking speed in gait analysis. *Gait Posture* 43, 216–219. doi: 10.1016/j.gaitpost.2015.09.026

Klencklen, G., Després, O., and Dufour, A. (2012). What do we know about aging and spatial cognition? Reviews and perspectives. *Ageing Res. Rev.* 11, 123–135. doi: 10.1016/j.arr.2011.10.001

Koo, T. K., and Li, M. Y. (2016). A guideline of selecting and reporting intraclass correlation coefficients for reliability research. *J. Chiropr. Med.* 15, 155–163. doi: 10.1016/j.jcm.2016.02.012

Lally, H., Hart, A. R., Bay, A. A., Kim, C., Wolf, S. L., and Hackney, M. E. (2020). Association between motor subtype and visuospatial and executive function in mild-moderate Parkinson disease. *Arch. Phys. Med. Rehabil.* 101, 1580–1589. doi: 10.1016/j.apmr.2020.05.018

Lexell, J. E., and Downham, D. Y. (2005). How to assess the reliability of measurements in rehabilitation. *Am. J. Phys. Med. Rehabil.* 84, 719–723. doi: 10.1097/01.phm.0000176452.17771.20

Liu, Y.-C., Yang, Y.-R., Yeh, N.-C., Ku, P.-H., Lu, C.-F., and Wang, R.-Y. (2021). Cognitive and motor dual task on multi-area brain activation and gait performance in individuals with Parkinson's disease. *Res. Sq.* [Preprint].

Lord, S., Galna, B., Yarnall, A. J., Morris, R., Coleman, S., Burn, D., et al. (2017). Natural history of falls in an incident cohort of Parkinson's disease: early evolution, risk and protective features. *J. Neurol.* 264, 2268–2276. doi: 10.1007/s00415-017-8620-y

Mahana, B., Bhatt, M., Gupta, A., Hobson, D. E., Ko, J. H., and Szturm, T. (2021). Does use of dual-task cognitive game-assisted treadmill system improve balance and gait in Parkinson's disease? A feasibility study. *Body Brain Cogn. J.* 9, 23–33.

Maidan, I., Nieuwhof, F., Bernad-Elazari, H., Reelick, M. F., Bloem, B. R., Giladi, N., et al. (2016). The role of the frontal lobe in complex walking among patients with Parkinson's disease and healthy older adults: an fNIRS study. *Neurorehabil. Neural Repair* 30, 963–971. doi: 10.1177/1545968316650426

Mak, M. K., Wong, A., and Pang, M. Y. (2014). Impaired executive function can predict recurrent falls in Parkinson's disease. *Arch. Phys. Med. Rehabil.* 95, 2390–2395. doi: 10.1016/j.apmr.2014.08.006

Messick, S. (1995). Standards of validity and the validity standards in performance assessment. *Educ. Meas. Issues Pract.* 14, 5–8. doi: 10.1111/j.1745-3992.1995.tb00881.x

Monchi, O., Petrides, M., Doyon, J., Postuma, R. B., Worsley, K., and Dagher, A. (2004). Neural bases of set-shifting deficits in Parkinson's disease. *J. Neurosci.* 24, 702–710. doi: 10.1523/jneurosci.4860-03.2004

Monchi, O., Petrides, M., Petre, V., Worsley, K., and Dagher, A. (2001). Wisconsin Card Sorting revisited: distinct neural circuits participating in different stages of the task identified by event-related functional magnetic resonance imaging. *J. Neurosci.* 21, 7733–7741. doi: 10.1523/jneurosci.21-19-07733.2001

Montero-Odasso, M., Almeida, Q. J., Burhan, A. M., Camicioli, R., Doyon, J., Fraser, S., et al. (2018). SYNERGIC TRIAL (SYNchronizing exercises, remedies in gait and cognition) a multi-centre randomized controlled double blind trial to improve gait and cognition in mild cognitive impairment. *BMC Geriatr.* 18:93. doi: 10.1186/s12877-018-0782-7

Montero-Odasso, M., Muir, S. W., and Speechley, M. (2012). Dual-task complexity affects gait in people with mild cognitive impairment: the interplay between gait variability, dual tasking, and risk of falls. *Arch. Phys. Med. Rehabil.* 93, 293–299. doi: 10.1016/j.apmr.2011.08.026

Nankar, M., Szturm, T., Marotta, J., Shay, B., Beauchet, O., and Allali, G. (2017). The interacting effects of treadmill walking and different types of visuospatial cognitive task: discriminating dual task and age effects. *Arch. Gerontol. Geriatr.* 73, 50–59. doi: 10.1016/j.archger.2017.07.013

Nasreddine, Z. S., Phillips, N. A., Bedirian, V., Charbonneau, S., Whitehead, V., Collin, I., et al. (2005). The montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment. *J. Am. Geriatr. Soc.* 53, 695–699. doi: 10.1111/j.1532-5415.2005.53221.x

O'Connor, S. M., and Kuo, A. D. (2009). Direction-dependent control of balance during walking and standing. *J. Neurophysiol.* 102, 1411–1419. doi: 10.1152/jn.00131.2009

Olchik, M. R., Ghisi, M., Freiry, A. M., Ayres, A., Schuh, A. F. S., Rieder, C. R. M., et al. (2017). Comparison trail making test between individuals with Parkinson's disease and health controls: suggestions of cutoff point. *Psychol. Neurosci.* 10, 77–82. doi: 10.1037/pne0000076

Paul, S. S., Sherrington, C., Canning, C. G., Fung, V. S., Close, J. C., and Lord, S. R. (2014). The relative contribution of physical and cognitive fall risk factors in people with Parkinson's disease: a large prospective cohort study. *Neurorehabil. Neural Repair* 28, 282–290. doi: 10.1177/1545968313508470

Penko, A. L., Streicher, M. C., Koop, M. M., Dey, T., Rosenfeldt, A. B., Bazyk, A. S., et al. (2018). Dual-task interference disrupts Parkinson's gait across multiple cognitive domains. *Neuroscience* 379, 375–382. doi: 10.1016/j.neuroscience.2018.03.021

Pickering, R. M., Grimbergen, Y. A., Rigney, U., Ashburn, A., Mazibrada, G., Wood, B., et al. (2007). A meta-analysis of six prospective studies of falling in Parkinson's disease. *Mov. Disord.* 22, 1892–1900. doi: 10.1002/mds.21598

Plotnik, M., Dagan, Y., Gurevich, T., Giladi, N., and Hausdorff, J. M. (2011). Effects of cognitive function on gait and dual tasking abilities in patients with Parkinson's disease suffering from motor response fluctuations. *Exp. Brain Res.* 208, 169–179. doi: 10.1007/s00221-010-2469-y

Raffegeau, T. E., Krehbiel, L. M., Kang, N., Thijs, F. J., Altmann, L. J. P., Cauraugh, J. H., et al. (2019). A meta-analysis: Parkinson's disease and dual-task walking. *Parkinsonism Relat. Disord.* 62, 28–35.

Rochester, L., Galna, B., Lord, S., and Burn, D. (2014). The nature of dual-task interference during gait in incident Parkinson's disease. *Neuroscience* 265, 83–94. doi: 10.1016/j.neuroscience.2014.01.041

Rochester, L., Hetherington, V., Jones, D., Nieuwboer, A., Willems, A. M., Kwakkel, G., et al. (2004). Attending to the task: interference effects of functional tasks on walking in Parkinson's disease and the roles of cognition, depression, fatigue, and balance. *Arch. Phys. Med. Rehabil.* 85, 1578–1585. doi: 10.1016/j.apmr.2004.01.025

Roheger, M., Kalbe, E., and Liepelt-Scarfone, I. (2018). Progression of cognitive decline in Parkinson's disease. *J. Parkinsons Dis.* 8, 183–193. doi: 10.3233/jpd-181306

Rosenberg-Katz, K., Herman, T., Jacob, Y., Mirelman, A., Giladi, N., Hendler, T., et al. (2015). Fall risk is associated with amplified functional connectivity of the central executive network in patients with Parkinson's disease. *J. Neurol.* 262, 2448–2456. doi: 10.1007/s00415-015-7865-6

Salazar, R. D., Ren, X., Ellis, T. D., Toraif, N., Barthelemy, O. J., Neargarder, S., et al. (2017). Dual tasking in Parkinson's disease: cognitive consequences while walking. *Neuropsychology* 31, 613–623. doi: 10.1037/neu0000331

Schäfer, T., and Schwarz, M. A. (2019). The meaningfulness of effect sizes in psychological research: differences between sub-disciplines and the impact of potential biases. *Front. Psychol.* 10:813. doi: 10.3389/fpsyg.2019.00813

Schlachetzki, J. C. M., Barth, J., Marxreiter, F., Gossler, J., Kohl, Z., Reinfelder, S., et al. (2017). Wearable sensors objectively measure gait parameters in Parkinson's disease. *PLoS One* 12:e0183989. doi: 10.1371/journal.pone.0183989

Schneider, J. S., Sendek, S., and Yang, C. (2015). Relationship between motor symptoms, cognition, and demographic characteristics in treated mild/moderate Parkinson's disease. *PLoS One* 10:e0123231. doi: 10.1371/journal.pone.0123231

Stegemöller, E. L., Wilson, J. P., Hazamy, A., Shelley, M. C., Okun, M. S., Altmann, L. J., et al. (2014). Associations between cognitive and gait performance during single- and dual-task walking in people with Parkinson disease. *Phys. Ther.* 94, 757–766. doi: 10.2522/ptj.20130251

Strouwen, C., Molenaar, E. A., Keus, S. H., Münks, L., Bloem, B. R., and Nieuwboer, A. (2016). Test-retest reliability of dual-task outcome measures in people with Parkinson disease. *Phys. Ther.* 96, 1276–1286. doi: 10.2522/ptj.20150244

Szturm, T., Beheshti, I., Mahana, B., Hobson, D. E., Goertzen, A., and Ko, J. H. (2020). Imaging cerebral glucose metabolism during dual-task walking in patients with Parkinson's disease. *J. Neuroimaging* 31, 356–362. doi: 10.1111/jon.12812

Szturm, T., Kolesar, T. A., Mahana, B., Goertzen, A. L., Hobson, D. E., Marotta, J. J., et al. (2021). Changes in metabolic activity and gait function by dual-task cognitive game-based treadmill system in Parkinson's disease: protocol of a randomized controlled trial. *Front. Aging Neurosci.* 13:680270. doi: 10.3389/fnagi.2021.680270

Szturm, T. J., Sakhalkar, V. S., Kanitkar, A., and Nankar, M. (2017). Computerized dual-task testing of gait and visuospatial cognitive functions; test-retest reliability and validity. *Front. Hum. Neurosci.* 11:105. doi: 10.3389/fnhum.2017.00105

Watt, J. R., Franz, J. R., Jackson, K., Dicharry, J., Riley, P. O., and Kerrigan, D. C. (2010). A three-dimensional kinematic and kinetic comparison of overground and treadmill walking in healthy elderly subjects. *Clin. Biomech.* 25, 444–449. doi: 10.1016/j.clinbiomech.2009.09.002

Wollesen, B., Voelcker-Rehage, C., Regenbrecht, T., and Mattes, K. (2016). Influence of a visual-verbal Stroop test on standing and walking performance of older adults. *Neuroscience* 318, 166–177. doi: 10.1016/j.neuroscience.2016.01.031

Wu, T., Hallett, M., and Chan, P. (2015). Motor automaticity in Parkinson's disease. *Neurobiol. Dis.* 82, 226–234. doi: 10.1016/j.nbd.2015.06.014

Yao, J., Guo, N., Xiao, Y., Li, Z., Li, Y., Pu, F., et al. (2019). Lower limb joint motion and muscle force in treadmill and over-ground exercise. *Biomed. Eng. Online* 18:89.

Zou, G. Y. (2012). Sample size formulas for estimating intraclass correlation coefficients with precision and assurance. *Stat. Med.* 31, 3972–3981. doi: 10.1002/sim.5466

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Human Neuroscience

BRIEF RESEARCH REPORT
published: 21 July 2021
doi: 10.3389/fnhum.2021.692651

In Patients With Parkinson's Disease in an OFF-Medication State, Does Bilateral Electrostimulation of Tibialis Anterior Improve Anticipatory Postural Adjustments During Gait Initiation?

Arnaud Delafontaine[1,2,3], Paul Fourcade[1,2], Ahmed Zemouri[1,2], D. G. Diakhaté[1,2,4], Gabriel Saiydoun[3,5,6,7] and Eric Yiou[1,2]*

[1] CIAMS, Univ. Paris-Sud., Université Paris-Saclay, Orsay, France, [2] CIAMS, Université d'Orléans, Orléans, France, [3] Unisurg, Paris, France, [4] UFR Sciences de l'Education de la Formation et du Sport, Gaston Berger University, Saint-Louis, Senegal, [5] Department of Cardiac Surgery, Henri Mondor University Hospital, APHP, Créteil, France, [6] University of Paris-Est Creteil, UFR Médecine-Pharmacie, Créteil, France, [7] Institut Mondor de Recherche Biomedicale, IMRB, Inserm U955, Faculté de Santé de Créteil, Creteil, France

OPEN ACCESS

Edited by:
Mariagiovanna Cantone, Sant'Elia Hospital, Italy

Reviewed by:
Angela Palomba, University of Campania Luigi Vanvitelli, Italy
Kaviraja Udupa, National Institute of Mental Health and Neurosciences, India

***Correspondence:**
Arnaud Delafontaine
arnaud.delafontaine@u-psud.fr

Specialty section:
This article was submitted to Motor Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *08 April 2021*
Accepted: *29 June 2021*
Published: *21 July 2021*

Citation:
Delafontaine A, Fourcade P, Zemouri A, Diakhaté DG, Saiydoun G and Yiou E (2021) In Patients With Parkinson's Disease in an OFF-Medication State, Does Bilateral Electrostimulation of Tibialis Anterior Improve Anticipatory Postural Adjustments During Gait Initiation? Front. Hum. Neurosci. 15:692651. doi: 10.3389/fnhum.2021.692651

A complete lack of bilateral activation of tibialis anterior (TA) during gait initiation (GI), along with bradykinetic anticipatory postural adjustments (APAs), often occurs in patients with Parkinson's disease (PD) in their OFF-medication state. Functional electrical stimulation (FES) is a non-pharmacological method frequently used in neurorehabilitation to optimize the effect of L-DOPA on locomotor function in this population. The present study tested the potential of bilateral application of FES on TA to improve GI in PD patients. Fourteen PD patients (OFF-medication state, Hoehn and Yahr state 2-3) participated in this study. They performed series of 10 GI trials on a force-plate under the following experimental conditions: (1) GI without FES (control group), (2) GI with 2Hz-FES (considered as a very low FES frequency condition without biomechanical effect; placebo group) and (3) GI with 40Hz-FES (test group). In (2) and (3), FES was applied bilaterally to the TA during APAs (300 mA intensity/300 μs pulse width). Main results showed that the peak of anticipatory backward center of pressure shift, the forward center of mass (COM) velocity and shift at foot off were significantly larger in the 40 Hz FES condition than in the control condition, while the duration of step execution was significantly shorter. In contrast, the capacity of participants to brake the fall of their COM remained unchanged across conditions. Globally taken, these results suggest that acute application of 40-Hz FES to the TA may improve the capacity of PD patients to generate APAs during GI, without altering their balance capacity. Future studies are required before considering that TA FES application might be a valuable tool to improve GI in PD patients and be relevant to optimize the effects of L-DOPA medication on locomotor function.

Keywords: Parkinson's disease, functional electrical stimulation, gait initiation, anticipatory postural adjustments, tibialis anterior

INTRODUCTION

Gait initiation (GI), the transient period between steady-standing posture and steady-state walking, is a functional task known to be altered in patients with Parkinson's Disease (PD) (Halliday et al., 1998). Alteration in GI has been identified as a source of fall in neurological patients (Stolze et al., 2004). GI is classically decomposed into three successive phases: the postural phase, which precedes the swing heel-off (and corresponding to the so-called "anticipatory postural adjustments," APAs), the unloading phase (from swing heel-off to toe-off) and the execution phase ending at the time of foot-contact. During APAs, the tibialis anterior (TA) are activated bilaterally, which is responsible of backward center-of-pressure (COP) shift. This COP shift is necessary to generate the initial forces to propel the center-of-mass (COM) forward during the execution phase, and reach the desired step length and velocity (Lepers and Breničre, 1995). During step execution, the COM falls under gravity effect, and this fall is actively braked by the activation of stance leg triceps surae, which acts to attenuate the impact of the swing limb at foot contact (Honeine et al., 2013).

A complete lack of bilateral TA activation, along with bradykinetic APAs often occurs in PD patients in their OFF-medication state (Halliday et al., 1998), which may be one of the factors responsible for the symptoms of "start hesitation" typical of this population (Delval et al., 2014). Altered active COM braking has also been reported in patients with severe PD patients (Chastan et al., 2009).

Classical treatment of PD includes L-DOPA administration (Palmisano et al., 2020). It is however noteworthy that the positive effects of this pharmacological treatment is controversial (Rocchi et al., 2002). L-DOPA may indeed induce dyskinesia (Curtze et al., 2015), which may alter balance control in PD patients in their ON-medication state when compared to their OFF-medication state (Armand et al., 2009).

Recent studies reported that Functional Electrical Stimulation (FES), a non-pharmacological rehabilitation method, may be relevant to optimize the effect of L-DOPA on locomotor function. FES is a means of producing an active muscle contraction controlled in such a way to provide functional movement to assist everyday tasks. Sijobert et al. (2016) showed that plantar sensitive electrical stimulation during steady-state walking reduced freezing by about 12% in PD patients. Mann et al. (2008) reported that the application of FES on the common peroneal nerve of PD patients increased the average stride length, increased the distance covered during a 3-min walk test, and decreased the risks of falls in this population. FES stimulation might also specifically ameliorate gait in patients with freezing of gait (FOG) (Djurić-Jovičić et al., 2013). However, it is noteworthy that Mancini and Horak (2010) stressed that the greatest limitation of these clinical approaches to rating balance is that they cannot specify what type of balance problem a subject suffers in order to direct a treatment.

To our knowledge, no studies to date investigated whether FES may be efficient to facilitate GI in PD patients. The present study thus tested the potential of bilateral application of FES on TA to improve GI in PD patients.

METHODS

Fourteen PD patients [11 men and 3 women, aged 69 ± 7 years, height 166 ± 8.2 cm, body-mass 66 ± 15 kg [(mean ± SD)]; see **Table 1**, classified Hoehn and Yahr states 2-3 were included in the experiment. Only PD patients in their OFF-medication state (i.e., after 12-h withdrawal from their antiparkinsonian's L-DOPA medications) were included because this is the condition where alterations in APAs development and associated TA activity mainly occur. All patients reported FOG. Exclusion criteria included: visual, hearing or orthopedic problems, other identified neurological troubles, dementia, severe dyskinesia, a score <25 on the Mini Mental State Exam, implanted deep brain stimulator and response fluctuations. The patients had no medical history of falling. All subjects gave informed written consent as required by the Declaration of Helsinki. The experiment was approved by the "Comité de Protection des Personnes Ile-de-France XI" under identification number 19028-60429.

MDS-UPDRS: Movement disorders society-Unified Parkinson's Disease Rating Scale; STS: Sit-to-Stand Task. STS score corresponds to the number of rising from a chair performed during 15 seconds; MMSE: Mini Mental State Exam.

Each participant performed series of GI trials at a spontaneous velocity on a force-plate (0.9 × 1.80 m, AMTI, Watertown, United States) following an acoustic signal delivered by the experimenter. Ten GI trials were performed in each of the three following experimental conditions (for a total of $N = 30$ trials): (1) GI without FES (control), (2) GI with 2 Hz FES (considered as a very low FES frequency condition without biomechanical effect), and (3) GI with 40 Hz FES. In (2) and (3), FES (referee Compex Wireless Professional®) was applied bilaterally to TA during APAs with an intensity of 300 mA and a pulse width of 300 μs. The order of the experimental conditions was randomly assigned across participants to avoid rank effects.

Force-plate data were low-pass filtered using a second order Butterworth filter with a 10 Hz cut-off frequency (Winter, 1990; Sinclair et al., 2013). The COP anteroposterior coordinate was computed from force-plate data. The instantaneous COM acceleration was determined from the ground reaction forces. COM velocity and position were computed with successive numerical integrations of COM acceleration (Yiou et al., 2016). Data were collected at a rate of 500 Hz. Data acquisition was controlled by a custom-made program written in MATLABTM [Version 5.3 (R11), The MathWorks Inc., United States].

Classical GI biomechanical parameters were analyzed. Temporal parameters included: duration of APAs (APAd, from onset variations of biomechanical traces to heel-off), unloading (UNL, from heel-off to toe-off) and execution phase (EXE, from toe-off to heel-contact). Spatial parameters included: peak backward COP shift (xP_{MAX}), forward COM velocity ($x'M_{TO}$) and COM position at toe-off (xM_{TO}), forward COM velocity at foot-contact ($x'M_{FC}$), step length (SL) and Braking Index (BI). GI biomechanical traces obtained in one representative PD subject and showing temporal parameters are reported in **Figure 1**.

Mean values and standard deviations were calculated for each dependent variable. Repeated-measures ANOVAs were used to test the effect of the condition (control, 2 Hz FES, 40 Hz FES) on

TABLE 1 | Demographic characteristics and clinical parameters of PD patients.

PD patients	Sex	Age (years)	Height (cm)	Body-mass (kg)	Disease duration (years)	Hoehn and Yahr stage	MDS-UPDRS motor examination (section III)	STS (numbers /15 s)	MMSE (points)
Subject 1	Male	63	158	62	4	3	28	8	30
Subject 2	Male	74	174	70	10	2	25	8	30
Subject 3	Male	80	170	62	5	3	24	4	25
Subject 4	Female	75	169	76	12	2	30	8	30
Subject 5	Male	70	170	76	8	2	19	11	30
Subject 6	Male	64	170	70	15	3	32	7	25
Subject 7	Female	62	158	45	12	2	19	8	30
Subject 8	Male	78	173	82	4	3	24	5	27
Subject 9	Male	70	176	87	6	3	28	6	27
Subject 10	Male	71	160	66	8	2	27	7	27
Subject 11	Male	68	160	52	7	2	19	9	29
Subject 12	Male	57	155	48	5	2	35	7	28
Subject 13	Male	63	157	40	8	3	21	8	30
Subject 14	Female	71	180	90	6	2	32	5	28
Mean (SD)	–	69 (7)	166 (8.2)	66 (15)	8 (3)	2 (0.5)	26 (5.3)	7 (2)	28 (2)

MDS-UPDRS, Movement disorders society-Unified Parkinson's Disease Rating Scale; STS, Sit-to-Stand Task, STS score corresponds to the number of rising from a chair performed during 15 s; MMSE, Mini Mental State Exam.

each variable after having checked normal distribution with the Shapiro-Wilk test. A significant outcome was followed up with the Tukey *post hoc* test. The threshold of significance was set at $p < 0.05$. The Cohen's d (d') was used to assess effect sizes. Effect sizes were classified as trivial (<0.2), small (0.2–0.49), medium (0.5–0.79), and large (≥0.8).

RESULTS

Statistical analysis showed that there was a significant effect of the condition on the following variables (**Figure 2**): xP_{MAX} [$F(2, 26) = 8.41$, $p < 0.01$], $x'M_{TO}$ [$F(2, 26) = 7.80$, $p < 0.01$], xM_{TO} [$F(2, 26) = 13.64$, $p < 0.001$] and EXE [$F(2, 26) = 4.15$, $p < 0.05$]. Specifically, *post hoc* test showed that xP_{MAX} ($p < 0.001$; $d' = 0.38$), $x'M_{TO}$ ($p < 0.05$; $d' = 0.58$) and xM_{TO} ($p < 0.001$; $d' = 0.17$) were significantly larger in the 40 Hz FES condition than in the control condition, while EXE was significantly shorter ($p < 0.05$, $d' = 0.62$, **Figure 2**). There was no significant effect of the condition on the following variables: APAd (590 ± 26 ms; mean of average values and standard deviation (SD) obtained in the three conditions together), UNL (163 ± 6 ms), SL (56 ± 1 cm), $x'M_{FC}$ (0.80 ± 0.01 m/s) and BI (65 ± 6%).

DISCUSSION

When gait is initiated at spontaneous velocity as in the present study, PD patients are known to develop APAs of lower amplitude than healthy age-matched participants, i.e., their APAs are hypometric (Halliday et al., 1998; Palmisano et al., 2020). The present study thus tested the potential of bilateral application of FES on TA to improve GI in PD patients. The finding that, in the 40 Hz FES condition, PD patients spontaneously initiated gait with a larger APAs amplitude (in terms of peak backward COP shift and forward COM velocity/displacement at foot-off) than in the control condition without modifying their APAs duration, suggests that this symptom was attenuated by the treatment. As APAs amplitude is related to TA activation (Lepers and Brenič̆re, 1995), this positive effect of FES can be ascribed to a putative increased in TA activation provided by the FES (not recorded). Furthermore, the duration of step execution was significantly shorter in the 40 Hz condition than in the control condition, while step length remained unchanged. In accordance with the literature (Lepers and Brenič̆re, 1995), this quicker step execution can likely be ascribed, at least partly, to the increased APAs amplitude.

These results are in agreement with two previous clinical studies focusing on the effects of ankle dorsi-flexors assistance provided by 40 Hz FES application to lower legs on gait in PD patients (Mann et al., 2008; Popa and Taylor, 2015). For example, in the feasibility study of Mann et al. (2008), seven PD patients who exhibited freezing in gait used an FES device for a period of 8 weeks. This study showed that the FES treatment improved some gait parameters over the tested period of use with a carryover effect that is maintained without stimulation during that time and an immediate reduction in the frequency of falls. An immediate effect of FES was demonstrated over a 3-min walk but not over a 20-m walk. Furthermore, these authors showed that these improvements in gait persisted on reassessment 4 weeks after FES withdrawal, although the frequency of falls returned to pretreatment levels. Similar beneficial effects of FES application on gait were also reported in the pilot study of Popa and Taylor (2015) involving 11 PD patients. These authors showed that the mean walking speed, step length, and cadence of gait increased following a 2 weeks lower legs FES application. These

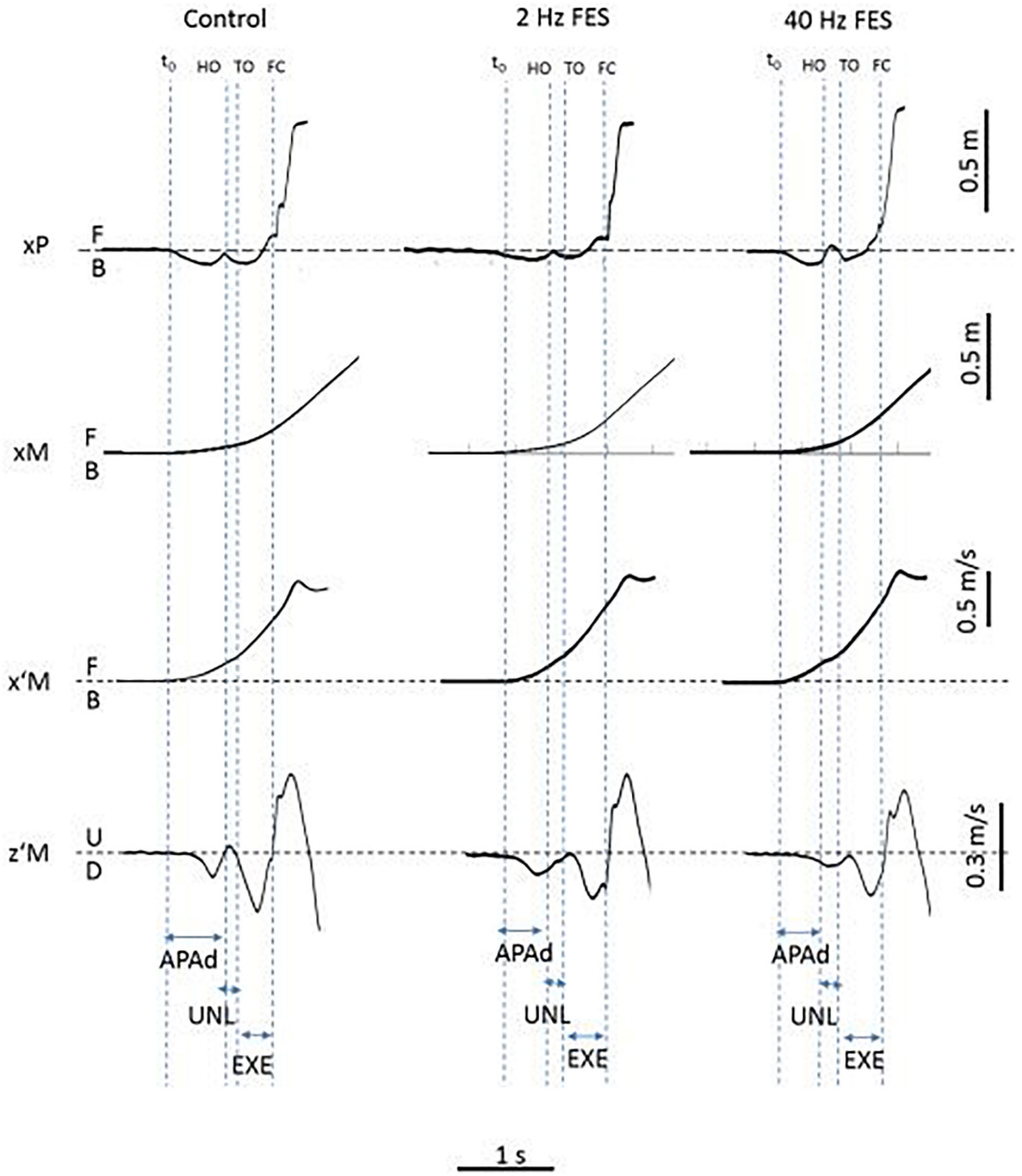

FIGURE 1 | Typical biomechanical traces of gait initiation obtained in the three experimental conditions (Control, 2 and 40 Hz FES) and showing each dependent variable (one trial in one representative PD patient). *Biomechanical traces*. xP, xM, x'M, z'M: cenete of pressure (COP) displacement, center of mass (COM) displacement and COM velocity along the anteroposterior (x) and vertical (z) axis, respectively. B, F, U, D: backward, forward, upward and downward direction, respectively. t0, HO, TO, FC: onset of biomechanical traces, swing heel-off, toe-off and foot-contact, respectively. *Experimental variables*. APAd, UNL, EXE: time-windows for APAs, unloading and execution phases of gait initiation.

authors further showed that FES treatment applied to the upper limb was also efficient to improve manual speed and dexterity. Interestingly, these motor improvements were associated with improvements in health related quality of life. These preliminary results thus suggest that FES application might be useful to attenuate both hypokinesia and bradykinesia in PD patients. However, it is clear that further studies involving a larger number of participants are required to confirm (or not) these beneficial effects of FES on the motor behavior of PD patients.

In the present study, it is noteworthy that, for the GI velocity spontaneously adopted by the PD patients, balance control was not altered by the FES since the active COM braking remained unchanged across conditions. COM braking is due to the activation of the stance leg triceps surae (TS) during the GI execution phase (Honeine et al., 2013). It therefore seems that the changes in TA activation with the 40 Hz FES application did not alter the TS antagonistic activity with a reciprocal inhibition effect from TA to TS. This finding was important to stress since

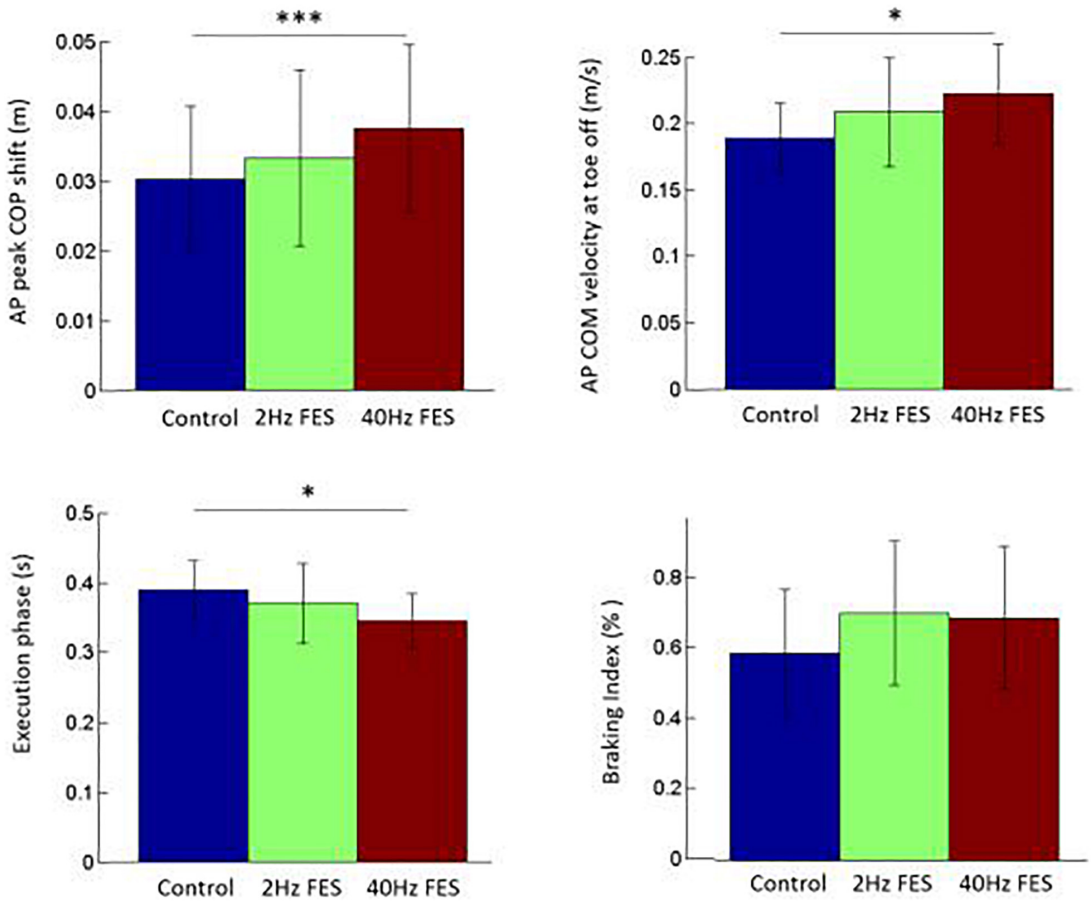

FIGURE 2 | Comparison of selected gait initiation parameters between the three conditions. Reported are mean values (all participants together) ± 1 SD. AP: anteroposterior direction. COM, COP: center of mass, center of pressure, respectively. *, *** indicates a significant difference between bars with $p < 0.05$ and $p < 0.001$ as revealed with the *post hoc* analysis.

the COM braking during GI is a main issue in PD patients (Chastan et al., 2009) and should not be further degraded by the treatment. Note that it was not possible to properly analyze EMG of lower leg muscles due to artifacts associated with FES application.

When compared to previous works in the literature on healthy elderly initiating gait at a spontaneous velocity (Halliday et al., 1998; Chastan et al., 2009; Palmisano et al., 2020), it seems that the GI parameters obtained by PD patients in the control condition were not dramatically altered. Note, however, that the peak backward COP shift (2.96 ± 1.02 cm) and the forward COM velocity at foot-off (0.18 ± 0.02 m/s) were both lower than values reported in healthy elderly (e.g., 3.54 ± 1.40 cm and 0.50 ± 0.13 m/s, respectively, in Halliday et al. (1998)). Following the 40 Hz FES application, the peak backward COP shift reached (3.67 ± 1.2 cm), a value which might be considered as within a normal range. The forward COM velocity at foot-off also increased (0.21 ± 0.03 m/s) but still remained below a normal range. In other words, it seems that acute application of 40 Hz FES failed to induce a complete recovery of APAs in PD patients, a finding that contrasts with the effects of L-dopa intake on the same APAs parameters as in the present study (Palmisano et al., 2020).

The present study adds to the growing efforts made by researchers to improve APA associated with GI in PD patients by the means of non-pharmacological/non-invasive devices such as powered ankle orthosis (Petrucci et al., 2019), self-triggered stimulus lowering stance side support surface, vibrations applied beneath the stance-side support surface (Creath et al., 2013), whole-body vibration (Fischer et al., 2019), lateral pull applied to the pelvis by motor-driven robotic system (Mille et al., 2007) or rhythmic auditory stimulus (Ghai et al., 2018). Study from our laboratory (not published) further suggests that acute ankle stretching may also be efficient to reduce ankle stiffness and improve APA in this population (see Vialleron et al., 2020 for a review on the effect of stretching on gait). Because gait and balance problems often respond poorly to treatment with anti-parkinsonian medications, and to other interventions such as deep brain stimulation (Bonnet et al., 1987; Krack et al., 2003), it is admitted that physical therapy interventions are an important clinical treatment for individuals with PD. These non-pharmacological methods might potentially be integrated

in physical training protocols and/or be used by PD patients to provide assistance during locomotor tasks such as gait initiation and/or steady-state gait. We acknowledge that this preliminary study has several limitations, among which: (1) the PD patients involved in the experiment had relatively low-level of motor impairment. It is not known whether acute TA FES application may also be beneficial to PD patients with more severe symptoms; (2) the sample size was relatively small (n = 14 participants). It follows that the results may not be generalizable to all PD participants; (3) only acute TA FES effects were considered. To what extent PD patients might beneficiate from long-term TA FES application is unknown; (4) the carry-over effects were not evaluated.

Despite these limitations, the results of the present preliminary study along with studies of the literature (Mann et al., 2008; Popa and Taylor, 2015; see also Sujith, 2008 for a review on FES on neurological disorders) are encouraging. Future studies should address these limitations before considering that TA FES application might be a valuable tool to improve GI in PD patients and be relevant to optimize the effects of L-DOPA medication on locomotor function.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Comité de Protection des Personnes Ile-de-France XI under identification number 19028-60429. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

AD and EY wrote the manuscript. PF performed the statistical analysis. EY, DD, AZ, and GS reviewed the manuscript. All authors contributed to the article and approved the submitted version.

REFERENCES

Armand, S., Landis, T., Sztajzel, R., and Burkhard, P. R. (2009). Dyskinesia-induced postural instability in Parkinson's disease. *Parkinsonism Relat. Disord.* 15, 359–364. doi: 10.1016/j.parkreldis.2008.08.007

Bonnet, A. M., Loria, Y., Saint-Hilaire, M. H., Lhermitte, F., and Agid, Y. (1987). Does long-term aggravation of Parkinson's disease result from nondopaminergic lesions? *Neurology* 37, 1539–1542. doi: 10.1212/wnl.37.9.1539

Chastan, N., Do, M. C., Bonneville, F., Torny, F., Bloch, F., Westby, G. W. M., et al. (2009). Gait and balance disorders in Parkinson's disease: impaired active braking of the fall of centre of gravity. *Mov. Disord.* 24, 188–195. doi: 10.1002/mds.22269

Creath, R. A., Prettyman, M., Shulman, L., Hilliard, M., Martinez, K., MacKinnon, C. D., et al. (2013). Self-triggered assistive stimulus training improves step initiation in persons with Parkinson's disease. *J. Neuroeng. Rehabil.* 10:11. doi: 10.1186/1743-0003-10-11

Curtze, C., Nutt, J. G., Carlson-Kuhta, P., Mancini, M., and Horak, F. B. (2015). Levodopa is a double-edged sword for balance and gait in people with Parkinson's disease. *Mov. Disord.* 30, 1361–1370. doi: 10.1002/mds.26269

Delval, A., Tard, C., and Defebvre, L. (2014). Why we should study gait initiation in Parkinson's disease. *Neurophysiol. Clin.* 44, 69–76. doi: 10.1016/j.neucli.2013.10.127

Djurić-Jovičić, M., Radovanović, S., Petrović, I., Azevedo, C., Mann, G., and Popović, M. B. (2013). The impact of functional electrical stimulation (FES) on freezing of gait (FOG) in patients with Parkinson's disease. *Clin. Neurophys.* 124:e11. doi: 10.1016/j.clinph.2012.12.019

Fischer, M., Vialleron, T., Laffaye, G., Fourcade, P., Hussein, T., Chčze, L., et al. (2019). Long-term effects of whole-body vibration on human gait: a systematic review and meta-analysis. *Front. Neurol.* 10:627. doi: 10.3389/fneur.2019.00627

Ghai, S., Ghai, I., Schmitz, G., and Effenberg, A. O. (2018). Effect of rhythmic auditory cueing on parkinsonian gait: a systematic review and meta-analysis. *Sci. Rep.* 8:506. doi: 10.1038/s41598-017-16232-5

Halliday, S. E., Winter, D. A., Frank, J. S., Patla, A. E., and Prince, F. (1998). The initiation of gait in young, elderly, and Parkinson's disease subjects. *Gait Posture* 8, 8–14. doi: 10.1016/s0966-6362(98)00020-4

Honeine, J. L., Schieppati, M., Gagey, O., and Do, M. C. (2013). The functional role of triceps-surae in human locomotion. *PLoS One* 8:e52943. doi: 10.1371/journal.pone.0052943

Krack, P., Batir, A., Van Blercom, N., Chabardes, S., Fraix, V., Ardouin, C., et al. (2003). Five-year follow-up of bilateral stimulation of the subthalamic nucleus in advanced Parkinson's disease. *N. Engl. J. Med.* 349, 1925–1934. doi: 10.1056/NEJMoa035275

Lepers, R., and Brenič re, Y. (1995). The role of anticipatory postural adjustments and gravity in gait initiation. *Exp. Brain Res.* 107, 118–124. doi: 10.1007/BF00228023

Mancini, M., and Horak, F. B. (2010). The relevance of clinical balance assessment tools to differentiate balance deficits. *Eur. J. Phys. Rehabil. Med.* 46, 239–248.

Mann, G. E., Finn, S. M., and Taylor, P. N. (2008). A pilot study to investigate the feasibility of electrical stimulation to assist gait in Parkinson's disease. *Neuromodulation* 11, 143–149. doi: 10.1111/j.1525-1403.2008.00157.x

Mille, M.-L., Johnson Hilliard, M., Martine, K. M., Simuni, T., and Rogers, M. W. (2007). Acute effects of a lateral postural assist on voluntary step initiation in patients with Parkinson's disease. *Mov. Disord.* 22, 20–27. doi: 10.1002/mds.21139

Palmisano, C., Brandt, G., Vissani, M., Pozzi, N. G., Canessa, A., Brumberg, J., et al. (2020). Gait initiation in Parkinson's disease: impact of dopamine depletion and initial stance condition. *Front. Bioeng. Biotechnol.* 8:137. doi: 10.3389/fbioe.2020.00137

Petrucci, M. N., MacKinnon, C. D., and Hsiao-Wecksler, E. T. (2019). Modulation of anticipatory postural adjustments using a powered ankle orthosis in people with Parkinson's disease and freezing of gait. *Gait Posture* 72, 188–194. doi: 10.1016/j.gaitpost.2019.05.002

Popa, L., and Taylor, P. (2015). Functional electrical stimulation may reduce bradykinesia in Parkinson's disease: a feasibility study. *J. Rehabil. Assist. Technol. Eng.* 2:2055668315607836. doi: 10.1177/2055668315607836

Rocchi, L., Chiari, L., and Horak, F. B. (2002). Effects of deep brain stimulation and levodopa on postural sway in Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry* 73, 267–274. doi: 10.1136/jnnp.73.3.267

Sijobert, B., Azevedo-Coste, C., Andreu, D., Verna, C., and Geny, C. (2016). Effects of sensitive electrical stimulation based cueing in Parkinson's disease: a preliminary study. *Eur. J. Transl. Myol.* 26:6018. doi: 10.4081/ejtm.2016.6018

Sinclair, J., Taylor, P. J., and Hobbs, S. J. (2013). Digital filtering of three-dimensional lower extremity kinematics: an assessment. *J. Hum. Kinet.* 39, 25–36. doi: 10.2478/hukin-2013-0065

Stolze, H., Klebe, S., Zechlin, C., Baecker, C., Friege, L., and Deuschl, G. (2004). Falls in frequent neurological diseases–prevalence, risk factors and aetiology. *J. Neurol.* 251, 79–84. doi: 10.1007/s00415-004-0276-8

Sujith, O. K. (2008). Functional electrical stimulation in neurological disorders. *Eur. J. Neurol.* 15, 437–444. doi: 10.1111/j.1468-1331.2008.02127.x

Vialleron, T., Delafontaine, A., Ditcharles, S., Fourcade, P., and Yiou, E. (2020). Effects of stretching exercises on human gait: a systematic review and meta-analysis. *F1000Res.* 9:984. doi: 10.12688/f1000research.25570.2

Winter, D. A. (1990). *Biomechanics and Motor Control of Human Movement*, 2nd Edn. New York, NY: Wiley.

Yiou, E., Artico, R., Teyssedre, C., Labaune, O., and Fourcade, P. (2016). Anticipatory postural control of stability during gait initiation over obstacles of different height and distance made under reaction-time and self-initiated instructions. *Front. Hum. Neurosci.* 10:449. doi: 10.3389/fnhum.2016.00449

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Human Neuroscience

METHODS
published: 22 July 2021
doi: 10.3389/fnhum.2021.690433

Motor Responses of Lumbar Erector Spinae Induced by Electrical Vestibular Stimulation in Seated Participants

*Amélie Desgagnés[1], Mikaël Desmons[1], Jean-Philippe Cyr[1], Martin Simoneau[1,2] and Hugo Massé-Alarie[1,3]**

[1] Centre Interdisciplinaire de Recherche en Réadaptation et en Intégration Sociale (CIRRIS), Laval University, Quebec City, QC, Canada, [2] Kinesiology Department, Laval University, Quebec City, QC, Canada, [3] Rehabilitation Department, Laval University, Quebec City, QC, Canada

Introduction: The study of motor responses induced by electrical vestibular stimulation (EVS) may help clarify the role of the vestibular system in postural control. Although back muscles have an important role in postural control, their EVS-induced motor responses were rarely studied. Moreover, the effects of EVS parameters, head position, and vision on EVS-induced back muscles responses remain little explored.

Objectives: To explore the effects of EVS parameters, head position, and vision on lumbar erector spinae muscles EVS-induced responses.

Design: Exploratory, cross-sectional study.

Materials and Methods: Ten healthy participants were recruited. Three head positions (right, left and no head rotation), 4 intensities (2, 3, 4, 5 mA), and 4 EVS durations (5, 20, 100, 200 ms) were tested in sitting position with eyes open or closed. EVS usually induced a body sway toward the anode (placed on the right mastoid). EMG activity of the right lumbar erector spinae was recorded. Variables of interest were amplitude, occurrence, and latency of the EVS-induced modulation of the EMG activity.

Results: The short-latency response was inhibitory and the medium-latency response was excitatory. Increased EVS current intensity augmented the occurrence and the amplitude of the short- and medium-latency responses (more inhibition and more excitation, respectively). EVS duration influenced the medium-latency response differently depending on the position of the head. Right head rotation produced larger responses amplitude and occurrence than left head rotation. Opposite head rotation (left vs. right) did not induce a reversal of the short- and medium-latency responses (i.e., the inhibition did not become an excitation), as typically reported in lower legs muscles. The eyes open condition did not modulate muscle responses.

Conclusion: Modulation of EVS parameters (current intensity and duration of EVS) affects the amplitude and occurrence of the lumbar erector spinae responses. In

OPEN ACCESS

Edited by:
Eric Yiou,
Université Paris-Saclay, France

Reviewed by:
Marco Schieppati,
Istituti Clinici Scientifici Maugeri (ICS Maugeri), Italy
Roberto Esposti,
University of Milan, Italy

****Correspondence:***
Hugo Massé-Alarie
hugo.masse-alarie@fmed.ulaval.ca

Specialty section:
This article was submitted to Motor Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *02 April 2021*
Accepted: *22 June 2021*
Published: *22 July 2021*

Citation:
Desgagnés A, Desmons M, Cyr J-P, Simoneau M and Massé-Alarie H (2021) Motor Responses of Lumbar Erector Spinae Induced by Electrical Vestibular Stimulation in Seated Participants. Front. Hum. Neurosci. 15:690433. doi: 10.3389/fnhum.2021.690433

contrast, vision did not influence the responses, suggesting its minimal contribution to vestibulomotor control in sitting. The lack of response reversal in sagittal plane may reflect the biomechanical role of lumbar erector spinae to fine-tune the lumbar lordosis during the induced body sway. This hypothesis remains to be further tested.

Keywords: electrical vestibular stimulation, back muscles, erector spinae, vision, postural control

INTRODUCTION

The vestibular system contributes to balance control and posture (Gandevia et al., 2012; Forbes et al., 2014; Kingma and van de Berg, 2016). The central integration of sensory inputs, such as vestibular, proprioceptive and visual, ensures adequate motor control to estimate self-motion and maintain a stable posture (Cullen, 2011; Gandevia et al., 2012). Electrical vestibular stimulation (EVS) (previously known as galvanic vestibular stimulation) (Dlugaiczyk et al., 2019; Sluydts et al., 2020) is a technique used to study the role of the vestibular system in postural control (Dlugaiczyk et al., 2019; Ertl and Boegle, 2019). The application of transcutaneous current changes the polarization of the eighth cranial nerve, resulting in the modulation of the activity of the vestibular afferents without the need to move the head (Fitzpatrick and Day, 2004; Ertl and Boegle, 2019). EVS modulates the continuous firing rate of vestibular afferent fibers and probably recruits vestibular hair cells (Gensberger et al., 2016): the firing rate increases on the cathodal side (depolarization) and decreases on the anodal side (hyperpolarization) (Fitzpatrick and Day, 2004). When applied in a standing position, EVS creates an illusion of movement toward the cathode and a postural sway toward the anode (Lund and Broberg, 1983; Fitzpatrick and Day, 2004) along the interaural line (Fitzpatrick and Day, 2004). The postural response may result from a counteraction from the balance system to maintain balance; it would be opposite to the EVS-perceived body sway (Fitzpatrick et al., 1994; Fitzpatrick and Day, 2004). Thus, EVS allows studying the postural response and its related electromyographic (EMG) activity (Fitzpatrick and Day, 2004). EVS induces motor responses when muscles are engaged in balance control (e.g., the *soleus* in standing) (Britton et al., 1993; Ali et al., 2003; Dakin et al., 2016). The typical EVS-induced motor responses have two components: a short- followed by a reversed medium-latency response (i.e., inhibitory and excitatory) (Britton et al., 1993). The direction of the EVS-induced response (e.g., inhibition or excitation) depends on the position of the anode and head orientation in relation to the body. For example, EVS applied while standing with the head rotated to the right and the anode positioned on the right mastoid process produces a backward body sway. In both *soleus* muscles, the resulting response corresponds to a short-latency inhibition followed by a medium-latency excitation in EMG activity (Britton et al., 1993). In contrast, rotating the head to the left while keeping the anode on the right mastoid process produces a forward body sway and reverses the direction of the responses (i.e., the short-latency becomes excitatory, and the medium-latency, inhibitory). Finally, when EVS is used while participants look forward, a body sway occurs toward the anode (i.e., in the frontal plane). Thus, EVS induces a sway in a particular direction (e.g. backward, forward, right, or left) depending on the head position.

Although back muscles are crucial in the control of balance and posture (Massion, 1992), few studies tested the effect of EVS on back muscles activation. There is emerging evidence that differences exist between limb and trunk vestibular control, which implies that the optimal stimulation parameters may differ when studying trunk muscles compared to lower limb muscles. First, a recent study highlighted that the EVS-induced responses in thoracic and lumbar *erector spinae* (LES) muscles were less flexible than those of *soleus* muscle (Guillaud et al., 2020). Although tasks reducing the contribution of the *soleus* in balance control (e.g., standing with head contact on a vertical panel compared to without) also attenuated the *soleus* responses amplitude, such modulation did not occur for LES motor responses. Also, Guillaud et al. (2020) did not observe the reversal of these responses in back muscles (i.e., short-latency, inhibitory vs. medium-latency, excitatory) when comparing EVS-induced body sway in anterior and posterior directions, although another study reported reversal in the frontal plane for at least one participant (Ali et al., 2003). Second, the phase frequency estimates of LES motor responses was smaller than in lower limb and neck muscles responses during a stochastic vestibular stimulation (i.e., an unpredictable current used to study the vestibular system) (Dakin et al., 2007; Forbes et al., 2013). The authors suggested that this could represent a limited functional contribution of the LES muscles compared to lower limb and neck muscles for controlling balance in standing (Forbes et al., 2014). Third, it was suggested that the amplitude of EVS-induced motor responses in back muscles was considerably smaller than in limb muscles (Ali et al., 2003). These results highlight the importance of studying the influence of parameters on EVS-induced responses especially in back muscles in relevant postural conditions (i.e., when back muscles are more likely to be involved).

Although three studies tested the LES motor responses during EVS (Ardic et al., 2000; Ali et al., 2003; Guillaud et al., 2020), there is still an important knowledge gap about the influence of EVS parameters on these motor responses. Only one study has tested the effect of EVS intensities (up to 4 mA). The authors reported that using EVS intensity of more than 2–2.5 mA induced short-latency response of greater amplitude than smaller intensity although it was not clarified if this was for the *soleus* or LES muscles, and no descriptive statistics were reported (Ali et al., 2003). Other EVS studies of LES muscles

Abbreviations: EMG, Electromyography; EVS, Electrical vestibular stimulation; LES, Lumbar *erector spinae* muscles; MVC, Maximal voluntary contraction; rms, Root mean square.

used only one stimulation intensity [0.6 mA (Ardic et al., 2000) or 3.5 mA (Guillaud et al., 2020)]. EVS intensity between 1 mA (Britton et al., 1993) or 6 mA (Fitzpatrick et al., 1994) were used in studies of neck and limbs muscles although the rationale was not justified. Also, although very-short duration of EVS (e.g., 2 ms) evoked short-latency response in sternocleidomastoid (Watson and Colebatch, 1998) and masseter (Deriu et al., 2003) muscles, most EVS studies of back muscles used relatively longer EVS duration [e.g., 175 ms (Guillaud et al., 2020), 400 ms (Ali et al., 2003)]. The use of a long duration stimulus complicates the interpretation of the measured latency since it is not possible to determine when nerve depolarization occurs. Thus, it is unclear what are the optimal parameters to evoke motor responses in LES muscles.

The balance task tested may modulate the EVS-induced response. For example, a less demanding task in terms of postural control for ankle muscles attenuates the response amplitude (Fitzpatrick et al., 1994; Guillaud et al., 2020). Besides, when balance control involves the upper limb (e.g., holding a handle), responses appear in the *triceps brachii* muscles (Britton et al., 1993). These examples suggest high task-dependent flexibility of the vestibular system to maintain balance. Testing EVS-induced responses in trunk muscles in a sitting position appears relevant considering their important contribution to balancing the upper body and the possibility to by-pass the contribution of lower leg muscles to maintain a stable posture in this position. Although one study reported responses in LES muscles in a sitting position and reported a smaller response than in standing, many methodological factors such as the lack of EMG activity control during postural tasks makes this result difficult to interpret (Ali et al., 2003). In addition, using a sitting position may enable to combine EVS with other neurophysiological techniques such as transcranial magnetic stimulation, in which participants are seated when testing back muscles (O'Connell et al., 2007; Tsao et al., 2011a,b; Massé-Alarie et al., 2013, 2016a,b; Masse-Alarie et al., 2018). Combining these techniques may help to better understand the central processing of the vestibular responses.

Visual cues contribute to upright and seated postural control (Day and Cole, 2002; Blouin et al., 2007). For example, occluded vision increases body sway and related EVS-induced responses (Fitzpatrick et al., 1994; Mackenzie and Reynolds, 2018). However, it is still unknown if the absence/presence of vision similarly influence LES motor responses in sitting. The availability of more tactile inputs from the thighs in sitting compared to standing could differently impact motor responses induced by EVS.

Overall, it remains unclear how the modification of EVS parameters (e.g., EVS current intensity and EVS duration), head rotation or vision influence the short- and medium-latency LES motor responses. This study aimed to explore the effect of EVS parameters and conditions on LES motor responses in sitting. The main objective was to determine the effect of head position, current intensity and duration of EVS current on the amplitude, latency and occurrence of the short- and medium-latency LES motor responses. A secondary objective was to determine the effect of vision on the amplitude, latency and occurrence of the short- and medium-latency LES motor responses. Considering that a condition (i.e., a combination of parameters) usually producing a backward sway was associated with larger activation of LES muscles, we hypothesized that the head position (usually producing a backward sway) would produce larger amplitude and more frequent occurrence of LES motor responses as well as a higher EVS current intensity, a longer EVS duration and an absence of vision.

MATERIALS AND METHODS

Participants

The study involved a convenience sample of ten healthy participants recruited from the *Centre Interdisciplinaire de Recherche en Réadaptation et en Intégration Sociale* (CIRRIS) in Quebec City from July 9th, 2019 to August 28th, 2019. To be eligible for the study, participants needed to be between 18 and 60 years old. Exclusion criteria were: (i) pathology of the vestibular system (e.g., Menière's disease, benign paroxysmal positional vertigo), (ii) pregnancy, (iii) allergy to tetracaine (the protocol involved the use of tetracaine-based analgesic cream), (iv) back pain, (v) idiopathic scoliosis, and (vi) any major pathologies interfering with the task tested in this study (e.g., neuropathy). We chose to exclude participants with scoliosis because of the imbalance in response to EVS between the right and left vestibular systems observed in these participants (Pialasse et al., 2015, 2016; Hatzilazaridis et al., 2019). The study was approved by the Ethics Research Committee of the *Centre Intégré Universitaire de Santé et de Services Sociaux de la Capitale-Nationale* (Project: #2019-1778), in accordance with the Declaration of Helsinki. All participants provided their written informed consent prior to the experiment.

Experimental Design

To test the effect of head position, EVS current intensity and EVS duration on the LES motor responses (main objective), participants sat on a chair without backrest with their arms along the body, feet touching the floor, and eyes closed. Participants had to maintain 15 $\pm$ 5% of the maximal voluntary contraction (MVC) of the right LES muscles by performing a slight active anterior pelvic tilt. Since participants had their eyes closed in most conditions, online auditory feedback helped maintaining a steady contraction using the pre-amplified EMG signal translated into an audio signal played through speakers. Online visual feedback [i.e., root mean square (rms) EMG] also helped the investigators to ensure muscle contractions accuracy. The investigators provided verbal feedback when necessary (i.e., instructions to increase or reduce the contraction). A period of training allowed participants to familiarize themselves with the procedure. Muscle activation was used to (i) standardize the pre-stimulus background EMG between participants and (ii) increase motoneuron excitability during EVS (Di Lazzaro et al., 1998). EVS studies consistently reported responses in muscles actively engaged in maintaining postural control [e.g., no responses in *tibialis anterior* muscle at rest (Fitzpatrick

et al., 1994) or in *soleus* muscle in sitting participants (Ali et al., 2003)].

Participants came to the laboratory for one session of ∼3 h. For the main objective, 48 conditions were tested for this part of the study. Each condition combined parameters of EVS current intensity (2, 3, 4, and 5 mA), EVS duration (5, 20, 100, and 200 ms), and head rotation (maximal comfortable right and left rotations, and no rotation). **Figure 1** presents the relationship between head rotation, electrodes positioning and usual induced body sway. For each condition, participants had their eyes closed and received a sequence of 15 stimulations, for a total of 720 stimulations. Fifteen stimulations per condition was chosen after the realization of pilot experiments to have an optimal balance between good signal-to-noise ratio and the duration of the session. EVS was randomly triggered between 5 and 8 s with respect to the last stimulation. The order of the conditions was randomized using two steps: (i) in function of the rotation of the head then (ii) in function of current intensity. The order of the EVS duration was not randomized and was always tested from the shortest to the longest EVS duration (5–200 ms). The condition with eyes open was tested after the same condition with eyes closed. Chin-acromion distance was measured to standardize the head rotation amplitude within-participant. In this way, the ranges of motion of right and left rotations were equal for a same participant. Participants maintained the same position throughout the experiment and avoided touching their legs or trunk since a light touch reduces the amplitude of LES motor responses (Maaswinkel et al., 2014). Rest periods were given as needed.

To test our secondary objective on the effect of vision on LES responses (secondary objective), participants completed two additional conditions with eyes open: (i) right head rotation and (ii) left head rotation (EVS current intensity: 4 mA, EVS duration: 200 ms). Due to time constraint and feasibility, we did not repeat all conditions with eyes open and selected parameters based on published EVS studies and on our results from pilot experiments. The position was the same as described previously.

Overall, participants received a total of 750 stimulations in 50 different conditions. The only adverse effect reported was a slight fatiguability of back muscles at the end of the session for some participants.

EMG and Maximal Voluntary Contraction

A pair of Ag/AgCl surface electrodes (Kendall Medi-trace 200, Covidien, Dublin, Ireland) was placed 2 cm lateral to the L3-L4 joint line onto the right LES belly following SENIAM recommendations (Hermens et al., 2000). A ground electrode was positioned on the right anterior superior iliac spine and iliac crest. EMG of leg muscles was not recorded considering that no response was observed in sitting (Ali et al., 2003; Fitzpatrick et al., 1994; Day et al., 1997). In sitting position, participants performed a MVC during 3 s. in anterior pelvic tilt and in resisted trunk extension at the thoracolumbar spine junction. MVC of the task producing most EMG activity in the right LES muscle was tested again twice to measure three MVCs using the same technique. This method was used since (i) some individuals are not able to produce MVC in anterior pelvic tilt or in resisted trunk extension (e.g., flexion of the lumbar spine during resisted trunk extension or inability to perform the anterior pelvic tilt) and (ii) it reduced the likelihood to underestimate the MVC. A smaller MVC will result in a smaller absolute value for the 15% MVC during the task and will potentially result in smaller responses to EVS. The evaluator provided instructions and demonstrations on how to perform these contractions. To ensure maximal contraction, the evaluator motivated each participant. Thirty seconds resting periods separated MVC trials. The largest peak of rms EMG was considered as MVC, regardless of the technique (i. e., pelvic tilt vs. resisted lumbar extension). EMG was bandpass filtered (10–500 Hz, bandwidth filter), amplified 1,000 times (NEO-210A Analog Output Module, NTI) and sampled at 1,000 Hz using Power 1401 Data Acquisition System and Spike2 software (Cambridge Electronic Design, Cambridge, United Kingdom).

Electrical Vestibular Stimulation

Application of tetracaine hydrochloride gel, i.e., anesthetic cream (AMETOP GEL 4%, Smith and Nephew Medical Ltd., Hull, United Kingdom) on both mastoid processes 30 min before installing the electrodes reduced nociceptive and tactile

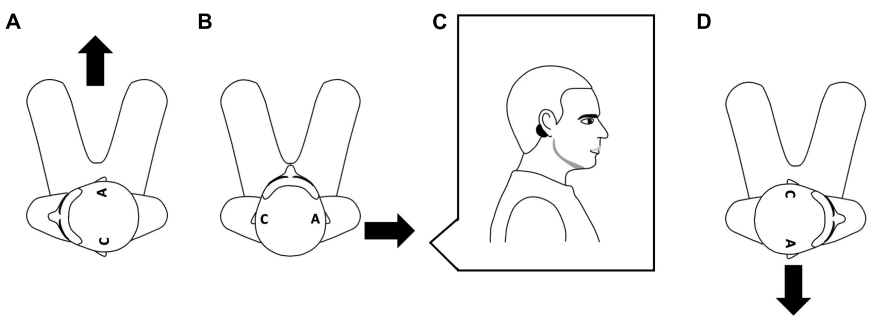

FIGURE 1 | Relationship between head rotation, electrodes position and usual direction of the induced body sway. The figure presents an aerial view of the seated participant. The letter "C" indicates the position of the cathode and the letter "A" indicates the position of the anode, and the black arrows indicate the direction of the induced body sway. Left head rotation with the anode on the right mastoid induces a forward sway **(A)**, no head rotation with the anode on the right mastoid usually induces a right body sway **(B)** and right head rotation with the anode of the right mastoid induces a backward sway **(D)**. **(C)** Depicts a side view of the participant to show the position of an electrode (black circle) on the mastoid process.

sensations produced by EVS (Ertl and Boegle, 2019). The duration of the 750 stimulations, regardless of the preparation period, the time to adjust the parameters and the pauses took approximately 80–90 min. A bipolar constant current stimulator (Digitimer DS5, United Kingdom) produced a binaural EVS (using square-wave pulse current, i.e., the intensity is the same throughout the stimulation duration) through round electrodes (3.2 cm diameter PALS, Axelgaard Manufacturing Co., Fallbrook, United States) placed on the right (anode) and left (cathode) mastoid processes. Participants wore a headband for optimal contact between the electrodes and skin. Square wave pulses were generated with the Spike2 software using the Graphical Editor Tool, that enables modifying current intensity, duration, and waveform, and to trigger externally the electrical stimulation (i.e., the DS5).

Data Extraction and Analysis

For each short- and medium-latency response, three variables were calculated: latency, rms EMG amplitude and occurrence in the software Spike2. For each condition, the average rectified EMG was analyzed. The averaged EMG comprised the signal of the 15 stimulations gated to stimulus events. Via a microcontroller (model Leonardo, Arduino) the output of the constant current stimulator produced a TTL pulse serving as an input to the data acquisition board. The event served as a reference (time zero) for the response latency. Studied time windows ranged from −200 to 300 ms around the event onset. A two-step process was used to quantify the amplitude of the motor responses depending on if a response was discernible or not. First, when a motor response was discernible, the onset and offset of the short- and medium-latency motor responses was determined visually. EVS, however, did not always evoke a discernible LES motor response, and in the first step of this analysis, the evaluator skipped these conditions. When all the conditions were analyzed, the average onset and offset of the discernible motor responses were used to determine time windows for both short- and medium-latency motor responses. Second, these time windows were used to measure rms amplitude in the conditions without discernible responses i.e., 45–70 and 75–100 ms for short- and medium-latency responses, respectively. This technique provided quantitative values in the absence of discernible motor responses. The amplitude of the motor response was calculated as a percentage of the MVC after subtracting the pre-stimulus rms EMG (from –110 to –10 ms). This method allowed determining the direction of the response (excitatory vs. inhibitory) relative to the participant's maximal contraction (Massé-Alarie et al., 2019). The occurrence was calculated as the percentage of participants having a discernible inhibitory/excitatory motor response (on the average rectified EMG signal of the 15 stimuli) on the total number of participants tested. The occurrence was measured for each condition. For example, a condition eliciting a discernible motor response in 8 out of 10 participants had an occurrence of 80%. The presence/absence of a motor response was determined visually. Published studies used similar visual strategies to identify motor-evoked potentials of back muscles using transcranial magnetic stimulation (Massé-Alarie et al., 2013; Masse-Alarie et al., 2016, 2018), withdrawal nociceptive reflex using electrical noxious stimulus of trunk muscles (Masse-Alarie et al., 2019) and anticipatory postural adjustment (Hodges and Bui, 1996).

Statistical Analysis

The statistical analysis was performed on SPSS (version 26 Premium, IBM corp., United States). Shapiro-Wilk's tests assessed the normality of the distribution. However, despite transformations, it was not possible to achieve a normal distribution. Thus, linear mixed models were realized on non-transformed data. Significance was set at $p < 0.05$. Results are presented as [mean (SD)].

The statistical model tested the rms EMG amplitude (% MVC) and the occurrence of the responses for both objectives. Due to many missing values for the latency (i.e., no discernible motor response), latency was described quantitatively without statistical analysis. To determine the effect of head position, EVS current intensity and EVS duration on the amplitude and occurrence of the short- and medium-latency motor responses (main objective), linear mixed models were independently computed on the short- and medium-latency variables. The model used a *scaled identity* covariance matrix with Rotation (right, left, no), EVS duration (5, 20, 100, 200 ms), and Current intensity (2, 3, 4, 5 mA) as fixed factors, and participants' intercept as the random factor (i.e., to consider the variability between participants' measurements). To determine the effect of vision on the responses of LES muscles (secondary objective), linear mixed models were independently computed on the short- and medium-latency variables. The model used a *scaled identity* covariance matrix with Rotation (right or left) and Vision (eyes open or closed) as fixed factors and participants' intercept as the random factor. Sidak's test corrected for multiple pairwise comparisons.

RESULTS

The mean age of participants (3 males, 7 females) was 24.3 (3.4) years. LES motor responses in one representative participant are presented in **Figure 2** according to current intensity, and in **Figure 3** according to EVS duration. The short- and medium-latency LES motor responses are obvious, especially at higher EVS current intensity. **Table 1** shows the amplitudes, occurrences and latencies of the short- and medium-latency motor responses. Note that the short-latency response was inhibitory and the medium-latency response was excitatory regardless of the direction of the head rotation for all participants.

Effect of Parameters on the Amplitude, Occurrence, and Latency of the Short-Latency Motor Response

The amplitude of the short-latency response showed a main effect of Current intensity [$F_{(3,\ 406.9)} = 13.13$; $p < 0.001$]. Pairwise comparisons show that EVS current intensities of 3 mA ($p = 0.041$), 4 mA ($p < 0.001$), and 5 mA ($p < 0.001$) produced a larger inhibition than 2 mA while current intensity of 5 mA

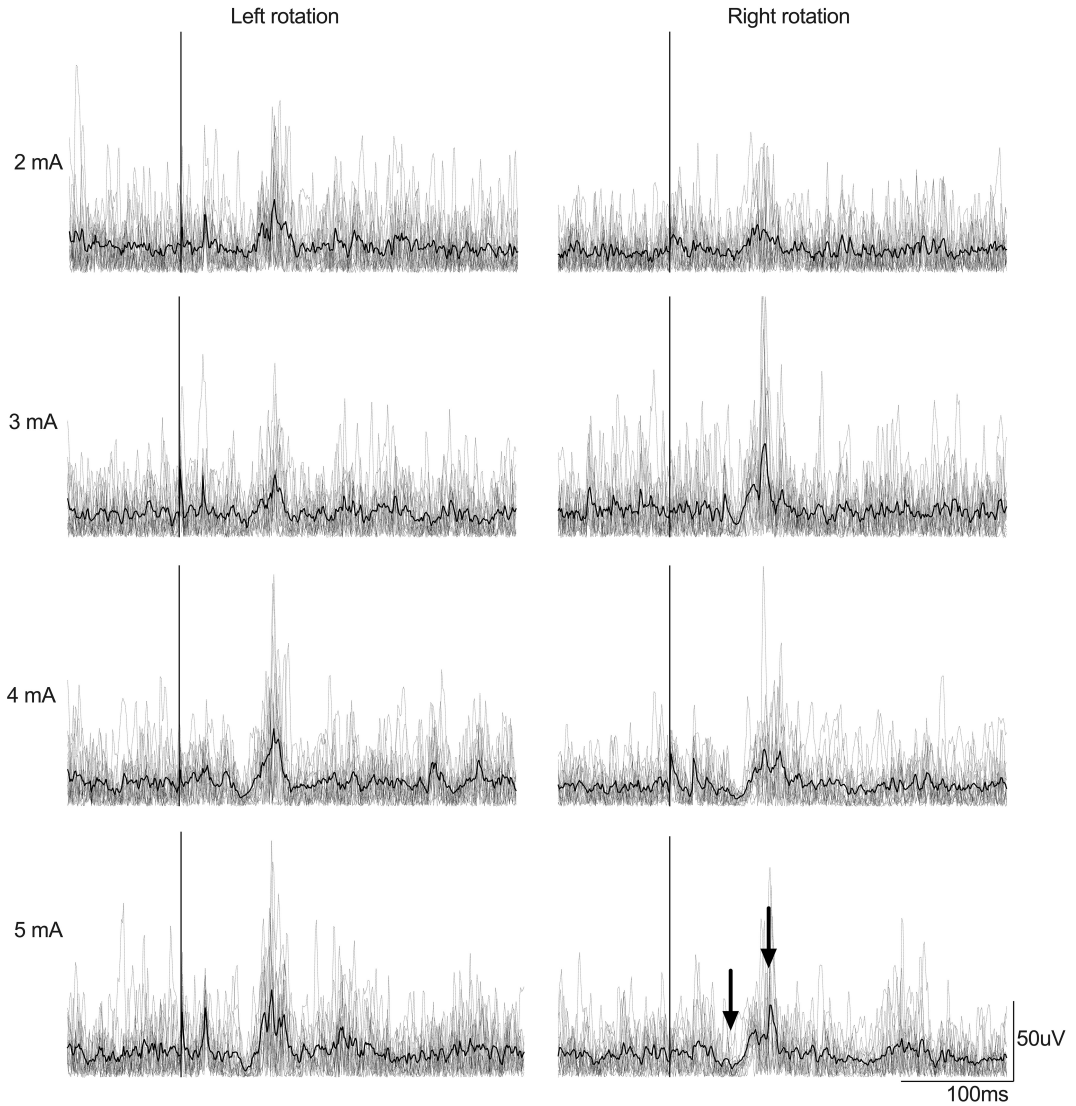

FIGURE 2 | Example of rectified EMG signals recorded from the right LES muscles from a participant according to EVS intensity (EVS duration was 20 ms). Left column depicts muscle amplitude for left head rotation and right column show muscle amplitude for right head rotation. Gray lines represent the EMG traces recorded for each 15 stimulations by condition whereas the black line represents the average EMG signal by condition. The stimulation is set at Time 0 (the vertical line). Arrows, respectively, show the short- and medium-latency responses.

inhibited more LES muscle activation than 3 mA (p = 0.004; **Figure 4A**).

The occurrence of the short-latency response showed main effects of Rotation [$F_{(2,\ 407{\cdot}9)}$ = 6.35; p = 0.002] and Current intensity [$F_{(3,\ 406{\cdot}9)}$ = 24.88; $p < 0.001$]. Pairwise comparisons were significant for the four EVS current intensities, except for the comparison between 4 and 5 mA (p = 0.841), indicating that higher EVS current intensities produced more frequently the short-latency response (**Figure 4B**). Also, pairwise comparisons showed that right head rotation induced more frequently the short-latency response compared to left (p = 0.003) and neutral (p = 0.02) head rotation (**Figure 5A**).

For all conditions combined, the mean latency of the short-latency response was 45.5 (5.3) ms. No obvious visual changes were present based on head rotation, EVS current intensity or EVS duration for the latency of the short-latency response.

Effect of Parameters on the Amplitude, Occurrence, and Latency of the Medium-Latency Motor Response

The amplitude of the medium-latency response showed a main effect of Current intensity [$F_{(3,\ 407{\cdot}0)}$ = 20.63; $p < 0.001$] and of Rotation by EVS duration interaction [$F_{(6,\ 407{\cdot}0)}$ = 2.56; p = 0.019]. Current intensities of 3 mA (p = 0.002), 4 mA ($p < 0.001$), and 5 mA ($p < 0.001$) all produced higher responses amplitude than 2 mA. Also, 5 mA produced a higher response amplitude than 3 mA ($p < 0.001$; **Figure 4C**). The

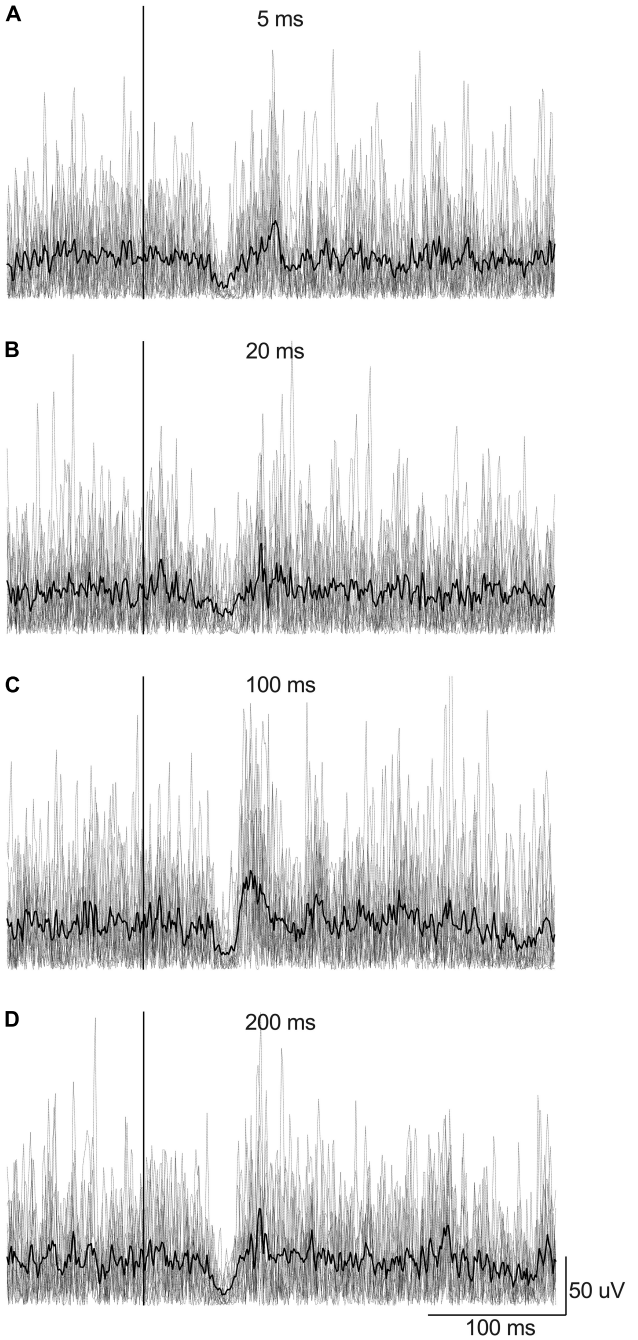

FIGURE 3 | Example of rectified EMG signals recorded from the right LES muscles from a participant according to EVS duration (EVS intensity was 4 mA with right head rotation): **(A)** 5 ms, **(B)** 20 ms, **(C)** 100 ms, and **(D)** 200 ms. Gray lines represent the EMG traces recorded for each 15 stimulations by condition whereas the black line represents the average EMG signal by condition. The stimulation is set at Time 0 (the vertical line).

Rotation x EVS duration interaction showed differences between Rotations only at 200 ms; the medium-latency response was larger in right (p = 0.001) and neutral (p < 0.001) than left head rotation (**Figure 6**). Also, the effect of EVS duration was different depending on head rotation. With the head in neutral position, 5-ms EVS produced a smaller response amplitude compared to 200 ms (p = 0.008) and 100 ms (p = 0.011). In left head rotation, 20-ms EVS produced a larger medium-latency response compared to 200 ms (p = 0.006; **Figure 6**). With the head rotated to the right, no difference was present between EVS duration.

Rotation [$F_{(2,\ 408.2)}$ = 3.953; p = 0.02] and Current intensity [$F_{(3,\ 407.0)}$ = 23.893; p < 0.001] significantly affected the occurrence of the medium-latency response. Pairwise comparisons showed that Right head rotation produced a higher occurrence of the response than Left head rotation (p = 0.016, **Figure 5B**). Except for the comparison between 4 and 5 mA (p = 0.542), larger EVS intensities produced more frequent responses (**Figure 4D**).

All conditions combined, the mean latency of the medium-latency response was 73.2 (5.1) ms. No obvious changes were present based on head rotation, EVS current intensity or EVS duration for the latency of the medium-latency response.

Effect of Vision

Vision showed no significant main effect or interaction on the amplitude [$F_{(1,\ 27)}$ = 1.10; p = 0.305] or occurrence [$F_{(1,\ 27)}$ = 1.90; p = 0.180] of the short-latency response, nor for the medium-latency response [amplitude: $F_{(1,\ 27)}$ = 0.43; p = 0.516 | occurrence: $F_{(1,\ 27)}$ = 0.45; p = 0.508].

DISCUSSION

This study explored the effect of EVS current intensity, EVS duration, head position and vision on the amplitude, occurrence and latency of the EVS-induced motor responses of right LES muscle. Based on our results, larger intensities of stimulation and right and neutral head rotations influenced the short- and medium-latency motor responses amplitude (i.e., more inhibited and more facilitated, respectively) and occurrence. Also, the EVS duration seemed to impact the medium-latency motor response depending on the head rotation. First, right and no head rotation compared to left head rotations produced larger motor response amplitude when using an EVS duration of 200 ms. Second, longer EVS duration produced larger medium-latency response amplitude only in no head rotation, whereas 20-ms EVS in left head rotation produced larger motor response amplitude than 200 ms. Visual cues did not influence the amplitude and occurrence of the short- and medium-latency motor responses.

Influence of EVS Parameters on Motor Responses

Some studies reported increased amplitude of short- and medium-latency motor responses with increased EVS current intensity (Fitzpatrick et al., 1994; Day et al., 1997). Modulation in EVS current intensity may lead to the recruitment of different afferent fibers. EVS primarily activates irregular vestibular afferent fibers transmitted by fast-conducting axons rather than regular vestibular afferent fibers transmitted by slow-conducting

TABLE 1 | Mean amplitudes, occurrences and latencies of the short- and medium LES motor responses by condition [mean (SD)].

Condition		Amplitude (% MVC)		Occurrence (%)		Latency (ms)	
mA	ms	(Short)	(Medium)	(Short)	(Medium)	(Short)	(Medium)
Right rotation (*n* = 10)							
2	5	−1.32 (1.84)	2.75 (2.73)	10	40	28.3 (n.a.)	80.1 (22.0)
	20	−1.63 (2.03)	3.28 (2.41)	30	40	46.1 (2.6)	69.0 (12.6)
	100	−1.91 (2.33)	2.17 (2.15)	30	40	57.2 (11.8)	83.7 (9.3)
	200	−1.84 (3.05)	1.87 (3.13)	30	20	49.0 (4.7)	68.9 (14.4)
3	5	−1.94 (1.94)	2.83 (3.56)	50	60	48.9 (4.9)	69.4 (7.1)
	20	−2.22 (3.34)	4.73 (4.28)	50	80	45.0 (10.8)	67.6 (7.6)
	100	−2.70 (2.69)	3.71 (3.43)	40	30	50.9 (3.5)	73.4 (5.2)
	200	−2.95 (2.34)	3.96 (3.60)	60	60	44.3 (13.7)	69.5 (5.4)
4	5	−4.28 (1.87)	3.04 (5.12)	70	60	47.6 (6.9)	75.2 (16.5)
	20	−2.13 (3.08)	4.42 (2.84)	60	70	46.4 (10.5)	67.4 (10.0)
	100	−3.31 (2.53)	3.74 (2.84)	70	60	50.7 (10.0)	77.7 (7.5)
	200	−3.56 (2.74)	4.33 (3.16)	70	70	47.9 (3.2)	70.4 (5.0)
5	5	−2.85 (2.47)	3.37 (4.53)	60	60	44.1 (5.9)	69.3 (14.5)
	20	−3.60 (2.78)	5.28 (3.91)	80	70	43.1 (7.0)	72.1 (4.3)
	100	−2.57 (4.10)	5.33 (2.79)	70	80	42.8 (10.8)	70.4 (12.5)
	200	−3.50 (2.98)	5.15 (3.09)	70	80	45.1 (4.2)	70.5 (4.7)
Left rotation (*n* = 10)							
2	5	−0.53 (1.69)	1.30 (3.29)	10	20	58.0 (n.a.)	86.3 (5.2)
	20	−0.18 (1.83)	1.87 (3.46)	0	10	n.a.	67.0 (n.a.)
	100	−3.15 (1.96)	1.50 (4.17)	60	20	39.7 (11.7)	72.3 (5.8)
	200	−0.31 (2.95)	1.82 (3.38)	10	40	48.6 (n.a.)	61.0 (12.5)
3	5	−1.09 (2.59)	2.43 (4.12)	20	40	44.7 (13.3)	70.7 (10.7)
	20	−2.80 (1.97)	3.76 (3.94)	50	50	51.2 (2.7)	73.4 (8.4)
	100	−2.53 (2.55)	2.03 (4.75)	40	30	55.0 (21.3)	68.2 (4.3)
	200	−1.62 (2.37)	1.56 (2.16)	10	30	52.9 (n.a.)	76.7 (19.7)
4	5	−3.05 (2.59)	3.31 (4.31)	50	50	42.3 (4.1)	72.3 (9.5)
	20	−2.24 (2.77)	4.41 (4.27)	50	70	45.1 (5.4)	76.0 (13.1)
	100	−2.09 (2.82)	3.27 (5.92)	40	40	41.1 (9.4)	68.9 (7.9)
	200	−1.88 (3.30)	2.86 (4.03)	40	50	40.3 (8.4)	61.3 (8.6)
5	5	−2.87 (3.03)	2.78 (4.30)	50	50	44.1 (3.4)	67.8 (4.7)
	20	−3.60 (3.09)	4.75 (4.30)	60	70	46.2 (3.0)	78.6 (13.1)
	100	−3.70 (3.18)	4.92 (2.97)	70	80	41.1 (5.8)	73.2 (10.2)
	200	−2.82 (2.65)	2.09 (4.76)	50	60	45.2 (2.8)	72.2 (6.5)
No rotation (*n* = 9)							
2	5	−0.40 (1.16)	1.42 (3.22)	0	11	n.a.	65.0 (n.a.)
	20	−1.77 (1.92)	0.99 (3.06)	11	11	55.3 (n.a.)	68.9 (n.a.)
	100	−1.46 (2.56)	2.97 (3.40)	33	44	42.9 (21.8)	74.3 (14.5)
	200	−0.64 (1.36)	2.02 (2.12)	0	22	n.a.	84.4 (13.6)
3	5	−1.93 (2.13)	1.40 (3.63)	33	22	41.3 (10.5)	67.8 (4.5)
	20	−1.93 (2.98)	3.55 (5.20)	33	44	51.1 (3.6)	73.1 (6.2)
	100	−2.01 (1.76)	3.24 (3.29)	22	44	42.5 (0.1)	79.0 (23.0)
	200	−1.33 (2.48)	4.12 (3.08)	33	67	50.6 (5.8)	86.0 (19.9)
4	5	−1.13 (3.05)	2.37 (3.21)	44	44	36.6 (12.0)	70.2 (7.5)
	20	−1.86 (2.82)	4.02 (2.81)	44	67	41.4 (5.4)	71.8 (20.1)
	100	−2.55 (3.05)	4.99 (3.32)	67	78	51.2 (7.1)	75.3 (13.5)
	200	−0.97 (4.38)	4.73 (1.95)	44	78	41.8 (5.0)	74.3 (10.1)
5	5	−1.67 (2.51)	3.68 (3.24)	44	56	44.0 (4.2)	68.5 (4.0)
	20	−3.02 (2.84)	5.58 (3.64)	78	78	43.0 (3.2)	70.2 (5.8)
	100	−3.27 (3.58)	5.14 (2.33)	44	78	40.0 (3.3)	79.7 (13.5)
	200	−2.96 (2.99)	5.67 (3.75)	44	78	46.7 (2.7)	73.9 (7.9)

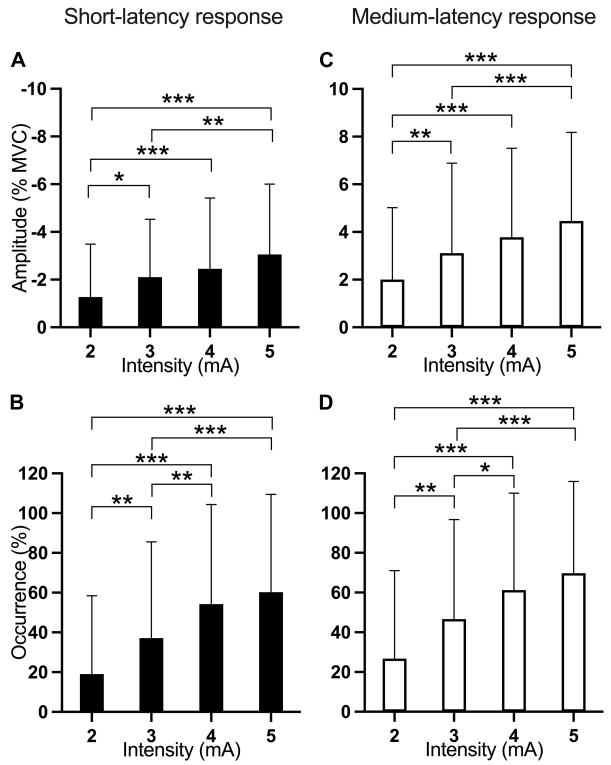

FIGURE 4 | Mean amplitude and occurrence of the short- and medium-latency responses according to current intensity (rotation and stimulus duration pooled within each EVS intensity). The first column of figures **(A,B**—black) is associated with the short-latency response while the second one **(C,D**—white) is associated with the medium-latency response. The first line of figures represents the amplitude **(A,C)** of the response while the second one represents the occurrence **(B,D)**. $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

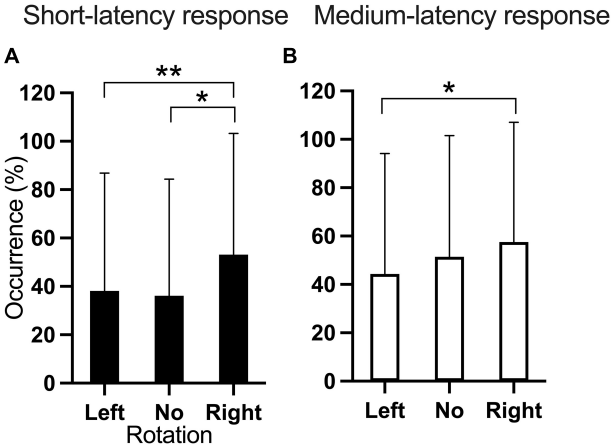

FIGURE 5 | Occurrence of the **(A)** short- and **(B)** medium-latency responses according to head rotation. $^{*}p < 0.05$; $^{**}p < 0.01$.

axons (Goldberg et al., 1984; Dlugaiczyk et al., 2019). Increased EVS current intensity recruits a more significant proportion of regular vestibular afferent fibers in monkeys (Goldberg et al., 1984). In humans, the recruitment of regular vestibular afferent fibers with the increase in EVS intensity could explain the higher occurrence and amplitude of short- and medium-latency motor responses as observed in animal studies.

EVS duration can also influence the motor responses. Although EVS studies of back muscles used longer stimulus duration [e.g., 175 ms (Guillaud et al., 2020), 400 ms (Ali et al., 2003)], using stimulus duration < 100 ms also result in LES motor responses. We observed that a 5-ms EVS duration induced a medium-latency motor response of smaller amplitude than for 20, 100, and 200 ms only in no head rotation condition. With the head rotated toward the right, the medium-latency motor response amplitude did not differ between EVS durations. In contrast, with the head toward the left, the medium-latency motor response amplitude was larger in 20 ms compared to other EVS durations. There was no effect of EVS duration on the short-latency motor response amplitude. Explaining the differences between the short- and medium-latency motor responses in different head positions remains challenging.

Overall, our results suggest that 5-ms EVS duration may induce motor responses, even though in few conditions their amplitude was smaller. EVS duration of 20 ms compared to 100- and 200-ms induced equal or larger motor responses, depending on the condition. Other studies reported that brief EVS duration might evoke responses. For example, EVS of 2-ms duration (5 mA) can evoke motor responses in the sternocleidomastoid (Watson and Colebatch, 1998) and masseter (Deriu et al., 2003) muscles, although they were only associated with movement of the head relative to the trunk rather than whole-body sway.

Influence of the Visual System

The EVS-induced motor response amplitude is highly context-dependent (Day et al., 1997; Fitzpatrick and Day, 2004; Gandevia et al., 2012; Maaswinkel et al., 2014; Ertl and Boegle, 2019). Biasing visual or proprioceptive input is frequently used to test their contribution to postural control. For example, if vision contributes to the motor responses, the absence of vision should increase its amplitude. In presence of visual input, the central nervous system could process the vestibular information induced by EVS as unphysiological or aberrant considering the mismatch between inputs coming from these sensory systems and reduce the gain on vestibular information. Vestibular-visual interaction occurs in standing, as authors reported much smaller EVS-induced motor responses with eyes open compared to closed (Britton et al., 1993; Fitzpatrick and Day, 2004). In contrast, our results do not support a significant contribution of vision on the amplitude and occurrence of the short- and medium latency motor responses in sitting. Increased gain of the somatosensory information while sitting could explain the small contribution of vision. In line, Fitzpatrick et al. (1994) concluded that visual input had a minor effect on EVS-induced responses when more somatosensory cues were available. In sitting, compared to upright standing, the large contact of the thighs and pelvis with the seat (i.e., involving more tactile receptors) may have provided large somatosensory input making postural control easier, even in the absence of vision. Future studies should test this hypothesis.

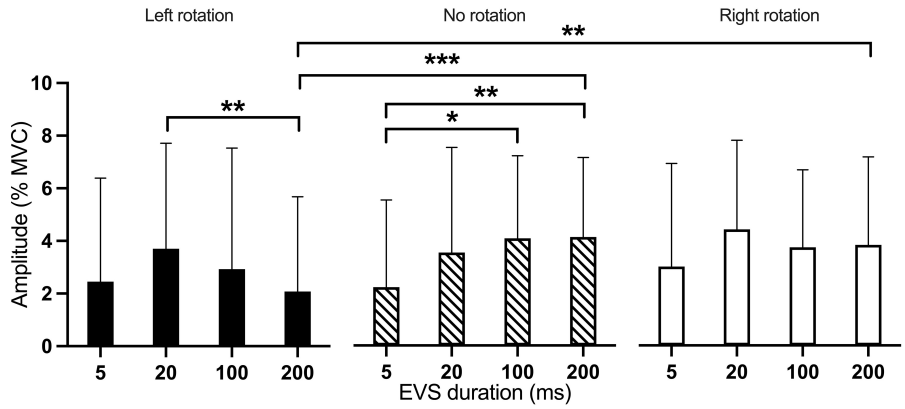

FIGURE 6 | Mean amplitude of the medium-latency response according to the interaction between EVS duration and head rotation. Results of the medium-latency response are represented as amplitude against EVS durations for the three head rotations. Black bar: left rotation; hatched bar: no rotation; White bar: right rotation. $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

Patterns of the Short- and Medium-Latency Motor Responses

In an upright standing position, short- and medium-latency responses in *soleus* muscles (Britton et al., 1993; Fitzpatrick et al., 1994) are opposite (i.e., inhibitory or excitatory). The direction of the response depends on the rotation of the head relative to the position of the anode/cathode. Britton et al. (1993) reported an inhibitory short-latency response followed by an excitatory medium-latency response in the *soleus* when the experimental conditions produced a backward sway (left head rotation and anode on the left). Opposite head rotation or the same rotation with the anode on the opposite mastoid process reversed the direction of the responses. Such a reversal did not occur in the current study: the short-latency response was always inhibitory and the medium-latency response, excitatory, regardless of the head rotation. A recent study from Guillaud et al. (2020) also reported no reversal of the short- and medium-latency LES motor responses when changing the polarity of the electrodes while standing with right head rotation. In another study, authors reported a reversed direction of LES motor responses by depicting EMG data from a single participant in frontal and sagittal planes of motion. However, it remains unclear whether the reversal was consistent across participants since no mean data or descriptive statistics were provided (Ali et al., 2003). This discrepancy could be explained by the sitting posture that was different between studies and the position of the electrodes that may capture the EMG signal from different back muscles having different biomechanical roles in lumbar spine control (i.e., prime mover vs. intervertebral control).

Although we did not measure body sway in sitting, Day et al. (1997) measured it and observed body sways in opposite directions when reversing EVS polarities, even though the amplitude was smaller compared to standing. Reversing EVS polarities (i.e., switching the anode and the cathode position) while keeping the same head rotation reverses the direction of body sway in the same manner than keeping the same EVS polarity but rotating the head rotation in the opposite direction. We suggest that the lack of reversal (i.e., the short-latency motor response was inhibitory and the medium-latency motor response was excitatory regardless of the direction of the head rotation) may reflect the biomechanical role of the LES muscle during body sway, i.e., that the central nervous system did not use the LES muscles as agonists of the body sway but rather as *"controllers"* of the lumbar spine posture. This hypothesis needs to be tested in future studies while recording multiple trunk/hip muscles on both sides of the body.

Although reversal was absent, head rotation modulated the amplitude of both short- and medium-latency motor responses. Indeed, the left head rotation produced smaller responses than right and no head rotations. A reduction in motor responses amplitude was observed during a condition corresponding to a forward body sway (e.g., left head rotation and anode placed to the right) compared to backward sway (e.g., right head rotation and anode placed to the right) (Ali et al., 2003; Guillaud et al., 2020). However, it remains difficult to compare the motor strategy in no head rotation with the available literature since we did not measure motor responses for LES on both sides.

Latencies and Pathways Underlying EVS Induced Motor Responses

In paraspinal muscles, the medium-latency response ranged between 47 and 110 ms (Ardic et al., 2000; Ali et al., 2003; Guillaud et al., 2020). We observed a similar range of the medium-latency motor response (range: 61.0–86.3 ms). No previous study reported the latency of the short-latency motor response. However, since measuring latencies for each condition was not possible, we did not perform statistical analysis for this parameter. Although studies suggested that an increase in EVS current reduced the motor response onset (Iles and Pisini, 1992; Rosengren and Colebatch, 2002; Ali et al., 2003), we did not observe such a trend.

EVS depolarizes the eighth cranial nerve axons, and the action potentials travel to the muscles through the vestibulospinal tract (for review Forbes et al., 2014). The latencies observed

for EVS-induced motor responses are 45.5 (5.3) ms for the short-latency response and 73.2 (5.1) ms for the medium-latency response. These relatively long latencies do not correspond to a monosynaptic fast-conducting pathway even when considering the latency between the vestibular organ and the vestibular nuclei. For example, the latency of the LES motor evoked potential (MEP) by transcranial magnetic stimulation of the primary motor cortex is between 14 and 18 ms (Tsao et al., 2011a; Jean-Charles et al., 2017). This latency is considered to represent a monosynaptic connection between the corticospinal cell and the α-motoneuron at the spinal level (Ferbert et al., 1992). Some authors argue that a long duration of central processing (e.g., by larger networks of interneurons at the vestibular nuclei and spinal cord levels) may cause these longer latencies (Forbes et al., 2014). For example, there is evidence in animal models that the vestibular pathways form direct (excitatory) or indirect (excitatory or inhibitory) connections with α-motoneurons (Lund and Pompeiano, 1968; Wilson and Yoshida, 1969; Grillner et al., 1970; Shinoda et al., 1986; Davies and Edgley, 1994). In other hand some could argue that the long latency of the EVS responses could be related to a late depolarization of the vestibular afferents due to long stimulus durations that are often used in EVS studies. However, the similarity of latencies (i) across EVS stimulus durations and (ii) between studies reinforce the validity of the observed EVS motor response latencies. Altogether, these results suggest that central processing of the vestibular afferents may occur at multiple levels of the central nervous system.

Limitations

Results need to be interpreted considering different methodological aspects. Even though attenuated by the application of anesthetic cream, tactile sensation induced by EVS can affect the responses (Ertl and Boegle, 2019). Moreover, the small number of participants combined with the large number of analyses carried out may have increased the likelihood of type II and I errors. EMG activity was only recorded in the right LES muscle, which prevented to confirm the absence of motor response reversal in the no head rotation condition (i.e., in the frontal plane of motion). Since the center of pressure or the trunk kinematics was not recorded, the analysis of the relationship between body sway and head rotation is based on the results of another study (Day et al., 1997). The number of stimulations per condition may be considered quite small when comparing to other studies (e.g., 160 stimulations; Ali et al., 2003). However, discernible motor responses without the need to integrate the EMG signal were observed in all participants. Also, the use of 15 conditions allowed to attain the study objectives, i.e., to identify optimal parameters. However, it is possible that more stimulations would have allowed to observe motor responses of smaller amplitude in some participants. Considering that not all conditions were repeated with eyes open, it is possible that vision could alter LES motor responses using untested EVS parameters and conditions. It is not possible to completely exclude the presence of an off-response for the 5 ms and the 20 ms-conditions, even though the results suggest a weak effect, if any, based on similar pattern of response and latency between EVS durations. We did not standardize head rotation between participants, considering the variability in individual cervical spine range of motion. Different amplitudes of head rotation between participants may have influenced the amplitude of the EVS-induced motor responses. However, we standardized head rotation (left vs. right) within-participant using the chin-acromion distance, which is rarely done in EVS studies.

CONCLUSION

This study explored the effect of head rotation, intensity, and duration of the EVS current, and vision on the EVS-induced motor responses in LES muscles. The EVS current intensity and EVS duration influenced the short- and medium-latency motor responses amplitude and occurrence. No reversal of the short- and medium-latency motor responses occurred in opposite head rotation (right vs. left). We suggest that this reflects the biomechanical role of the LES muscles to fine-tune the position of the lumbar lordosis during induced body sway. Finally, the presence of vision did not modulate the motor response amplitude and occurrence, suggesting a minimal contribution of vision to vestibulomotor control in sitting position.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Research Committee of the Centre Intégré Universitaire de Santé et de Services Sociaux de la Capitale-Nationale. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

HM-A, MS, and AD conceived the idea for the manuscript. J-PC elaborated a microcontroller, necessary to collect data, and provided essential technical assistance. MD and AD processed to the recruitment of participants and the collection of data. AD and HM-A performed the data analysis. All authors were involved in drafting the article and or revising it critically for important intellectual content.

FUNDING

This work was funded by the Discovery grant from the Natural Sciences and Engineering Research Council of Canada (RGPIN-2019-06529). HM-A was supported by a research scholar from Fonds de recherche du Québec—Santé (respectively #281961). AD was supported by a scholarship from the Faculté de médecine, Université Laval.

REFERENCES

Ali, A. S., Rowen, K. A., and Iles, J. F. (2003). Vestibular actions on back and lower limb muscles during postural tasks in man. *J. Physiol.* 546(Pt 2), 615–624. doi: 10.1113/jphysiol.2002.030031

Ardic, F. N., Latt, L. D., and Redfern, M. S. (2000). Paraspinal muscle response to electrical vestibular stimulation. *Acta Otolaryngol.* 120, 39–46. doi: 10.1080/000164800760370819

Blouin, J., Teasdale, N., and Mouchnino, L. (2007). Vestibular signal processing in a subject with somatosensory deafferentation: the case of sitting posture. *BMC Neurol.* 7:25. doi: 10.1186/1471-2377-7-25

Britton, T. C., Day, B. L., Brown, P., Rothwell, J. C., Thompson, P. D., and Marsden, C. D. (1993). Postural electromyographic responses in the arm and leg following galvanic vestibular stimulation in man. *Exp. Brain Res.* 94, 143–151.

Cullen, K. E. (2011). The neural encoding of self-motion. *Curr. Opin. Neurobiol.* 21, 587–595. doi: 10.1016/j.conb.2011.05.022

Dakin, C. J., Héroux, M. E., Luu, B. L., Inglis, J. T., and Blouin, J. S. (2016). Vestibular contribution to balance control in the medial gastrocnemius and soleus. *J. Neurophysiol.* 115, 1289–1297. doi: 10.1152/jn.00512.2015

Dakin, C. J., Son, G. M., Inglis, J. T., and Blouin, J. S. (2007). Frequency response of human vestibular reflexes characterized by stochastic stimuli. *J. Physiol.* 583(Pt 3), 1117–1127. doi: 10.1113/jphysiol.2007.133264

Davies, H. E., and Edgley, S. A. (1994). Inputs to group II-activated midlumbar interneurones from descending motor pathways in the cat. *J. Physiol.* 479(Pt 3), 463–473. doi: 10.1113/jphysiol.1994.sp020310

Day, B. L., and Cole, J. (2002). Vestibular-evoked postural responses in the absence of somatosensory information. *Brain* 125(Pt 9), 2081–2088. doi: 10.1093/brain/awf212

Day, B. L., Séverac Cauquil, A., Bartolomei, L., Pastor, M. A., and Lyon, I. N. (1997). Human body-segment tilts induced by galvanic stimulation: a vestibularly driven balance protection mechanism. *J. Physiol.* 500(Pt 3), 661–672. doi: 10.1113/jphysiol.1997.sp022051

Deriu, F., Tolu, E., and Rothwell, J. C. (2003). A short latency vestibulomasseteric reflex evoked by electrical stimulation over the mastoid in healthy humans. *J. Physiol.* 553(Pt 1), 267–279. doi: 10.1113/jphysiol.2003.047274

Di Lazzaro, V., Restuccia, D., Oliviero, A., Profice, P., Ferrara, L., Insola, A., et al. (1998). Effects of voluntary contraction on descending volleys evoked by transcranial stimulation in conscious humans. *J. Physiol.* 508(Pt 2), 625–633. doi: 10.1111/j.1469-7793.1998.625bq.x

Dlugaiczyk, J., Gensberger, K. D., and Straka, H. (2019). Galvanic vestibular stimulation: from basic concepts to clinical applications. *J. Neurophysiol.* 121, 2237–2255. doi: 10.1152/jn.00035.2019

Ertl, M., and Boegle, R. (2019). Investigating the vestibular system using modern imaging techniques-A review on the available stimulation and imaging methods. *J. Neurosci. Methods* 326:108363. doi: 10.1016/j.jneumeth.2019.108363

Ferbert, A., Caramia, D., Priori, A., Bertolasi, L., and Rothwell, J. C. (1992). Cortical projection to erector spinae muscles in man as assessed by focal transcranial magnetic stimulation. *Electroencephalogr. Clin. Neurophysiol.* 85, 382–387. doi: 10.1016/0168-5597(92)90051-c

Fitzpatrick, R., Burke, D., and Gandevia, S. C. (1994). Task-dependent reflex responses and movement illusions evoked by galvanic vestibular stimulation in standing humans. *J. Physiol.* 478(Pt 2), 363–372. doi: 10.1113/jphysiol.1994.sp020257

Fitzpatrick, R. C., and Day, B. L. (2004). Probing the human vestibular system with galvanic stimulation. *J. Appl. Physiol. (Bethesda, Md: 1985).* 96, 2301–2316. doi: 10.1152/japplphysiol.00008.2004

Forbes, P. A., Dakin, C. J., Vardy, A. N., Happee, R., Siegmund, G. P., Schouten, A. C., et al. (2013). Frequency response of vestibular reflexes in neck, back, and lower limb muscles. *J. Neurophysiol.* 110, 1869–1881. doi: 10.1152/jn.00196.2013

Forbes, P. A., Siegmund, G. P., Schouten, A. C., and Blouin, J. S. (2014). Task, muscle and frequency dependent vestibular control of posture. *Front. Integr. Neurosci.* 8:94. doi: 10.3389/fnint.2014.00094

Gandevia, S. C., Proske, U., and Stuart, D. G. (2012). *Sensorimotor Control of Movement and Posture*. New York, NY: Springer Science & Business Media.

Gensberger, K. D., Kaufmann, A. K., Dietrich, H., Branoner, F., Banchi, R., Chagnaud, B. P., et al. (2016). Galvanic vestibular stimulation: cellular substrates and response patterns of neurons in the vestibulo-ocular network. *J. Neurosci.* 36, 9097–9110. doi: 10.1523/jneurosci.4239-15.2016

Goldberg, J. M., Smith, C. E., and Fernández, C. (1984). Relation between discharge regularity and responses to externally applied galvanic currents in vestibular nerve afferents of the squirrel monkey. *J. Neurophysiol.* 51, 1236–1256. doi: 10.1152/jn.1984.51.6.1236

Grillner, S., Hongo, T., and Lund, S. (1970). The vestibulospinal tract. Effects on alpha-motoneurones in the lumbosacral spinal cord in the cat. *Exp. Brain Res.* 10, 94–120. doi: 10.1007/bf00340521

Guillaud, E., Faure, C., Doat, E., Bouyer, L. J., Guehl, D., and Cazalets, J. R. (2020). Ancestral persistence of vestibulospinal reflexes in axial muscles in humans. *J. Neurophysiol.* 123, 2010–2023. doi: 10.1152/jn.00421.2019

Hatzilazaridis, I., Hatzitaki, V., Antoniadou, N., and Samoladas, E. (2019). Postural and muscle responses to galvanic vestibular stimulation reveal a vestibular deficit in adolescents with idiopathic scoliosis. *Eur. J Neurosci.* 50, 3614–3626. doi: 10.1111/ejn.14525

Hermens, H. J., Freriks, B., Disselhorst-Klug, C., and Rau, G. (2000). Development of recommendations for SEMG sensors and sensor placement procedures. *J. Electromyogr. Kinesiol.* 10, 361–374. doi: 10.1016/s1050-6411(00)00027-4

Hodges, P. W., and Bui, B. H. (1996). A comparison of computer-based methods for the determination of onset of muscle contraction using electromyography. *Electroencephalogr. Clin. Neurophysiol.* 101, 511–519. doi: 10.1016/s0013-4694(96)95190-5

Iles, J. F., and Pisini, J. V. (1992). Vestibular-evoked postural reactions in man and modulation of transmission in spinal reflex pathways. *J. Physiol.* 455, 407–424. doi: 10.1113/jphysiol.1992.sp019308

Jean-Charles, L., Nepveu, J. F., Deffeyes, J. E., Elgbeili, G., Dancause, N., and Barthelemy, D. (2017). Interhemispheric interactions between trunk muscle representations of the primary motor cortex. *J. Neurophysiol.* 118, 1488–1500. doi: 10.1152/jn.00778.2016

Kingma, H., and van de Berg, R. (2016). Anatomy, physiology, and physics of the peripheral vestibular system. *Handb. Clin. Neurol.* 137, 1–16. doi: 10.1007/0-387-21567-0_1

Lund, S., and Broberg, C. (1983). Effects of different head positions on postural sway in man induced by a reproducible vestibular error signal. *Acta Physiol. Scand.* 117, 307–309. doi: 10.1111/j.1748-1716.1983.tb07212.x

Lund, S., and Pompeiano, O. (1968). Monosynaptic excitation of alpha motoneurones from supraspinal structures in the cat. *Acta Physiol. Scand.* 73, 1–21. doi: 10.1111/j.1748-1716.1968.tb04075.x

Maaswinkel, E., Veeger, H. E., and Dieen, J. H. (2014). Interactions of touch feedback with muscle vibration and galvanic vestibular stimulation in the control of trunk posture. *Gait Posture* 39, 745–749. doi: 10.1016/j.gaitpost.2013.10.011

Mackenzie, S. W., and Reynolds, R. F. (2018). Differential effects of vision upon the accuracy and precision of vestibular-evoked balance responses. *J. Physiol.* 596, 2173–2184. doi: 10.1113/jp275645

Massé-Alarie, H., Beaulieu, L. D., Preuss, R., and Schneider, C. (2016a). Corticomotor control of lumbar multifidus muscles is impaired in chronic low back pain: concurrent evidence from ultrasound imaging and double-pulse transcranial magnetic stimulation. *Exp. Brain Res.* 234, 1033–1045. doi: 10.1007/s00221-015-4528-x

Massé-Alarie, H., Beaulieu, L.-D., Preuss, R., and Schneider, C. (2016b). Influence of paravertebral muscles training on brain plasticity and postural control in chronic low back pain. *Scand. J. Pain.* 12, 74–83. doi: 10.1016/j.sjpain.2016.03.005

Masse-Alarie, H., Elgueta Cancino, E., Schneider, C., and Hodges, P. (2016). Paired-pulse TMS and fine-wire recordings reveal short-interval intracortical inhibition and facilitation of deep multifidus muscle fascicles. *PLoS One* 11:e0159391. doi: 10.1371/journal.pone.0159391

Massé-Alarie, H., Flamand, V. H., Moffet, H., and Schneider, C. (2013). Peripheral neurostimulation and specific motor training of deep abdominal muscles improve posturomotor control in chronic low back pain. *Clin. J. Pain* 29, 814–823. doi: 10.1097/ajp.0b013e318276a058

Masse-Alarie, H., Neige, C., Bouyer, L. J., and Mercier, C. (2018). Modulation of corticospinal excitability of trunk muscles in preparation of rapid arm movement. *Neuroscience* 369, 231–241. doi: 10.1016/j.neuroscience.2017.11.024

Massé-Alarie, H., Salomoni, S. E., and Hodges, P. W. (2019). The nociceptive withdrawal reflex of the trunk is organized with unique muscle receptive

fields and motor strategies. *Eur. J. Neurosci.* 50, 1932–1947. doi: 10.1111/ejn.14369

Masse-Alarie, H., Salomoni, S. E., and Hodges, P. W. (2019). The nociceptive withdrawal reflex of the trunk is organized with unique muscle receptive fields and motor strategies. *Eur. J. Neurosci.* 50, 1932–1947. doi: 10.1111/ejn.14369

Massion, J. (1992). Movement, posture and equilibrium: interaction and coordination. *Prog. Neurobiol.* 38, 35–56. doi: 10.1016/0301-0082(92)90034-c

O'Connell, N. E., Maskill, D. W., Cossar, J., and Nowicky, A. V. (2007). Mapping the cortical representation of the lumbar paravertebral muscles. *Clin. Neurophysiol.* 118, 2451–2455. doi: 10.1016/j.clinph.2007.08.006

Pialasse, J. P., Descarreaux, M., Mercier, P., Blouin, J., and Simoneau, M. (2015). The vestibular-evoked postural response of adolescents with idiopathic scoliosis is altered. *PLoS One* 10:e0143124. doi: 10.1371/journal.pone.0143124

Pialasse, J. P., Mercier, P., Descarreaux, M., and Simoneau, M. (2016). Sensorimotor control impairment in young adults with idiopathic scoliosis compared with healthy controls. *J. Manipulat. Physiol. Ther.* 39, 473–479. doi: 10.1016/j.jmpt.2016.06.001

Rosengren, S. M., and Colebatch, J. G. (2002). Differential effect of current rise time on short and medium latency vestibulospinal reflexes. *Clin. Neurophysiol.* 113, 1265–1272. doi: 10.1016/s1388-2457(02)00121-9

Shinoda, Y., Ohgaki, T., and Futami, T. (1986). The morphology of single lateral vestibulospinal tract axons in the lower cervical spinal cord of the cat. *J. Comp. Neurol.* 249, 226–241. doi: 10.1002/cne.902490208

Sluydts, M., Curthoys, I., Vanspauwen, R., Papsin, B. C., Cushing, S. L., Ramos, A., et al. (2020). Electrical vestibular stimulation in humans: a narrative review. *Audiol. Neurootol.* 25, 6–24. doi: 10.1159/000502407

Tsao, H., Danneels, L., and Hodges, P. W. (2011a). Individual fascicles of the paraspinal muscles are activated by discrete cortical networks in humans. *Clin. Neurophysiol.* 122, 1580–1587. doi: 10.1016/j.clinph.2011.01.048

Tsao, H., Danneels, L. A., and Hodges, P. W. (2011b). ISSLS prize winner: smudging the motor brain in young adults with recurrent low back pain. *Spine (Phila Pa 1976)* 36, 1721–1727. doi: 10.1097/brs.0b013e31821c4267

Watson, S. R., and Colebatch, J. G. (1998). Vestibulocollic reflexes evoked by short-duration galvanic stimulation in man. *J. Physiol.* 513(Pt 2), 587–597. doi: 10.1111/j.1469-7793.1998.587bb.x

Wilson, V. J., and Yoshida, M. (1969). Comparison of effects of stimulation of Deiters' nucleus and medial longitudinal fasciculus on neck, forelimb, and hindlimb motoneurons. *J. Neurophysiol.* 32, 743–758. doi: 10.1152/jn.1969.32.5.743

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Bioengineering and Biotechnology

METHODS
published: 29 July 2021
doi: 10.3389/fbioe.2021.678006

Proof-of-Concept of the Virtual Reality Comprehensive Balance Assessment and Training for Sensory Organization of Dynamic Postural Control

Sanghee Moon[1,2], Chun-Kai Huang[2], Maryam Sadeghi[2], Abiodun E. Akinwuntan[2,3] and Hannes Devos[2]**

[1] Department of Physical Therapy, Ithaca College, Ithaca, NY, United States, [2] Laboratory for Advanced Rehabilitation Research in Simulation, Department of Physical Therapy, Rehabilitation Science, and Athletic Training, University of Kansas Medical Center, Kansas City, KS, United States, [3] Office of the Dean, School of Health Professions, University of Kansas Medical Center, Kansas City, KS, United States

OPEN ACCESS

Edited by:
Eric Yiou,
Université Paris-Saclay, France

Reviewed by:
Arnaud Delafontaine
Staps Orsay, CIAMS Paris-Saclay, France
Romain Artico,
Université Paris-Sud, France

***Correspondence:**
Sanghee Moon
smoon2@ithaca.edu
Hannes Devos
hdevos@kumc.edu

Specialty section:
This article was submitted to Biomechanics, a section of the journal Frontiers in Bioengineering and Biotechnology

Received: *08 March 2021*
Accepted: *10 June 2021*
Published: *29 July 2021*

Citation:
Moon S, Huang C-K, Sadeghi M, Akinwuntan AE and Devos H (2021) Proof-of-Concept of the Virtual Reality Comprehensive Balance Assessment and Training for Sensory Organization of Dynamic Postural Control. Front. Bioeng. Biotechnol. 9:678006. doi: 10.3389/fbioe.2021.678006

Accurate quantification of the impact of visual, somatosensory, and vestibular systems on postural control may inform tailor-made balance intervention strategies. The aim of this proof-of-concept study was to determine the safety, sense of presence, system usability, and face validity of a newly developed Virtual Reality Comprehensive Balance Assessment and Training (VR-ComBAT) in healthy young individuals. The VR-ComBAT included six balance condition: (1) stable surface with fixed virtual reality (VR) surroundings; (2) stable surface with blacked out VR surroundings; (3) stable surface with VR visual conflict; (4) unstable surface with fixed VR surroundings; (5) unstable surface with blacked out VR surroundings; and (6) unstable surface with VR visual conflict. Safety was evaluated using the number of adverse events, including scores on the Simulator Sickness Questionnaire. Sense of presence was evaluated using the igroup Presence Questionnaire (iPQ). System usability was assessed using the Systems Usability Scale (SUS). Friedman analyses with *post hoc* Wilcoxon Signed Rank tests were employed to demonstrate face validity by quantifying center of pressure (COP) changes in mean distance, mean velocity, and mean frequency in the anteroposterior (AP) and mediolateral (ML) direction across the six conditions. Twenty-three participants (27.4 ± 8.0 years old; 13 women) reported no adverse events. Participants scores on average 44.9 ± 9.6 on the iPQ and 79.7 ± 9.9 on the SUS. *Post hoc* analyses showed significant changes in COP-based measures when compared to baseline. The mean frequency change of COP showed direction-dependence in which increased frequency change in AP was observed while decreased change in ML was noted. The VR-ComBAT provides a safe, feasible, and cost-effective VR environment that demonstrates consistent sensory re-weighting between visual, somatosensory, and vestibular systems. Future studies should investigate whether VR-ComBAT can be used to inform precision rehabilitation of balance and fall prevention in older adults without and with neurological conditions.

Keywords: virtual reality, balance, sensory organization test, postural control, center of pressure

INTRODUCTION

Postural control requires the brain to integrate information from vision, somatosensory, and vestibular cues in order to respond timely and accurately to changes in the body's alignment and tone with respect to visual surroundings, support surface, internal references, and gravity (Alcock et al., 2018; Ivanenko and Gurfinkel, 2018). These sensory systems sometimes provide conflicting information (Nashner and Peters, 1990). To illustrate, while sitting on a moving bus, the eyes inform the brain that the surroundings appear to be moving whereas the somatosensory system provides information that the body is stationary. In such cases, the brain needs to ignore or prioritize conflicting information to accomplish postural control (Gaerlan, 2010). Discrepancies in these systems become even more apparent in individuals with neurological conditions, resulting in increased postural imbalance, a higher risk of falls, and, in many cases, a higher fear of falling (Horak, 2006; Cronin et al., 2017). Accurate detection of the system that affects postural control in neurological conditions is key to tailor balance intervention and fall prevention programs to the needs of individuals at risk of falls.

Several computerized balance assessment tools have been developed, including dynamic posturography [e.g., Neurocom® SMART EquiTest®, Bertec® computerized dynamic posturography (CDP/IVR), Biodex® Balance] or wearable motion sensors (e.g., APDM Opal). These computerized balance assessment tools enable quantitative assessment of postural control (Mancini and Horak, 2010), reduce test performance variability, increase sensitivity to subtle changes (Visser et al., 2008), and determine the systems that may underly impaired postural control (Mancini and Horak, 2010). Of those, the Neurocom® SMART EquiTest® system (Natus, San Carlos, CA, United States) and Bertec computerized dynamic posturography (Bertec®, Columbus, OH, United States) are considered the gold standard of dynamic posturography assessment. These computerized sensory organization tests (SOT) challenge the visual, somatosensory, and vestibular systems to provide a detailed assessment of the underlying sensory deficits affecting balance. Although effective in evaluating and treating balance disorders (Alahmari et al., 2014), the high cost ($80,000–$180,000), space needs for the equipment, lack of portability, and time needed for training, have limited the use of the computerized SOT in clinical practice (Visser et al., 2008). The Clinical Test of Sensory Interaction on Balance (CTSIB) was developed to discern the relative contributions of the visual, somatosensory, and vestibular systems to postural control (Shumway-Cook and Horak, 1986). This test includes six static balance conditions with eyes open, eyes closed, and the use of a dome to create visual conflict combining with feet on firm or foam surface. This test was later modified to only four conditions, excluding the visual dome from the test procedures as the balance tasks with the visual dome did not differ from those in the eyes closed conditions (Cohen et al., 1993). Although clinically useful, the scoring system is crude, semi-objective, and may not be sensitive enough to detect subtle changes in postural control in neurodegenerative conditions (Suttanon et al., 2011).

The advent of portable force platforms with head-mounted virtual reality (VR) technology may provide a clinical, cost-effective, and user-friendly dynamic posturography assessment without compromising the evaluative and rehabilitative effectiveness of current computerized SOT. Although VR technology has emerged in the rehabilitation realm as a promising intervention tool to improve balance and gait (de Rooij et al., 2016; Cano Porras et al., 2018, 2019; Massetti et al., 2018; Chen et al., 2020), only few studies utilized VR to assess the sensory organization of postural balance (Lubetzky et al., 2018, 2019; Trueblood et al., 2018; Wittstein et al., 2020). However, it is not clear whether the SOT administered using a head-mounted VR set is safe and easy to use, provides a realistic experience to the user, and discriminates between postural control conditions that test different balance systems.

Unlike the Equilibrium Score calculated from the force platform of the Equitest® that evaluates postural balance through center of pressure (COP) displacement only in the anteroposterior (AP) direction, portable force platforms provide a multidimensional assessment of postural control. Quiet standing on a foam increased COP displacement in the AP direction by 8%, and in the mediolateral (ML) direction by 21% (Reynard et al., 2019). Adding assessment of ML sway and sway area has shown to quantify fall risk in neurological conditions, such as changes in postural sway characteristics while standing with eyes closed in Parkinson's disease (Błaszczyk et al., 2007). Additionally, measuring COP frequency in AP and ML directions brings perspective of adopting different strategies to maintain balance. For example, evidence suggests that changes in perturbation conditions alter COP AP or ML frequency characteristics (Creath et al., 2005). Previous study also noted that postural sway in AP and ML directions can be attributed to ankle and hip control, respectively (Saffer et al., 2008).

The aim of this proof-of-concept study was to demonstrate the safety, sense of presence, system usability, and face validity of the Virtual Reality Comprehensive Balance Assessment and Training (VR-ComBAT) in healthy individuals. The overall hypothesis was that the VR-ComBAT will provide a safe and standardized VR-based balance testing environment in the healthy population. To test our hypothesis, we gauged sense of presence and system usability in the VR environment and satisfaction with our novel VR-based test. Face validity of the VR-ComBAT was evaluated by comparing multidirectional COP displacement and frequency measures across different postural control conditions.

MATERIALS AND EQUIPMENT

Hardware and Software Specifications

The VR-ComBAT consists of a computer that processes the VR input and output [Alienware (Intel® Core™ i7-7800X CPU @ 3.50GHz; 16.0 GB RAM), Dell USA Corporation, Round Rock, TX, United States], a commercially available, head-mounted

device (HMD) with integrated VR (HTC VIVE Pro Eye, HTC, Taoyuan, Taiwan), and two VR tracking sensors (Steam VR Base Stations, HTC, Taoyuan, Taiwan). The HTC VIVE Pro Eye headset includes dual-OLED 3.5-inch displays with a combined resolution of 2,880 × 1,600 pixels. The refresh rate of the screen is 90 Hz. The field of view is 110 degrees. The Steam VR (version 1.13, Valve, Bellevue, WA, United States) was used to simultaneously link the computer and the VR headset.

The VR headset was integrated with a force plate (AMTI Optima, Watertown, MA, United States) to measure the displacement and velocity of COP. The sampling frequency of the force plate was 200 Hz. The force plate was manually synchronized with the VR system by simultaneously starting the VR conditions and force plate measurement at each trial. The experimental setup is shown in **Figure 1**.

Unity 3D (version 2019.3.0; San Francisco, CA, United States) was utilized to create the VR-ComBAT environment. The executable application is available at http://bit.ly/VR-ComBAT (github). The basic setup of the VR environment includes three panels (one front, and two side panels), positioned at 90-degree angle to each, with multi-colored triangular patterns to help participants with visual fixation on the VR environment (**Figure 2**).

Balance Conditions

The VR-ComBAT emulates six different conditions, that, in combination, test visual, somatosensory, and vestibular systems of balance (**Figure 2**). These conditions mimic the six conditions in the SOT of the Equitest®: (1) stable surface with fixed VR surrounding; (2) stable surface with blacked out VR surroundings; (3) stable surface with VR visual conflict; (4) unstable surface with fixed VR surroundings; (5) unstable surface with blacked out VR surroundings; and (6) unstable surface with VR visual conflict.

Condition 1 is a baseline that measures static balance on a fixed surface. The surrounding panels in the VR environment remain stationary. Participants can use input from visual, somatosensory, and vestibular systems to maintain balance. In condition 2, participants cannot rely on vision to remain upright since the VR surroundings are blackened out. Condition 3 creates a conflict between normal input from the somatosensory and vestibular systems and the visual information from the moving VR panels. The surrounding panels are moving in the anteroposterior direction with a maximum of 20 degrees and a maximum velocity of 15 degrees/s. Conditions 4, 5, and 6 are identical to 1, 2, and 3, respectively. However, in conditions 4, 5, and 6, a foam (Amazon Basics Balance Pad for Exercise Training, 35 cm × 5 cm × 40 cm, density = 0.04 g/cm^3) is placed between the feet and the force plate, thus challenging the somatosensory system.

METHODS

Participants

This study was conducted in the Laboratory for Advanced Rehabilitation Research in Simulation, at the University of Kansas Medical Center. This proof-of-concept study recruited 23 healthy participants if they were (1) between 19 and 65 years of age; (2) had no walking or balance impairment [>45 in Berg Balance Scale (BBS; Berg et al., 1992) and >20 in Mini Balance Evaluation Systems Test (Mini-BESTest; Leddy et al., 2011)]; and (3) were able to understand and follow instructions in English. We excluded individuals who (1) had a history of neurological or vestibular conditions and (2) had visual acuity or visual field impairment that could not be resolved by corrective lenses. All participants signed written informed consent. The study ethics was approved by the Institutional Review Board at the University of Kansas Medical Center (#STUDY00145395).

Study Protocol

Following written consent, demographic information (age, sex, and education) was collected. The BBS (total score: 56, lower score indicating higher risk of balance problems) and Mini-BESTest (total score: 28, lower score indicating the higher risk of balance problems) were administered to confirm the absence of any balance impairments. Cognitive impairments were ruled out using the Montreal Cognitive Assessment (MOCA; Nasreddine et al., 2005). Next, participants were fitted with the VR headset and asked to step on the force plate. Then, participants stood on the force plate (conditions 1–3) or on the foam surface (conditions 4–6) with their feet shoulder width apart and hands naturally placed at their sides. Participants were asked to remain in the same position during each VR-ComBAT task (**Figure 3**). All participants were newly recruited and had no previous exposure to the VR-ComBAT system. There was no practice or learning trial before the recording, since all the conditions in VR-ComBAT were thoroughly explained by the lead researcher and were easy to perform for healthy young participants. Participants with glasses wore the VR headset without taking their glasses off, which allowed participants to experience the VR environment with their normal vision or corrected-to-normal vision. Participants were instructed to stand as still as possible. Each condition consisted of three trials that lasted 20 s per trial. Between each trial, a 5-s break was given. For conditions 2 and 4 (blacked out VR surroundings), the light of the testing room was also turned off to create a completely dark VR environment by removing any lights coming from the gaps of the VR headset. During the experiment, safety was assured by a gait belt and a research team member next to a participant in case of a fall or near-fall event. The experimental protocol is shown in **Figure 4**.

Outcome Measures

Safety

The number of adverse events (e.g., falls) was recorded. VR HMD is believed to increase simulator sickness (similar to motion sickness) compared to remote VR displays (Kim et al., 2014; Dennison et al., 2016). This increased proneness to simulator sickness is thought to stem from the high-fidelity, stereoscopic rendering of VR images. The realistic images displayed in VR HMD can create discrepancies between the perceived and expected visual sensory information, leading to increased symptoms of simulator sickness (Chang et al., 2020). We administered the Simulator Sickness Questionnaire (SSQ) after condition 6, which is the condition that was expected to induce

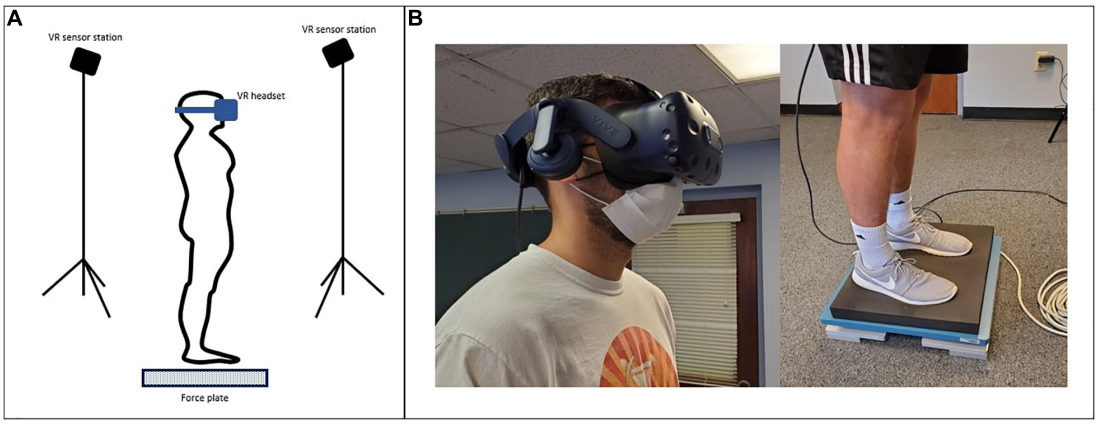

FIGURE 1 | (A) Virtual Reality Comprehensive Balance Assessment and Training (VR-ComBAT) setup; **(B)** A participant wears the VR headset and stands on the foam surface placed over the force plate.

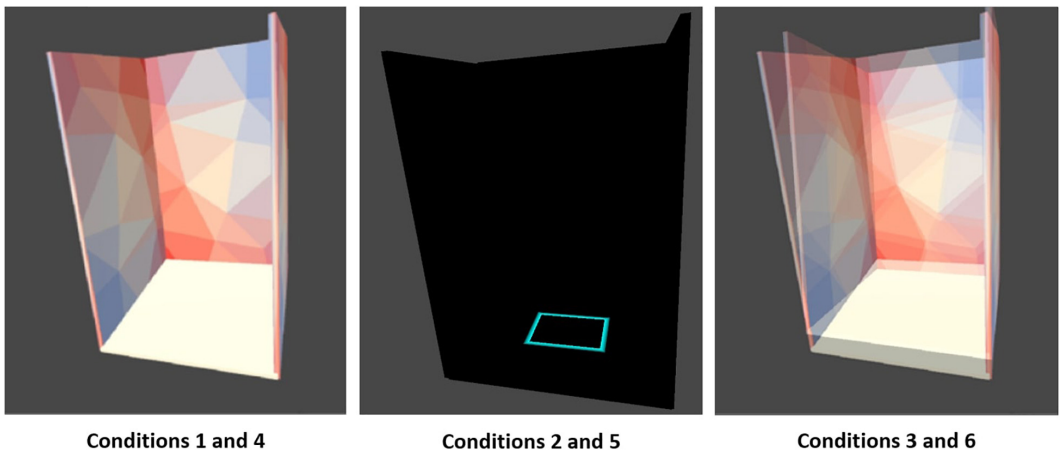

FIGURE 2 | Six VR-ComBAT conditions. (1) stable surface with fixed virtual reality (VR) surroundings; (2) stable surface with blacked out VR surroundings; (3) stable surface with VR visual conflict; (4) unstable surface with fixed VR surroundings; (5) unstable surface with blacked out VR surroundings; and (6) unstable surface with VR visual conflict.

most simulator sickness. The SSQ is regarded as the current gold standard in calculating simulator sickness in research (Kennedy et al., 1993; Jinjakam and Hamamoto, 2012). The SSQ is accurate and reliable to measure simulator sickness in high-fidelity VR environments such as driving simulators, flight simulators, and other VR systems (Kennedy et al., 1993). The score is comprised of three subsections, each with seven symptoms, in which there is some overlap: disorientation, nausea, and oculomotor. The symptoms include general discomfort, fatigue, headache, eyestrain, difficulty focusing, increased salivation, sweating, nausea, difficulty concentrating, the fullness of head, blurred vision, dizziness (eyes open and closed), vertigo, stomach awareness, and burping. The weighted score formula was used to calculate the global index, which reflects the total discomfort level, as well as the scores for the three subsections.

According to previous research (Kennedy et al., 1993), the three subscale scores were calculated by summing scores associated with each subscale and multiplying them by an appropriate weighting factor (9.54 for SSQ-Nausea, 7.58 for SSQ-Oculomotor, and 13.92 for SSQ-Disorientation). To calculate the total score of SSQ, the result was equal to the sum of the three unweighted subscale scores, multiplied by 3.74. A person with a total score of >100 is considered actively ill due to simulator sickness (Kennedy et al., 1993).

Sense of Presence

Sense of presence was evaluated using the iPQ. The iPQ is a multidimensional scale assessing the sense of presence in a VR environment. Sense of presence refers to the subjective feeling of being in a virtual environment. The reliability and validity of the iPQ have been established in previous work (Panahi et al., 2009). The 14 items of the questionnaire are scores on questionnaire contains 14 items, scored on an ordinal scale ranging from 1 to 5. One item reflects general sense of presence. The other items are categorized into sense of spatial presence (5 items), involvement (4 items), and experienced realism (4 items) (Hein et al., 2018).

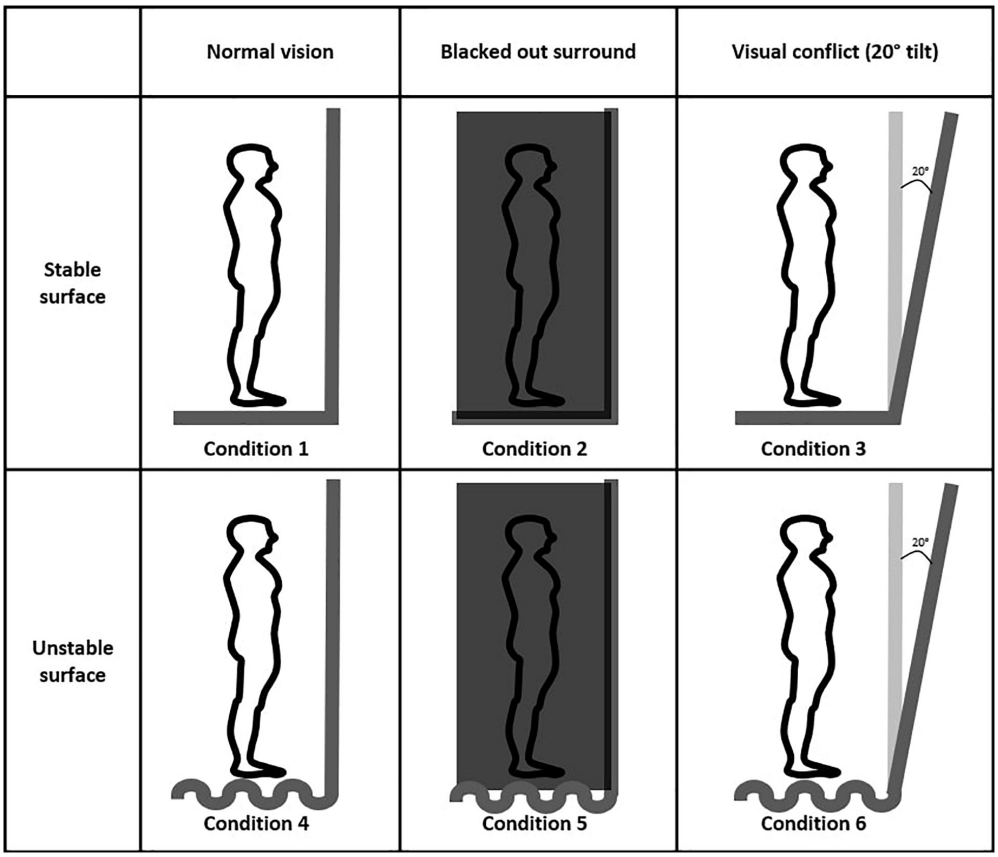

FIGURE 3 | Six VR-ComBAT conditions in the virtual environment. Conditions 1 and 4, conditions 2 and 5, and conditions 3 and 6 share the same VR balance testing environments.

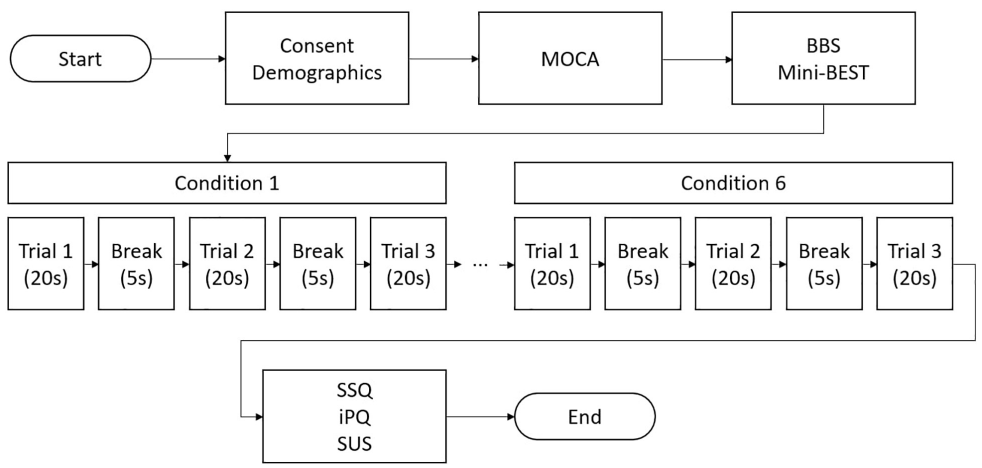

FIGURE 4 | A flow chart of VR-ComBAT experimental procedure (BBS = Berg Balance Scale; iPQ = igroup Presence Questionnaire; Mini-BEST = Mini Balance Evaluation Systems Test; MOCA = Montreal Cognitive Assessment; SSQ = Simulator Sickness Questionnaire; SUS = System Usability Scale).

System Usability

The SUS was administered to capture participants' viewpoints on effectiveness, efficiency, and satisfaction levels of the VR-ComBAT (Brooke, 1996; Bangor et al., 2008). The questionnaire contains 10 items, each scored on a range from ranges from 0 to 100. The SUS total scores representing a composed measure of the system's overall usability on a scale from 0 to 100.

Face Validity

Face validity evaluates the extent to which the measured variable appears to adequately measure the conceptual variable (Thomas et al., 1992). The face validity of VR-ComBAT to discriminate between different postural control conditions was evaluated using quantitative COP measures. These COP data were extracted from the force plate and processed using the MATLAB application (MathWorks, Natick, MA, United States) to calculate the following outcomes (Prieto et al., 1996):

- Mean distance in the AP (MeanAP) or ML (MeanML) direction: The average distance in the AP/ML direction from the mean COP.
- Mean velocity in the AP (VelAP) or ML (VelML) direction: The average velocity of COP in the AP/ML direction.
- 95% confidence ellipse area (95%Area): The area that encloses approximately 95% of the points on the COP path.
- Mean frequency in the AP (MfAP) or ML (MfML) direction: The frequency (Hz) of a sinusoidal oscillation with an average value of total path length of excursions in AP (or ML) over MeanAP (or MeanML).

Statistical Analysis

All statistical analyses were performed using SPSS (version 26, IBM Corporation, Armonk, NY, United States). The distribution of data was examined for normality using the Shapiro–Wilk test. Since the number of participants of this study was small and almost all data were not normally distributed, the Friedman test was conducted to examine the differences between conditions followed by *post hoc* Wilcoxon Signed Rank test. We identified *a priori* four pairwise comparisons to minimize committing type 1 error. We compared (1) condition 2 to condition 1 to tease out somatosensory system contributions; (2) condition 4 to condition 1 to tease out visual system contributions; and (3) condition 5 to condition 1 and (4) condition 6 to condition 5 to tease out vestibular system contributions (Shumway-Cook, 2011; Pletcher et al., 2017). The effect size ($r = \frac{Z}{\sqrt{n}}$) was adopted to indicate the strength of two conditions of VR-ComBAT. Of note, given that Wilcoxon Signed-rank test was conducted in this study, to more accurately reflect this non-parametric approach, we calculated the effect size (r) according to Rosenthal et al. instead of Cohen's d effect size (Rosenthal et al., 1994). The significance levels of all analyses were set $\alpha = 0.05$.

RESULTS

Participants (13 women and 10 men) were on average 27.4 ± 8 years old and reported 19.2 ± 2.5 years of education. None of the participants showed any impairment in static or dynamic balance, as evidenced by maximum scores on the BBS (56 ± 0) and on the Mini-BESTest (28 ± 0). Participants scored on average 28.3 ± 1.4 on the MOCA, indicating no cognitive impairments (**Table 1**).

Safety

No adverse events were reported during or after the study visit. SSQ total scores were on average 33.3 ± 66.1. Average SSQ average subscores were 2.9 ± 6.1 for nausea, 3 ± 5.9 for oculomotor, and 3 ± 7.2 for disorientation. Participants either scored none or slight on each item of the SSQ.

Sense of Presence

The average iPQ score of total iPQ was 44.9 ± 9.6 with average subscores of 18.8 ± 3.7 for spatial presence, 11.3 ± 3.5 for involvement, and 10.7 ± 2.7 for experienced realism.

System Usability

The SUS demonstrated nearly a total score of 80 in system usability (79.7 ± 9.9).

Face Validity

The Friedman test revealed significant differences across the six conditions for all COP-based measures ($p < 0.01$). *Post hoc* analyses (**Table 2**) showed that participants exhibited worse performance on most COP measures in conditions 2, 4, and 5 compared to condition 1.

In the frequency-based analysis, an inverse trend between MfAP and MfML was observed across the conditions. Pairwise comparisons showed that MfAP increased while MfML decreased with respect to increased task difficulty (**Figure 5**).

DISCUSSION

The aim of this proof-of-concept study was to determine the safety, sense of presence, systems usability, and face validity of the newly developed VR-ComBAT in healthy young individuals. We gauged sense of presence in the VR environment and satisfaction with our novel VR-based system as important outcomes of sense of presence. We also included comprehensive quantitative comparisons of multidirectional COP outcomes across the six conditions. The results of this study support our hypotheses that the VR-ComBAT is safe, highly acceptable, and able to detect multidirectional changes of postural control in terms of COP amid different conditions from healthy young participants.

The VR-ComBAT provided a safe and feasible virtual balance testing environment. As Howarth and Costello noted (Howarth and Costello, 1997), VR environments can induce temporary side effects such as general discomfort, fatigue, headache, nausea, and irritating eyes. However, in our study, no adverse events were reported by participants. In addition, the results of SSQ suggested that the VR-ComBAT did not cause any adverse effects of VR throughout the experiment.

Our findings on the sense of presence of the VR-ComBAT measured by iPQ and SUS demonstrated that our novel VR system was well accepted by participants. The total iPQ (44.9) was 9.9-point above neutral presence (35 = 70/2), demonstrating that participants indicated being present in the VR-ComBAT environment. The means of the three subscales of iPQ all contributed to the averaged overall score [spatial

TABLE 1 | Demographic and clinical characteristics.

	Age	Sex	BBS	Mini-BESTest	MOCA
Participants (*N* = 23)	27.4 ± 8.0	13 female,10 male	56 ± 0	28 ± 0	28.3 ± 1.4

BBS, Berg Balance Scale; Mini-BESTest, Mini Balance Evaluation Systems Test; MOCA, Montreal Cognitive Assessment.

TABLE 2 | COP-based measures across the six VR-ComBAT conditions (*N* = 23).

	Condition 1	Condition 2	Condition 3	Condition 4*	Condition 5*	Condition 6
MeanAP (mm)	3.71 (1.02)	4.17 (1.90) *0.21 [0.12–0.36]*	3.90 (1.26) *0.18 [0.13–0.22]*	5.50 (1.57) *0.61 [0.49–0.74]*	5.92 (1.83) *0.62 [0.78–0.46]*	5.92 (2.16) *0.62 [0.46–0.78]*
MeanML (mm)	1.33 (0.65)	1.61 (0.82)* *0.34 [0.3–0.38]*	1.73 (1.41) *0.37 [0.32–0.42]*	3.15 (1.08) *0.62 [0.49–0.75]*	3.24 (1.19) *0.62 [0.48–0.75]*	3.12 (1.19) *0.62 [0.49–0.75]*
VelAP (mm/s)	17.31 (3.46)	18.71 (4.03)* *0.4 [0.25–0.56]*	18.89 (3.22) *0.42 [0.25–0.58]*	29.73 (7.56) *0.62 [–0.25 to 1.49]*	32.96 (8.19) *0.62 [–0.49 to 1.72]*	29.59 (7.61)** *0.62 [–0.24 to 1.49]*
VelML (mm/s)	9.22 (1.21)	9.82 (1.65)* *0.38 [0.31–0.45]*	9.56 (1.74) *0.20 [0.12–0.27]*	15.40 (3.93) *0.62 [0.18–1.05]*	15.88 (3.30) *0.62 [0.15–1.09]*	14.39 (3.02) ** *0.62 [0.25–0.98]*
95%Area (mm^2)	148.99 (102.53)	190.46 (152.39)* *0.26 [–10.1 to 10.61]*	209.30 (239.64) *0.21 [–13.14 to 13.56]*	530.12 (314.76) *0.62 [–23.99 to 25.23]*	574.78 (342.18) *0.62 [–29.91 to 31.15]*	569.81 (450.65) *0.62 [–29.24 to 30.48]*
MfAP (Hz)	0.92 (0.29)	0.96 (0.37) *0.05 [0.01–0.09]*	0.96 (0.27) *0.1 [0.09–0.12]*	1.03 (0.32) *0.31 [0.3–0.33]*	1.06 (0.27) *0.41 [0.4–0.43]*	0.98 (0.30) ** *0.23 [0.22–0.24]*
MfML (Hz)	1.49 (0.56)	1.39 (0.64) *0.25 [0.23–0.27]*	1.38 (0.63) *0.34 [0.34–0.35]*	0.96 (0.28) *0.6 [0.56–0.76]*	0.96 (0.29) *0.58 [0.53–0.61]*	0.91 (0.25) ** *0.59 [0.55–0.64]*

Each cell represents the mean (standard deviation) on top and effect size r [95% CI] compared to condition 1 at bottom in italics.
**Significant differences when compared to condition 1 ($p < 0.05$).*
***Significant decrease when compared to condition 5 ($p < 0.05$).*
MeanAP/MeanML, Mean distance of COP in the anteroposterior/mediolateral direction; VelAP/VelML, Mean velocity of COP in the anteroposterior/mediolateral direction; 95%Area, 95% confidence ellipse area of COP; MfAP/MfML, Mean rotational frequency of COP in the anteroposterior/mediolateral direction.

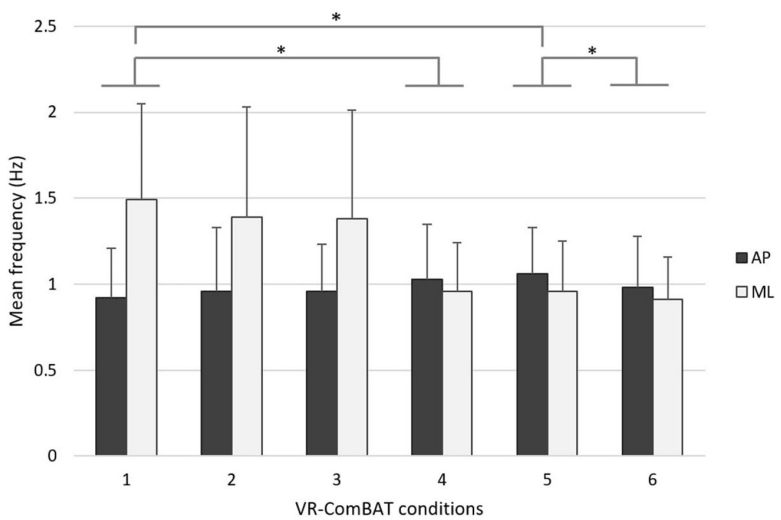

FIGURE 5 | Mean rotational frequency of COP in anteroposterior (black) and mediolateral (gray) directions across the 6 VR-ComBAT conditions. *Significant differences ($p < 0.05$).

presence (18.8 out of 25), involvement (11.3 out of 20), and experience realism (10.7 out of 20)]. The average total score of SUS was approximately 80 out of 100, which demonstrated high effectiveness, efficiency, and satisfaction levels of the VR-ComBAT. The high system usability of VR was also reported in a VR-based rehabilitation study (Meldrum et al., 2012).

The six conditions of the VR-ComBAT emulate an environment equivalent to the SOT. Combined, they are purported to evaluate the sensory systems involved in postural control. Comparing conditions 2, 4, and 5 versus condition 1, our findings are consistent with results from previous SOT studies in healthy younger and older adults (Cohen et al., 1996;

Pletcher et al., 2017). When the somatosensory system is confronted with a challenging environment (e.g., conditions 4 and 5), healthy young participants reweighted appropriately to their vision and vestibular systems to maintain postural control. The large effect sizes observed in condition 4 vs. 1 and condition 5 vs. 1 support postural control reliance on vision and vestibular systems, respectively (Pletcher et al., 2017). When comparing condition 6 (unstable surface with VR visual conflict) to condition 5 (unstable surface with blacked out VR surroundings), the significant decreased mean velocity and mean frequency indicate that blacking out the VR surroundings compromised postural control more so than providing conflicting visual information through a moving VR surround. Our results demonstrate that the perturbed somatosensory system might be compensated for by the visual-guided scene through the VR-ComBAT. Vision contributes to balance during quiet standing, and a previous study showed that individuals with impaired vision failed to maintain their postural stability in challenging conditions (Ray et al., 2008). To this end, future studies identifying the changes of COP-based measures in patients with sensory deficits using VR-ComBAT are warranted.

In addition to the findings in the AP direction, the COP-based measures in the ML direction (e.g., MeanML, VelML, and MfML) demonstrated significant changes in this study (e.g., conditions 2, 4, 5 vs. condition 1). Specifically, the change of mean COP frequency of this study is direction-dependent where the mean frequency increases in the AP direction while it decreases in the ML direction with respect to increased task difficulty (**Figure 5**). While confronted with a challenging environment, healthy young adults seem to restrict ML movement to maintain postural control. This direction-dependent phenomenon was in line with current evidence that additional energy expenditure, such as muscular effort, is required to maintain lateral stability during walking (Kuo and Donelan, 2010). More evidence is required to elucidate whether there is a relationship between COP frequency changes in different directions and energy expenditure. Future studies using the VR-ComBAT will examine whether this direction-dependent phenomenon of COP frequency alters in older adults or patients with deficits in sensory integration.

A previous study that integrated VR HMD with posturography provided similar conditions as the Equitest® SOT (Wittstein et al., 2020) and demonstrated a moderate reliability and a weak correlation between the developed VR SOT and the EquiTest® (Wittstein et al., 2020). The VR-ComBAT of this study emulates conditions that are equivalent to those in the EquiTest® as illustrated in **Figure 2**. In addition, our study provided a quantitative analysis of COP distance, velocity, area, and frequency in the anteroposterior and mediolateral direction. The importance of including multidirectional COP outcomes was illustrated in our direction-dependent phenomenon of frequency changes in the anteroposterior and mediolateral direction.

There are limitations to this proof-of-concept study. The current study included a relatively small number of healthy young adults. Therefore, we did not adjust for multiple comparisons in the *post hoc* analyses. Although we established the safety of the VR-ComBAT in healthy individuals, further studies are warranted to validate the VR-ComBAT in people with balance impairments. In addition, the balance testing conditions in the VR-ComBAT system were based on the testing conditions that originate from the EquiTest®. Although the current study demonstrated the face validity of the novel system, our new test requires validation against the EquiTest®. We list future directions of work to overcome the limitations observed in the current work and optimize the utilization of the VR-ComBAT. First, we plan to integrate the VR-ComBAT with a cognitive assessment to evaluate the effect of dual-tasking on reweighting for postural control. The eye-tracking integrated VR system such as HTC VIVE Pro Eye can be used to extract pupillary response, which is a valid measure of cognitive workload in demanding postural conditions (Orlosky et al., 2017). Second, we will employ the VR-ComBAT in older and/or patient populations to confirm the sensitivity of the VR-ComBAT in evaluating sensory organization of postural control. Third, not all clinical settings can afford a relatively expensive force plate system. One of the overarching goals of the VR-ComBAT development is to provide a cost-effective system. We developed the VR-ComBAT for research purposes. Thus, the cost of the current setup including force platform system ($10,000–$20,000) and VR HMD system ($500–$2,000) may be expensive for most clinics. However, we plan to create a clinically affordable VR-ComBAT by replacing the force plate with cost-effective COP measures such as Nintendo Wii Fit or gyroscope/accelerometers in smartphones. Lastly, our study found meaningful outcomes of COP changes in ML direction. Future VR-ComBAT conditions should include ML tilting in VR to further elucidate the effect of visual conflict on ML postural control.

In conclusion, this current proof-of-concept study demonstrates the safety, sense of presence, and face validity of the VR-ComBAT integrated with a COP measuring system.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by IRB at University of Kansas Medical Center. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

SM and HD designed the study. SM performed the experiments. SM, C-KH, MS, and HD analyzed the collected data. All authors wrote the manuscript, discussed the results, and commented on the manuscript.

REFERENCES

Alahmari, K. A., Marchetti, G. F., Sparto, P. J., Furman, J. M., and Whitney, S. L. (2014). Estimating postural control with the balance rehabilitation unit: measurement consistency, accuracy, validity, and comparison with dynamic posturography. *Arch. Phys. Med. Rehabil.* 95, 65–73. doi: 10.1016/j.apmr.2013.09.011

Alcock, L., O'brien, T. D., and Vanicek, N. (2018). Association between somatosensory, visual and vestibular contributions to postural control, reactive balance capacity and healthy ageing in older women. *Health Care Women Int.* 39, 1366–1380. doi: 10.1080/07399332.2018.1499106

Bangor, A., Kortum, P. T., and Miller, J. T. (2008). An empirical evaluation of the system usability scale. *Int. J. Hum. Comp. Interact.* 24, 574–594. doi: 10.1080/10447310802205776

Berg, K. O., Wood-Dauphinee, S. L., Williams, J. I., and Maki, B. (1992). Measuring balance in the elderly: validation of an instrument. *Can. J. Public Health* 83(Suppl. 2), S7–S11.

Błaszczyk, J. W., Orawiec, R., Duda-Kłodowska, D., and Opala, G. (2007). Assessment of postural instability in patients with Parkinson's disease. *Exp. Brain Res.* 183, 107–114. doi: 10.1007/s00221-007-1024-y

Brooke, J. (1996). "Sus: a "quick and dirty'usability," in *Usability Evaluation in Industry*, eds P. W. Jordan, B. Thomas, I. McLelland, and B. A. Weerdmeester (London: Taylor and Francis), 189.

Cano Porras, D., Sharon, H., Inzelberg, R., Ziv-Ner, Y., Zeilig, G., and Plotnik, M. (2019). Advanced virtual reality-based rehabilitation of balance and gait in clinical practice. *Ther. Adv. Chronic Dis.* 10:2040622319868379.

Cano Porras, D., Siemonsma, P., Inzelberg, R., Zeilig, G., and Plotnik, M. (2018). Advantages of virtual reality in the rehabilitation of balance and gait. *Syst. Rev.* 90, 1017–1025. doi: 10.1212/wnl.0000000000005603

Chang, E., Kim, H. T., and Yoo, B. (2020). Virtual reality sickness: a review of causes and measurements. *Int. J. Hum. Comput. Interact.* 36, 1658–1682. doi: 10.1080/10447318.2020.1778351

Chen, Y., Gao, Q., He, C. Q., and Bian, R. (2020). Effect of virtual reality on balance in individuals with Parkinson disease: a systematic review and meta-analysis of randomized controlled trials. *Phys. Ther.* 100, 933–945. doi: 10.1093/ptj/pzaa042

Cohen, H., Blatchly, C. A., and Gombash, L. L. (1993). A study of the clinical test of sensory interaction and balance. *Phys. Ther.* 73, 346–351; discussion 351–344.

Cohen, H., Heaton, L. G., Congdon, S. L., and Jenkins, H. A. (1996). Changes in sensory organization test scores with age. *Age Ageing* 25, 39–44. doi: 10.1093/ageing/25.1.39

Creath, R., Kiemel, T., Horak, F., Peterka, R., and Jeka, J. (2005). A unified view of quiet and perturbed stance: simultaneous co-existing excitable modes. *Neurosci. Lett.* 377, 75–80. doi: 10.1016/j.neulet.2004.11.071

Cronin, T., Arshad, Q., and Seemungal, B. M. (2017). Vestibular deficits in neurodegenerative disorders: balance, dizziness, and spatial disorientation. *Front. Neurol.* 8:538. doi: 10.3389/fneur.2017.00538

de Rooij, I. J., Van De Port, I. G., and Meijer, J. G. (2016). Effect of virtual reality training on balance and gait ability in patients with stroke: systematic review and meta-analysis. *Phys. Ther.* 96, 1905–1918. doi: 10.2522/ptj.20160054

Dennison, M. S., Wisti, A. Z., and D'zmura, M. (2016). Use of physiological signals to predict cybersickness. *Displays* 44, 42–52. doi: 10.1016/j.displa.2016.07.002

Gaerlan, M. G. (2010). *The Role of Visual, Vestibular, and Somatosensory Systems in Postural Balance*. Ph. D. thesis. Las Vegas, NV: University of Nevada.

Hein, D., Mai, C., and Hußmann, H. (2018). "The usage of presence measurements in research: a review," in *Proceedings of the International Society for Presence Research Annual Conference (Presence)*, (Prague: The International Society for Presence Research), 21–22.

Horak, F. B. (2006). Postural orientation and equilibrium: what do we need to know about neural control of balance to prevent falls? *Age Ageing* 35(Suppl. 2), ii7–ii11.

Howarth, P. A., and Costello, P. J. (1997). The occurrence of virtual simulation sickness symptoms when an HMD was used as a personal viewing system. *Displays* 18, 107–116. doi: 10.1016/s0141-9382(97)00011-5

Ivanenko, Y., and Gurfinkel, V. S. (2018). Human postural control. *Front. Neurosci.* 12:171. doi: 10.3389/fnins.2018.00171

Jinjakam, C., and Hamamoto, K. (2012). "Simulator sickness in immersive virtual environment," in *Proceedings of the 5th 2012 Biomedical Engineering International Conference*, Muang, 1–4.

Kennedy, R. S., Lane, N. E., Berbaum, K. S., and Lilienthal, M. G. (1993). Simulator sickness questionnaire: an enhanced method for quantifying simulator sickness. *Int. J. Aviat. Psychol.* 3, 203–220. doi: 10.1207/s15327108ijap0303_3

Kim, K., Rosenthal, M. Z., Zielinski, D. J., and Brady, R. (2014). Effects of virtual environment platforms on emotional responses. *Comput. Methods Programs Biomed.* 113, 882–893. doi: 10.1016/j.cmpb.2013.12.024

Kuo, A. D., and Donelan, J. M. (2010). Dynamic principles of gait and their clinical implications. *Phys. Ther.* 90, 157–174. doi: 10.2522/ptj.20090125

Leddy, A. L., Crowner, B. E., and Earhart, G. M. (2011). Utility of the Mini-BESTest, BESTest, and BESTest sections for balance assessments in individuals with Parkinson disease. *J. Neurol. Phys. Ther.* 35, 90–97. doi: 10.1097/npt.0b013e31821a620c

Lubetzky, A. V., Harel, D., Kelly, J., Hujsak, B. D., and Perlin, K. (2019). Weighting and reweighting of visual input via head mounted display given unilateral peripheral vestibular dysfunction. *Hum. Mov. Sci.* 68:102526. doi: 10.1016/j.humov.2019.102526

Lubetzky, A. V., Kary, E. E., Harel, D., Hujsak, B., and Perlin, K. (2018). Feasibility and reliability of a virtual reality oculus platform to measure sensory integration for postural control in young adults. *Physiother. Theory Pract.* 34, 935–950. doi: 10.1080/09593985.2018.1431344

Mancini, M., and Horak, F. B. (2010). The relevance of clinical balance assessment tools to differentiate balance deficits. *Eur. J. Phys. Rehabil. Med.* 46, 239–248.

Massetti, T., Da Silva, T. D., Crocetta, T. B., Guarnieri, R., De Freitas, B. L., Bianchi Lopes, P., et al. (2018). The clinical utility of virtual reality in neurorehabilitation: a systematic review. *J. Cent. Nerv. Syst. Dis.* 10:1179573518813541.

Meldrum, D., Glennon, A., Herdman, S., Murray, D., and Mcconn-Walsh, R. (2012). Virtual reality rehabilitation of balance: assessment of the usability of the Nintendo Wii® Fit Plus. *Disabil. Rehabil. Assist. Technol.* 7, 205–210. doi: 10.3109/17483107.2011.616922

Nashner, L. M., and Peters, J. F. (1990). Dynamic posturography in the diagnosis and management of dizziness and balance disorders. *Neurol. Clin.* 8, 331–349. doi: 10.1016/s0733-8619(18)30359-1

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., et al. (2005). The montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment. *J. Am. Geriatr. Soc.* 53, 695–699. doi: 10.1111/j.1532-5415.2005.53221.x

Orlosky, J., Itoh, Y., Ranchet, M., Kiyokawa, K., Morgan, J., and Devos, H. (2017). Emulation of physician tasks in eye-tracked virtual reality for remote diagnosis of neurodegenerative disease. *IEEE Trans. Vis. Comput. Graph.* 23, 1302–1311. doi: 10.1109/tvcg.2017.2657018

Panahi, S. M., Fathi, A. A., Azad, F. P., and Montazer, G. A. (2009). Reliability and validity of igroup presence questionnaire (ipq). *J. Behav. Sci.* 3, 27–34.

Pletcher, E. R., Williams, V. J., Abt, J. P., Morgan, P. M., Parr, J. J., Wohleber, M. F., et al. (2017). Normative data for the NeuroCom sensory organization test in US military special operations forces. *J. Athl. Train.* 52, 129–136. doi: 10.4085/1062-6050-52.1.05

Prieto, T. E., Myklebust, J. B., Hoffmann, R. G., Lovett, E. G., and Myklebust, B. M. (1996). Measures of postural steadiness: differences between healthy young and elderly adults. *IEEE Trans. Biomed. Eng.* 43, 956–966. doi: 10.1109/10.532130

Ray, C. T., Horvat, M., Croce, R., Mason, R. C., and Wolf, S. L. (2008). The impact of vision loss on postural stability and balance strategies in individuals with profound vision loss. *Gait Posture* 28, 58–61. doi: 10.1016/j.gaitpost.2007.09.010

Reynard, F., Christe, D., and Terrier, P. (2019). Postural control in healthy adults: determinants of trunk sway assessed with a chest-worn accelerometer in 12 quiet standing tasks. *PLoS One* 14:e0211051. doi: 10.1371/journal.pone.0211051

Rosenthal, R., Cooper, H., and Hedges, L. (1994). Parametric measures of effect size. *Handb. Res. Synth.* 621, 231–244.

Saffer, M., Kiemel, T., and Jeka, J. (2008). Coherence analysis of muscle activity during quiet stance. *Exp. Brain Res.* 185, 215–226.

Shumway-Cook, A. (2011). *Motor control*. Alphen aan den Rijn: Wolters Kluwer press.

Shumway-Cook, A., and Horak, F. B. (1986). Assessing the influence of sensory interaction of balance. Suggestion from the field. *Phys. Ther.* 66, 1548–1550. doi: 10.1093/ptj/66.10.1548

Suttanon, P., Hill, K. D., Dodd, K. J., and Said, C. M. (2011). Retest reliability of balance and mobility measurements in people with mild to moderate Alzheimer's disease. *Int. Psychogeriatr.* 23, 1152–1159. doi: 10.1017/s1041610211000639

Thomas, S. D., Hathaway, D. K., and Arheart, K. L. (1992). Face validity. *West. J. Nurs. Res.* 14, 109–112.

Trueblood, P. R., Rivera, M., Lopez, C., Bentley, C., and Wubenhorst, N. (2018). Age-based normative data for a computerized dynamic posturography system that uses a virtual visual surround environment. *Acta Otolaryngol.* 138, 597–602. doi: 10.1080/00016489.2018.1429653

Visser, J. E., Carpenter, M. G., Van Der Kooij, H., and Bloem, B. R. (2008). The clinical utility of posturography. *Clin. Neurophysiol.* 119, 2424–2436.

Wittstein, M. W., Crider, A., Mastrocola, S., and Gonzalez, M. G. (2020). Use of virtual reality to assess dynamic posturography and sensory organization: instrument validation study. *JMIR Serious Games* 8:e19580. doi: 10.2196/19580

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

frontiers in Neurology

SYSTEMATIC REVIEW
published: 09 September 2021
doi: 10.3389/fneur.2021.720662

Physical and Psychological Factors Associated With Walking Capacity in Patients With Lumbar Spinal Stenosis With Neurogenic Claudication: A Systematic Scoping Review

Marième Houle[1]*, *Jean-Daniel Bonneau*[2], *Andrée-Anne Marchand*[2] and *Martin Descarreaux*[3]

[1] Department of Anatomy, Université du Québec à Trois-Rivières, Trois-Rivières, QC, Canada, [2] Department of Chiropractic, Université du Québec à Trois-Rivières, Trois-Rivières, QC, Canada, [3] Department of Human Kinetics, Université du Québec à Trois-Rivières, Trois-Rivières, QC, Canada

Objective: The purpose of this study was to evaluate the current state of scientific knowledge regarding physical and psychological factors associated with walking capacity in patients with lumbar spinal stenosis (LSS) with neurogenic claudication.

Design: Systematic scoping review.

Literature Search: We searched CINAHL (Cumulative Index to Nursing and Allied Health Literature), MEDLINE, Cochrane, PsycINFO, and SPORTDiscus databases.

Study Selection Criteria: Cohorts and cross-sectional studies reporting on associations between physical or psychological factors and impaired walking capacity in patients with symptomatic LSS were included.

Data Synthesis: Data were synthetized to identify associations between physical or psychological factors and either walking capacity, gait pattern characteristics, or functional tasks.

Results: Twenty-four studies were included. Walking capacity was significantly correlated with several pain outcomes, disability, estimated walking distance, and cross-sectional area of the lumbar spine. Gait pattern characteristics such as speed and stride were strongly and positively correlated with disability outcomes. Functional tasks were significantly correlated with lower back and upper limb disability, lower limb endurance strength, ranges of motion, and speed. Associations with psychological factors were mostly conflicting except for the Rasch-based Depression Screener and the Pain Anxiety Symptom Scale (PASS-20) questionnaire that were associated with a decreased performance in functional tasks.

Conclusion: Physical and psychological factors that are associated with walking capacity in patients with symptomatic LSS were identified. However, many associations reported between physical or psychological factors and walking capacity were conflicting, even more so when correlated with walking capacity specifically.

Keywords: lumbar spinal stenosis, neurogenic claudication, walking capacity, gait pattern characteristics, functional task

OPEN ACCESS

Edited by:
Francesco Monaco,
Azienda Sanitaria Locale Salerno, Italy

Reviewed by:
Koji Otani,
Fukushima Medical University, Japan
Stanley Golovac,
Florida Pain TPI, United States

***Correspondence:**
Marième Houle
marieve.houle@uqtr.ca

Specialty section:
This article was submitted to Neurorehabilitation, a section of the journal Frontiers in Neurology

Received: *08 June 2021*
Accepted: *10 August 2021*
Published: *09 September 2021*

Citation:
Houle M, Bonneau JD, Marchand AA and Descarreaux M (2021) Physical and Psychological Factors Associated With Walking Capacity in Patients With Lumbar Spinal Stenosis With Neurogenic Claudication: A Systematic Scoping Review. Front. Neurol. 12:720662. doi: 10.3389/fneur.2021.720662

INTRODUCTION

Symptomatic lumbar spinal stenosis (LSS), characterized by a limited walking capacity due to leg pain, is a leading cause of disability in the elderly (1, 2). Narrowing of the lumbar spinal canal or lateral foramina, as well as compression or decreased blood flow to the nerve roots (3, 4) are considered the main causes of pain in this musculoskeletal condition. Lumbar spinal stenosis is affecting between 11 and 39% (5, 6) of the global population, especially people over the age of 65 (6, 7). The acquired form of LSS arises from degenerative changes, including disc degeneration (herniation or bulging), hypertrophy of the ligamentum flavum, and spondylolisthesis and/or facet osteoarthritis (3, 4, 8) and can involve the central canal, lateral recess, foramina, or any combination of these anatomical sites (8). Congenital LSS is due to abnormalities during development, leading up to smaller pedicles length, which directly affects the antero-posterior diameter of the spinal canal (9).

In patients with LSS, self-reported symptoms combined with a physical examination represent the main assessment components of the clinical portrait severity, considering that symptoms and associated disability do not always correlate with results from magnetic resonance imaging (MRI). Advanced imaging provides information on the presence and extent of lumbar spine degenerative changes and on the lumbar spinal canal size, but does not translate information on functional capacity (6). Indeed, a number of patients will show clear and severe signs of stenosis on imaging but will experience few or no symptoms. Commonly reported symptoms of LSS include leg pain, numbness, cramps, fatigue, and weakness (8, 10). These symptoms can be grouped under one appellation: neurogenic claudication (NC). The presence of NC is modulated by the patient's posture, as it is brought on by lumbar extension when standing or walking and relieved by lumbar flexion (i.e., sitting or bending forward) (8).

Neurogenic claudication is triggered by performing daily activities that require prolonged standing postures such as walking, and patients often face a decrease in quality of life (QoL) due to important walking and functional limitations. The assessment of walking limitations plays a central role in LSS management, both in the decision-making process regarding the diagnosis (11) and treatment options (12). Most recent studies evaluating treatment effects in patients with LSS have measured walking abilities using different assessment methods. Some of these studies focused on walking distance (13–15), while others focused on walking time (16, 17), or both (18, 19) to report on walking capacity. Indeed, severe symptoms combined with a decrease in walking capacity, and subsequently in QoL, prompt neurosurgeons to opt for surgery in patients with LSS (20, 21).

Walking impairment is a major issue in LSS, and many physical and psychological factors are related to this decrease in functional capacity. Several gait measures such as step length, cadence, step width, and gait cycle have been assessed in LSS patients, but it is not clear if and how they relate to the decline in walking capacity. It is also known that walking limitations can negatively influence or be influenced by psychological factors such as a perceived low QoL and self-efficacy, and increased anxiety and kinesiophobia (22, 23). Assessing physical and psychological factors may provide relevant information that would improve our understanding of how LSS affects daily activities.

The purpose of this study was to evaluate the current state of scientific knowledge regarding physical and psychological factors associated with walking capacity in patients with LSS and associated NC.

METHODS

As systematic scoping reviews are used to inform future research directions, this study design was deemed the most appropriate to capture information from heterogeneous studies, map existing literature and identify knowledge gaps (24). This scoping review was based on the framework of Levac et al. using a 5-step review method (25) and on the framework of Peters et al. for the systematic aspect of the study conduct (24). This study was registered on Open Science Framework (https://osf.io/6az7c/?view_only=15ad45d1f1f14517b3706b154af12bb6).

Step 1: Identifying the Research Question

This scoping review was conducted to answer the following question: What are the physical and psychological factors associated with walking capacity in patients with LSS and associated NC?

The main focus of this systematic scoping review was walking capacity in patients with LSS and associated NC. Exploring associations between physical or psychological factors and walking capacity or performance in functional tasks should provide critical information regarding the impact of LSS on daily functioning. Interventions targeting physical and psychological factors associated with the decline in walking capacity could improve patients' walking capacity and QoL and support surgical decision-making.

Step 2: Identifying Relevant Studies

The search strategy was elaborated in collaboration with a university librarian and was conducted using CINAHL (Cumulative Index to Nursing and Allied Health Literature), MEDLINE, Cochrane, PsycINFO, and SPORTDiscus databases from inception to October 4, 2019. Then, an update of the literature was completed on June 18, 2020. A combination of keywords and MeSH terms was used to identify relevant studies. The lead investigator (MH) conducted the literature search. The search strategy was first developed for MEDLINE and adapted to other databases when needed (see **Supplement Material 1**). Other sources such as Google Scholar and reference lists of relevant studies were hand-searched to ensure a comprehensive overview of the subject. An EndNote library (version X9, Clarivate Analytics, Boston, MA, USA) was created to import all citations from the search strategy. Then, all duplicates were identified and removed.

Step 3: Study Selection

Definitions of Key Concepts

Symptomatic LSS was defined as back and/or leg pain causing NC in patients diagnosed with degenerative LSS. The targeted outcome was walking capacity which was considered from two

different perspectives: walking capacity defined as a distance or time spent walking, and walking capacity defined as performance during a functional task that repetitively involve lower limbs and/or trunk movement (e.g., the Timed Up and Go test or stairs climbing). Associated factors of walking capacity were regarded as either physical or psychological. Physical factors were divided into patient-reported outcome measures (PROMs) [e.g., pain, disability and QoL] and objectives measures [e.g., gait pattern characteristics (e.g., speed, cadence, and step width), lower limb strength and range or motion (ROM)] while psychological factors of interest included anxiety, depression, kinesiophobia, frailty, and self-efficacy.

Inclusion and Exclusion Criteria

To be included in this scoping review, studies had to be limited to human participants and be published in peer-reviewed scientific journals in either French, English, or Spanish language. Study designs were limited to cohort, and cross-sectional studies. Randomized controlled trials were also considered provided that they present baseline data of participants with LSS and associated NC and reported on correlation or regression prior to the beginning of the intervention. In addition, assessments had to include at least one physical and/or psychological outcome measures. To be include, studies needed to fulfill inclusion criteria regarding the specific populations (P), intervention (I), and outcomes measures (O) that are presented in **Table 1**. In addition, studies that included participants with congenital LSS, scoliosis, or vascular claudication were excluded. The following types of publication were also excluded: validation study, case study, cases series, systematic review and meta-analysis, gray literature, and governmental documents.

Screening

All potentially eligible articles were independently screened by a pair of reviewers (MH, MERP) in two phases, using a standardized Excel spreadsheet. In phase one screening, titles and abstracts were classified as relevant, possibly relevant, or irrelevant according to the eligibility criteria. Then during phase two screening, the full text of possibly relevant articles was reviewed by the same pair of reviewers for final determination of eligibility. Reviewers discussed disagreement to reach consensus for both phases of screening and a third independent reviewer (AAM) was consulted to achieve consensus if needed.

Step 4: Charting the Data

The following descriptive variables were extracted from all relevant studies using a standardized extraction form: authors, year of publication, title, country, study design, sample size, definitions of both LSS and NC, description of the study population (number of participants with LSS, LSS type, age, and gender ratio), independent variables, dependent variables, and key findings from study results. A pair of researchers independently extracted data (MH, JDB) and if necessary, a third person (AAM) was involved to resolve disagreements.

Step 5: Collating, Summarizing, and Reporting Results

Study Designs and Participants

Data regarding study designs, sample sizes, and patients' characteristics were summarized to provide an overall picture of the populations studied.

Quality Assessment

Quality assessment of all eligible studies was independently completed by two reviewers (MH, JDB) using the Appraisal tool for Cross-sectional Studies (AXIS) (26). When a disagreement between the two reviewers occurred, a third person (AAM) was involved to reach consensus. The AXIS tool contains 20 questions that address three different domains: study design (7 questions), study quality (7 questions) and risk of bias (6 questions). Each question is answered by either "yes" (1 point), "no" (0 point), or "do not know" (0 point). A sum of all "yeses" is calculated to provide an overall score with higher scores indicating higher quality. As none of the studies reported a description of the non-responders (question 7), question 14 ("If appropriate, was information about non-responders described?") became non-applicable and therefore was removed from the quality assessment checklist, bringing the maximum possible score to 19. Furthermore, question 19 ("Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the result?") was given one point when it was specified that there were no conflicts of interest.

TABLE 1 | Inclusion criteria regarding population, intervention, and outcomes measures.

Inclusion criteria	P	I	C	O
	• Patients with LSS: Localization: - Central - Foraminal - Lateral • With or without spondylolisthesis • Coexisting LSS types (e.g., central + foraminal) • Presenting with NC • Having at least 18 years old	• Associations provided before any medical intervention is initiated • Data collected during one of these situations: - Walking - Climbing stairs - Running - Functional tasks	• Non-applicable	• Physical and psychological factors related to: - Walking capacity - Functional tasks - Gait pattern characteristics

If there was a mixed sample (e.g., LSS and healthy participants), the study was kept only if data from patients with LSS could be extracted separately.
P, Population; I, Intervention; C, Comparison; O, Outcome measures; LSS, lumbar spinal stenosis; NC, neurogenic claudication.

Results Organization

Results were first organized into two broad categories based on the nature of the reported associations. The categories were defined as follow: associations in relation to [1] walking capacity, and [2] functional tasks. Then, within each category, results were organized based on outcome measure types (i.e., PROMs, objective outcome measures, and any other relevant outcome whenever applicable).

RESULTS

The initial literature search identified 6,034 possible studies for inclusion in the scoping review. Following the removal of duplicates ($n = 1{,}665$), 4,369 studies remained. Initial screening of titles and abstracts resulted in the exclusion of 4315 articles that did not meet inclusion criteria. Out of the remaining 54 full-text articles, 21 fulfilled the inclusion criteria. Frequent updates of the search strategy were conducted during the review process. In light of the last update conducted on July 15, 2021, three additional articles fulfilling inclusion criteria were found bringing the final number of included studies to 24. All studies were published between 2007 and 2020 from 11 different countries over 3 continents (see **Supplement Material 2** *for more details*). **Figure 1** presents the study selection flowchart.

Participants

Out of the 24 studies, seventeen were cross-sectional studies, five were prospective observational studies, one was a secondary analysis of a RCT, and one was a retrospective observational study. Sample sizes ranged from 12 to 1009 participants. In

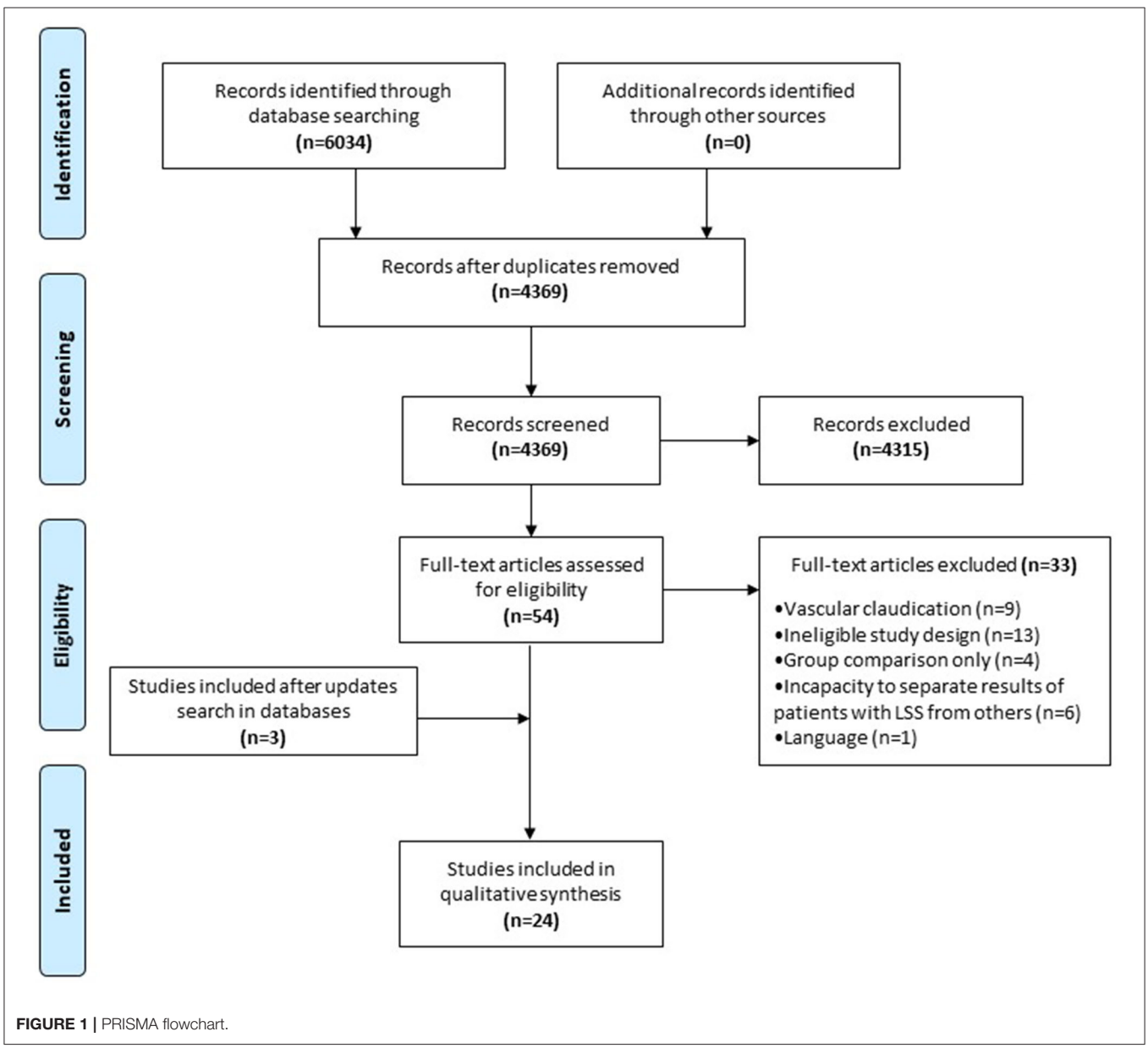

FIGURE 1 | PRISMA flowchart.

addition, out of the 2,973 participants included in the 24 studies, 1,694 had symptomatic LSS with NC. In most studies ($n = 17$), LSS was diagnosed using a combination of clinical assessment such as patient's history and/or physical examination, and findings of MRI. Regarding NC, only seven studies described NC as pain, numbness, weakness, or tingling in the lower extremity brought on by lumbar extension, standing, or walking. Based on criteria provided for inclusion of participants (or introduction section when inclusion criteria prevented the definitive identification of LSS subtypes), 974 presented with central LSS, 246 presented with combined central LSS and spondylolisthesis, 66 presented with either central or foraminal stenosis, 54 with either central or lateral stenosis, 49 with either central LSS or a combination of central and foraminal stenosis or lateral stenosis and 14 presented with lateral LSS. Finally, there were 291 patients for which the exact LSS type (e.g., central) was not explicitly described. Mean age of participants ranged from 58 to 76.9 years old across studies. Extracted data regarding population are presented in **Supplement Material 2**.

Quality Assessment

The 24 studies were assessed for quality using the AXIS tool. Two studies (27, 28) scored between 6 and 10, 14 studies (15, 19, 21, 29–39) scored between 11 and 15, and 8 studies (40–47) scored between 16 and 19. The items from the AXIS tool are reported in **Supplement Material 3**.

Associations

Surprisingly, no study investigated associations between gait pattern characteristics and walking capacity or functional tasks. However, a few studies reported associations between either physical or psychological factors and gait pattern characteristics. Considering that gait pattern characteristics do have a direct impact on walking capacity, these unplanned associations have been extracted and are now presented as a third category of associations along with walking capacity and functional tasks. All reported associations (significant or not) between either physical or psychological factors, and measures of walking capacity, functional tasks, or gait pattern characteristics are presented in **Supplementary Table 1**.

There was significant heterogeneity within both PROMs and objective measures used to assess physical and psychological factors for each category of outcome measures among the studies. **Figure 2** illustrates the range of outcome measures reported.

As a large range of associated factors were retrieved from the 24 studies, only significant associations with walking capacity, functional tasks, and gait pattern characteristics are reported herein. Additional details regarding non-significant associations are reported in **Supplement Material 4**. All associations are illustrated in **Figure 3**.

Physical and Psychological Factors Associated With Walking Capacity

PROMs

Pain. Overall, conflicting results were found based on the four studies reporting on the association between leg and/or back pain and walking capacity (distance or time). More specifically, Ishimoto et al. reported a weak positive association between symptomatic LSS (lower limb and/or buttock pain) and the 6-m walking time at maximal pace (vs. usual pace) (31). Tomkins-Lane and Battie (15) reported moderate positive correlations between walking distance and number of years with back pain and number of years with leg pain. They also reported moderate negative associations between walking capacity and intensity of leg pain before walking, and the items 8 (pain and discomfort over the past week affecting activities) and 15 (pain and discomfort over the past week requiring medication) of the Health Utilities Index Mark 3 (HUI) questionnaire (15). The other two studies did not report significant associations between pain and walking capacity (28, 40).

Disability. Overall, conflicting results were found based on the six studies reporting on the association between disability and walking capacity (distance or time).

Three studies (28, 40, 44) measured disability using the Quebec Back Pain Disability Scale (QBPDS), of which only one showed a strong negative correlation between the total QBPDS score and walking distance (40). When looking at the questionnaire individual subscales, four (walk, reach, run, and groceries) were strongly and negatively correlated with total walking distance and one (stand) was strongly and negatively correlated with walking time to first symptoms.

All four studies using the Swiss Spinal Stenosis Questionnaire found moderate to strong negative correlations with walking capacity (15, 40, 41, 46). Specifically, Drury et al. reported a moderate association between walking distance and the SSSQ total score. Regarding the SSSQ individual subscales, results among the four studies were conflicting. Drury et al. reported moderate to strong negative correlations between walking capacity and the physical function and each component of the symptom subscale (pain, sensory and neuroischemic) (41). Thornes et al. reported a moderate negative correlation between walking capacity and the physical function subscale and Tomkins and Battie reported a moderate negative correlation between walking capacity and the symptom subscale. However, two studies also reported no correlation between walking capacity and some SSSQ subscales (40, 46).

All three studies using the Oswestry Disability Index (ODI) found weak to strong correlations with total walking distance (15, 40, 44). However, Conway et al. reported a non-significant correlation between the ODI and walking capacity regarding time to first symptoms (40).

Quality of Life. Overall, conflicting results were found based on the five studies reporting on the association between quality of life and walking capacity (distance or time) (15, 37, 40, 41, 44).

All three studies reporting on QoL using the 36-item Short Form Health Survey (SF-36) reported at least one significant associations of varying strength with walking distance (37, 40, 41). Of these, one reported a strong positive correlation between SF-36 and walking distance (41). When looking at the questionnaire individual subscales, three studies reported moderate to strong positive correlations between the physical functioning (PF) subscale and walking distance (37, 40, 41). Moreover, Drury et al. (41) reported moderate positive correlations between four of the subscales (role physical, bodily

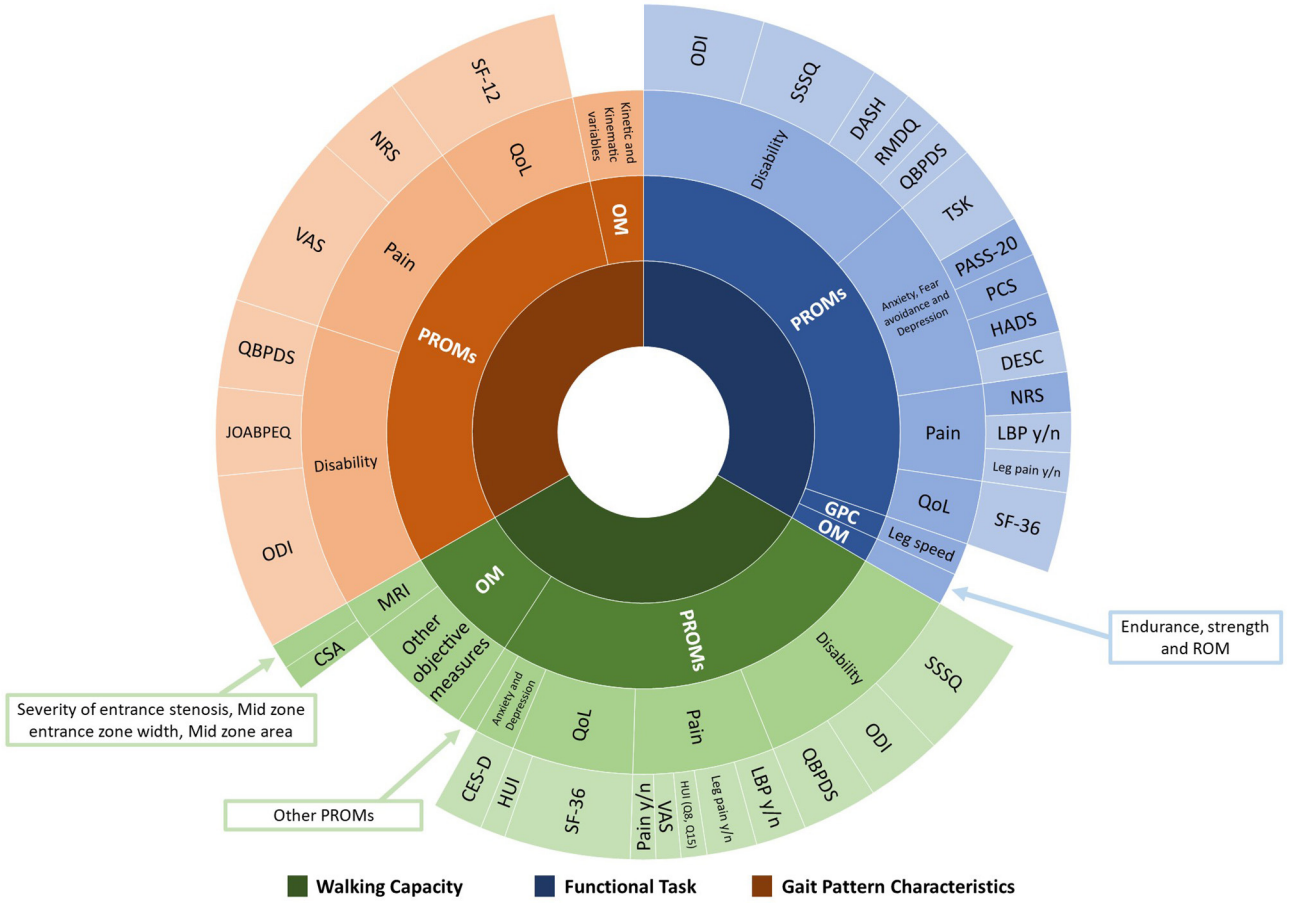

FIGURE 2 | Range and proportion of tools used to assess physical and psychological factors associated with walking capacity, functional task, and gait pattern characteristics. PROMs, Patient-Reported Outcome Measures; OM, Objective Measures; GPC, Gait Pattern Characteristics; QoL, Quality of Life; MRI, Magnetic Resonance Imaging; ODI, Oswestry Disability Index; SSSQ, Swiss Spinal Stenosis Questionnaire; DASH, Disability of the Arm, Shoulder and Hand questionnaire; RMDQ, Roland-Morris Disability Questionnaire; QBPDS, Quebec Back Pain Disability Scale; TSK, Tampa Scale of Kinesiophobia; PASS-20, Pain Anxiety Symptoms Scale; PCS, Pain Catastrophizing Scale; HADS, Hospital Anxiety and Depression Scale; DESC, Rasch-based Depression Screener; NRS, Numeric Rating Scale; LBP, Low Back Pain; SF-36, 36-item Short Form Health Survey; SF-12, Medical Outcomes Short-Form 12; HUI, Health Utilities Index Mark 3; VAS, Visual Analog Scale; CES-D, Center of Epidemiological Studies Depression Scale; CSA, Cross-sectional area; JOABPEQ, Japanese Orthopedic Association Back Pain Evaluation Questionnaire.

pain, general health index and social functioning) and walking distance whereas they reported a weak positive correlation between the vitality subscale and walking distance. Out of the two studies reporting on the association between the mental health subscale and walking distance (37, 41), only one reported a moderate positive correlation (37). One study used a shorter version of the SF-36 (SF-12) and reported no significant association (44). Finally, one study reported a moderate positive correlation between health-related QoL using the HUI questionnaire and walking capacity (15).

Anxiety and Depression. One study assessed depression using the CES-D and reported no significant correlation between depression status and walking distance (19).

Estimated Walking Distance. One study assessed estimated walking distance and showed a strong significant correlation between this estimated and measured walking distances (40).

Objective Outcome Measures

MRI Findings. Overall, conflicting results were found based on the three studies reporting on the association between MRI characteristics and walking capacity (distance or time) (19, 27, 33). One study reported a negative association between the cross-sectional area of the dural tube measured at L1/L2 and walking distance (19). Two studies reported no significant correlation between MRI findings and walking distance (27, 33).

Other Objective Outcome Measures. Overall, conflicting results were found based on the six studies reporting on the association between other objective measures and walking capacity (15, 19, 30, 36, 40). Specifically, one study reported a strong positive correlation between maximum time of continuous activity per day over a 7-day period (at a minimum of low intensity) and walking distance (40), and another study reported a moderate positive correlation between daily step count and walking

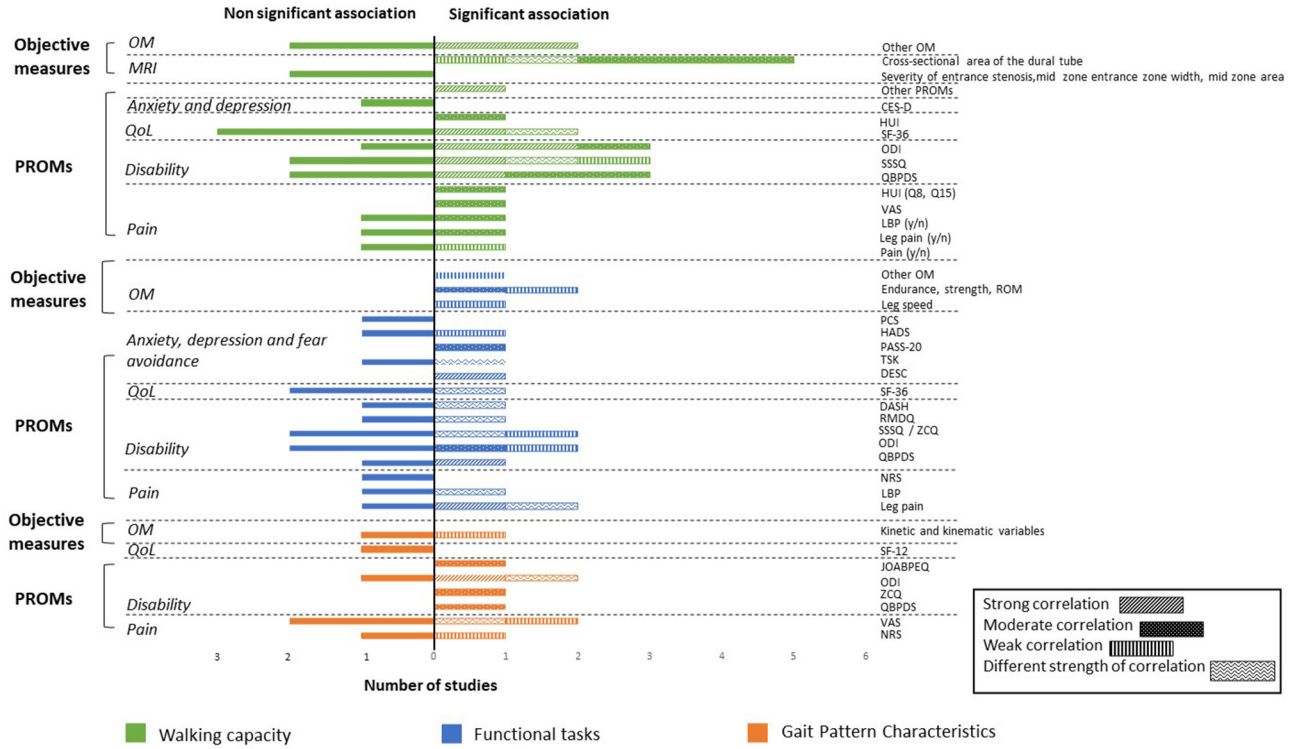

FIGURE 3 | Associations between walking capacity, gait pattern characteristics, functional tasks, and PROMs and objective measures expressed in number of studies. PROMs, Patient-Reported Outcome Measures; OM, Objective Measures; QoL, Quality of Life; MRI, Magnetic Resonance Imaging; CES-D, Center of Epidemiological Studies Depression Scale; HUI, Health Utilities Index Mark 3; SF-36, 36-item Short Form Health Survey; SF-12, Medical Outcomes Short-Form 12; ODI, Oswestry Disability Index; SSSQ, Swiss Spinal Stenosis Questionnaire; ZCQ, Zurich Claudication Questionnaire; QBPDS, Quebec Back Pain Disability Scale; LBP, Low Back Pain; VAS, Visual Analog Scale; ROM, Range of Motion; PASS-20, Pain Anxiety Symptoms Scale; PCS, Pain Catastrophizing Scale; HADS, Hospital Anxiety and Depression Scale; TSK, Tampa Scale of Kinesiophobia; DESC, Rasch-based Depression Screener; DASH, Disability of the Arm, Shoulder and Hand questionnaire; RMDQ, Roland-Morris Disability Questionnaire; NRS, Numeric Rating Scale; JOABPEQ, Japanese Orthopedic Association Back Pain Evaluation Questionnaire.

distance (35). One study showed a moderate negative correlation between balance problems and walking capacity (15). One study reported a negative association between BMI and walking distance, and a positive association between functional status (combination of tests) and walking distance (19). One study reported a strong negative correlation between trunk postural sway and maximum walking distance (36). Two of these studies also showed no significant association between other objectives measures and walking capacity (36, 40). Finally, one study reported a moderate negative correlation between handgrip strength and walking time and a weak positive correlation between handgrip strength and walking distance (30).

Physical and Psychological Factors Associated With Functional Tasks

PROMs

Pain. Overall, conflicting results were found based on the four studies reporting on the association between pain outcomes and functional tasks (31, 35, 38, 40). More specifically, strong positive correlations were found between leg pain severity and overall activity per day measured with an activity monitor, as well as maximum time of continuous activity per day (40).

Pryce et al. reported moderate to strong correlations between back pain (intensity and related function), leg pain (related function), and physical activity (volume and duration). Physical activity intensity was not associated with either back or leg pain intensity and function. They also reported moderate to strong negative correlations between back or leg pain intensity and bout length or maximum bout length of meaningful activity. However, back pain intensity was negatively correlated with bout length and maximum bout length only at meaningful physical activity intensity, while leg pain intensity was only correlated at moderate intensity (between 1.5 and 2.99 METs) (38). All other associations between pain and functional tasks were non-significant (31, 35).

Disability. Overall, conflicting results were found based on the five studies reporting on the association between disability and functional tasks (32, 35, 38, 40, 46, 47).

Conway et al. reported strong negative correlations between disability, measured using the run subscale of the QBPDS questionnaire, and overall activity per day, as well as

between disability and time of continuous activity. All other correlations between the QBPDS and functional tasks were not significant (40).

Four studies conducted correlation analyses between the ODI and functional tasks (32, 38, 40, 47). Results from Pryce et al. (38) showed moderate to strong negative correlations between disability and physical activity volume, intensity, and duration. They also showed moderate to strong negative correlations between disability and maximum bout length at meaningful intensity and at moderate intensity during ambulatory behavior. The ODI was only correlated with bout length during ambulatory behavior at moderate intensity. Thornes et al. reported an association between stability in gait and the total ODI score. All other associations between ODI and functional tasks were not significant (32, 40).

The Roland-Morris Disability Questionnaire (RMDQ) was used in the study by Pryce et al. (38) to assess disability. In this study, authors reported moderate to strong negative correlations between disability and physical activity volume, intensity, and duration. They also reported moderate to strong negative correlations between disability and bout length and maximum bout length during ambulatory behavior (38).

Three studies reported on the correlation between the SSSQ [also known as the Zurich Claudication Questionnaire (ZCQ)] total score or subscales and functional tasks (35, 46, 47). The results of Thornes et al. (46) showed negative moderate correlations between the symptoms subscale and the 30-second Sit-to-Stand test, and the One Leg Stance test while they showed a positive moderate correlation between the symptoms subscale and the stair climbing test. The authors also reported a moderate correlation between the physical function subscale and stair climbing (46) and a weak association between the physical function subscale and the score of the Mini-BESTest (47). However, Minetama et al. (35) reported non-significant correlations between daily step count and the symptom subscale or the physical function subscale of the SSSQ.

Finally, Price et al. reported moderate to strong negative correlations between disability measured using the DASH questionnaire and physical activity volume, intensity, and duration, as well as bout length and maximum bout length during ambulatory behavior (38).

Quality of Life. Overall, conflicting results were found based on the two studies reporting on the association between QoL and functional tasks (38).

Pryce et al. reported moderate to strong positive correlations between the SF-36 total score and physical activity (volume, duration, intensity), and ambulatory behavior (bout length and maximum bout length) at both meaningful and moderate intensity (38). Further details about correlations between functional task and all SF-36 subscales are presented in **Supplementary Table 1**.

Depression, Anxiety, and Fear Avoidance. Two studies reported on the association between either depression or fear avoidance and functional tasks (21, 35). Depression was strongly and negatively correlated with the patient's participation in social, daily and work-related activities using the Aachen Activity and Participation Index (AAPI). Depression was also moderately and positively correlated with lower extremity function using the RehaCAT lower extremity subscale and with activities of daily living when using the RehaCAT lower extremity subscale. Minetama et al. (35) reported moderate negative correlations between daily step count and the total score, the cognitive anxiety subscale, the escape/avoidance subscale, and the fear subscale of the Pain Anxiety Symptom Scale (PASS-20). The authors also reported a weak negative correlation between daily step count and depression as measured by the Hospital Anxiety and Depression Scale (HADS) but no correlation with anxiety also measured by the HADS (35).

Furthermore, two studies reported on the association between kinesiophobia and functional tasks (21, 35). The somatic focus subscale of the Tampa Scale of Kinesiophobia (TSK) was strongly and positively correlated with the RehaCAT lower extremity subscale while the activity avoidance subscale was moderately and positively correlated with the RehaCAT lower extremity subscale. The score of the RehaCAT activities of daily living subscale was moderately and positively correlated with the somatic focus and the activity avoidance subscales of the TSK (21). The correlation between daily step count and kinesiophobia was not significant (35).

Finally, one study reported a correlation between daily step count and pain catastrophizing as measured with the Pain Catastrophizing Scale (PCS) (35). However, the correlations between each subscale of the PCS were not significantly correlated with daily step count.

Objective Outcome Measures

Other Objective Outcome Measures. Two studies reported on the associations between other objective measures and functional tasks performance. Schmidt et al. (39) reported weak associations between either trunk extensor muscle endurance, leg strength asymmetry, or leg speed during a leg press and the Short Physical Performance Battery score. They also reported weak associations between either trunk extensor muscle endurance, knee flexion ROM, or knee extension strength asymmetry and the Habitual Gait Speed test, and a weak association between leg strength and the Chair Stand test (39). Finally, one study reported a moderate negative correlation between handgrip strength and walking steps (30).

Physical and Psychological Factors Associated With Gait Pattern Characteristics

PROMs

Pain Severity. Overall, conflicting results were found based on the three studies reporting on the association between pain severity and gait pattern characteristics (29, 34, 43). To assess pain severity, one study used the 11-point Numeric Rating Scale (NRS) and two studies used a Visual Analog Scale (VAS) (29, 34, 43). Only back pain, measured using the NRS, was weakly and positively correlated to walking velocity (29). Regarding leg pain, Kuwahara et al. (34) reported a moderate negative correlation between leg pain and peak trunk tilt during walking (34). Other significant correlations were reported between pain

severity (location unspecified) and width of base of support, the Gait Disability Index (GDI), peak lumbar tilt pre- and post-walking, and changes in pelvis tilt variation during stance (43). All other gait pattern characteristics measured in these studies were non-significant.

Disability. Overall, conflicting results were found based on the three studies reporting on the association between disability and gait pattern characteristics (29, 42, 44).

Out of two studies using the ODI to assess disability (29, 44), one study reported strong positive correlations between disability and gait velocity and step length, as well as a weak positive correlation between disability and base of support (29). The same authors also reported that other gait pattern characteristics such as cadence, lumbar proprioception (except for left lateral bending) and ROM were not correlated with the ODI score. The second study reported a strong correlation between disability and free walking speed (44).

One study reported a moderate correlation between disability, measured using the QBPDS, and free walking speed (44).

Finally, one study reported weak positive associations between disability, measured using the JOABPED total score or its individual subscales, and short stride when walking (42).

Quality of Life. One study reported non-significant correlations between QoL using the SF-12 and gait pattern characteristics (29).

Objective Outcome Measures

Other Objective Outcome Measures. One study reported weak positive correlations between anterior trunk flexion angle during walking and step length as well as maximum ankle plantar flexion moment (45).

DISCUSSION

This systematic scoping review explored the current state of scientific knowledge regarding the associations between physical or psychological factors and walking capacity in patients with LSS. Results show that physical factors are more commonly studied than psychological factors with 22 studies reporting on physical factors and 3 reporting on psychological factors. The systematic scoping review highlighted the use of a wide range of PROMs and objective measures, with disability being the most frequently reported outcome measure followed by pain. Among objective measures, reported tools were heterogenous with most used in no more than one study. A third outcome category (gait pattern characteristics) was added following data extraction given that no study directly assessed gait pattern characteristics in relation to walking capacity. Considering the impact of gait pattern characteristics on decreased walking capacity, associations between physical or psychological factors and gait pattern characteristics were reported. Results among studies were conflicting regarding associations between PROMs and either walking capacity, functional tasks, or gait pattern characteristics. Results were also conflicting for associations between objective measures and either walking capacity, functional tasks, or gait pattern characteristics. Some outcome measures, however, were clearly associated with several measures related to walking capacity. For instance, walking capacity was significantly associated with pain outcomes, disability, estimated walking distance, and cross-sectional area of the dural tube in the lumbar spine L1/L2. Among the included studies, functional tasks were associated with physical factors such as lower back and upper limb disability, and lower limb endurance, strength, ROM, and speed. Strong significant correlations were also found between gait pattern characteristics (speed and stride) and disability outcomes. These results clearly highlight the intricate and heterogeneous presentation of symptomatic LSS.

Conflicting results can possibly be explained by the heterogeneity of walking capacity tests used across studies. Most tests were not validated in people with symptomatic LSS (28, 31–33, 36, 41, 44, 46), although a few were validated in elderly individuals (31, 32, 44). Out of nine walking tests, only four (Self-Pace walking tests, Shuttle walking test, Treadmill walking test and 6-meter walking test) were validated and/or reliable specifically for patients with LSS (see **Supplement Material 5** for further details). Further studies are needed to assess the validity of commonly used walking tests in patients with symptomatic LSS. Validated walking test for patient with LSS should be used to better understand walking limitations caused by LSS.

The most commonly reported psychological factor was depression and results were conflicting. The Rasch-based Depression Screener (DESC) and PASS-20 questionnaire were associated with decreased performance in functional tasks. Other psychological factors including anxiety, depression and kinesiophobia were either not associated or showed conflicting evidence of association with walking capacity, functional tasks, or gait pattern characteristics. A comprehensive assessment of walking capacity combined with a better knowledge of the physical and psychological factors associated with walking capacity will help health care professionals identified targeted rehabilitation strategies.

The present systematic scoping review highlighted conflicting results among studies reporting on the association between PROMs or objectives measures and measures related to walking capacity (i.e., walking capacity, functional tasks, and gait pattern characteristics). The wide range of questionnaires used to assess the same outcome could also explain some of these conflicting results. For instance, disability was reported using 6 different questionnaires, with only one being specifically validated for LSS (the SSSQ). Low back pain and/or leg pain were also reported among studies using different tools (presence or absence thereof, VAS, NRS, or HUI). The most commonly reported QoL questionnaire used was the SF-36. However, its association with walking capacity and functional tasks was unclear. On the other hand, the HUI, also used to assess QoL, was associated with greater walking capacity. Objective measures were all different across studies and such heterogeneity impeded our ability to determine whether specific outcome measures are related to walking capacity in patients with LSS. In addition, no study specifically assessed gait pattern characteristics such as stride, walking phases, or walking velocity in relation to walking distance or walking time. It seems important to evaluate

these characteristics in order to establish if deviations from normal gait pattern are present in patients with symptomatic LSS. Knowing that risk of fall is increased in populations with mobility impairment (32), a better understanding of walking gait characteristics that can modify walking capacity is needed to know if these walking parameters can also contribute to an increased risk of fall. As such, slower walking speed seems to be related to increased fear of falling (48). Given that some changes in gait pattern normally occur with aging, it is important to know if additional changes are brought on by symptomatic LSS.

Another possible explanation for the conflicting results is the lack of a clear definition for LSS in the studies. Diagnostic ascertainment for inclusion of participants was not clearly mentioned in some studies. Furthermore, many studies reported only the range of included LSS subtypes among participant instead of providing the exact number of individuals per subtype. They also did not clearly describe affected levels.

Clinical Implications

For clinicians, understanding which walking parameters are modified in patients with LSS would provide new insights on the consequences brought on by LSS on gait. If any of these parameters are identified as associated factors, clinicians will be able to establish a treatment plan and monitor clinical evolution more closely over time. Clinicians are also aware that the patient's psychological state can have an impact on the prognosis of musculoskeletal disorders. For instance, patients with LSS reporting depression or at high risk of developing depression show poorer outcomes over time (49). However, more studies are needed to inform the possible implications of psychological status on walking-related functions in patients with LSS.

The Self-Paced Walking Test (SPWT) was the most used test to assessed walking capacity in patients with LSS and was the only reliable and validated one for this specific population. Results from the present systematic scoping review suggest that subjective evaluation tools such as the SSSQ and ODI were the disability-related questionnaires the most used and for which there were many significant associations with the three domains (walking capacity, functional tasks, and gait pattern characteristics). Regarding QoL, the most used questionnaire was the SF-36 but results were conflicting across studies. MRI findings (cross-sectional area) were associated with walking capacity. Regarding objective measures and psychological factors, current evidence suggests that further studies are needed to be able to better formulate recommendations for clinicians. Exploring other biomechanical walking parameters such as minimal toe clearance, speed, simple and double stance and step width can be interesting indicators to consider when assessing walking capacity in future studies.

Strengths and Limitations

To our knowledge, this is the first systematic scoping review to assess physical and psychological factors associated with walking capacity in patients with LSS. One strength of this review is that every step was consistent with the current standards for conducting a systematic scoping review (24, 25). It is not, however, without limitation. The first limitation of our study was the low number of studies that provided a direct evaluation of walking capacity. Only studies published in English, French or Spanish were considered for this scoping review. We cannot rule-out that additional relevant evidence may have been published in other languages. Moreover, most of the studies did not specify the level and location of the LSS limiting the clinical interpretation of the results with regards to distinction of LSS subtypes.

CONCLUSION

The present systematic scoping review allowed to identify physical and psychological factors that are associated with walking capacity in patients with symptomatic LSS. However, a large number of associations reported between walking capacity and physical or psychological factors were conflicting especially when correlated directly with the assessment of walking capacity.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

MH was the principal investigator of this scoping review, participated in the study design, literature search, data extraction, results formatting, and as well as the manuscript writing. JBD participated in the data extraction and results formatting. AAM and MD participated in the study design, overall supervision of the project, and manuscript writing and revision. AAM was also involved in the screening process as the third person to obtain consensus (sorting and quality rating). All authors read and approved the final manuscript.

FUNDING

The study was funded by the Chaire de recherche internationale en santé neuromusculosquelettique and its partner the Centre intégré universitaire de santé et de services sociaux de la Mauricie-et-du-Centre-du-Québec.

ACKNOWLEDGMENTS

Thanks to the laboratory assistant Marie-Élisabeth Roy-Poulin for her help at different stages of the screening process.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2021.720662/full#supplementary-material

REFERENCES

1. Ammendolia C, Côté P, Southerst D, Schneider M, Budgell B, Bombardier C, et al. Comprehensive nonsurgical treatment versus self-directed care to improve walking ability in lumbar spinal stenosis: a randomized trial. *Arch Phys Med Rehabil.* (2018) 99:2408–19 e2. doi: 10.1016/j.apmr.2018.05.014
2. Budithi S, Dhawan R, Cattell A, Balain B, Jaffray D. Only walking matters-assessment following lumbar stenosis decompression. *Eur Spine J.* (2017) 26:481–7. doi: 10.1007/s00586-016-4881-x
3. Kobayashi S. Pathophysiology, diagnosis and treatment of intermittent claudication in patients with lumbar canal stenosis. *World J Orthop.* (2014) 5:134–45. doi: 10.5312/wjo.v5.i2.134
4. Hartvigsen J, Hancock MJ, Kongsted A, Louw Q, Ferreira ML, Genevay S, et al. What low back pain is and why we need to pay attention. *Lancet.* (2018) 391:2356–67. doi: 10.1016/S0140-6736(18)30480-X
5. Kalichman L, Cole R, Kim DH, Li L, Suri P, Guermazi A, et al. Spinal stenosis prevalence and association with symptoms: the Framingham Study. *Spine J.* (2009) 9:545–50. doi: 10.1016/j.spinee.2009.03.005
6. Jensen RK, Jensen TS, Koes B, Hartvigsen J. Prevalence of lumbar spinal stenosis in general and clinical populations: a systematic review and meta-analysis. *Eur Spine J.* (2020) 29:2143–63. doi: 10.1007/s00586-020-06339-1
7. Comer CM, Redmond AC, Bird HA, Conaghan PG. Assessment and management of neurogenic claudication associated with lumbar spinal stenosis in a UK primary care musculoskeletal service: a survey of current practice among physiotherapists. *BMC Musculoskelet Disord.* (2009) 10:121. doi: 10.1186/1471-2474-10-121
8. Genevay S, Atlas SJ. Lumbar spinal stenosis. *Best Pract Res Clin Rheumatol.* (2010) 24:253–65. doi: 10.1016/j.berh.2009.11.001
9. Singh K, Samartzis D, Vaccaro AR, Nassr A, Andersson GB, Yoon ST, et al. Congenital lumbar spinal stenosis: a prospective, control-matched, cohort radiographic analysis. *Spine J.* (2005) 5:615–22. doi: 10.1016/j.spinee.2005.05.385
10. Lurie J, Tomkins-Lane C. Management of lumbar spinal stenosis. *BMJ.* (2016) 352:h6234. doi: 10.1136/bmj.h6234
11. Tomkins-Lane C, Melloh M, Wong A. Diagnostic tests in the clinical diagnosis of lumbar spinal stenosis: consensus and results of an International Delphi Study. *Europ Spine J.* (2020) 29:2188–97. doi: 10.1007/s00586-020-06481-w
12. Tomkins-Lane CC, Holz SC, Yamakawa KS, Phalke VV, Quint DJ, Miner J, et al. Predictors of walking performance and walking capacity in people with lumbar spinal stenosis, low back pain, and asymptomatic controls. *Arch Phys Med Rehabil.* (2012) 93:647–53. doi: 10.1016/j.apmr.2011.09.023
13. Williamson E, Ward L, Vadher K, Dutton SJ, Parker B, Petrou S, et al. Better Outcomes for Older people with Spinal Trouble (BOOST) trial: a randomised controlled trial of a combined physical and psychological intervention for older adults with neurogenic claudication, a protocol. *BMJ Open.* (2018) 8:e022205. doi: 10.1136/bmjopen-2018-022205
14. Barz T, Melloh M, Staub L, Roeder C, Lange J, Smiszek F-G, et al. The diagnostic value of a treadmill test in predicting lumbar spinal stenosis. *Europ Spine J.* (2008) 17:686–90. doi: 10.1007/s00586-008-0593-1
15. Tomkins-Lane CC, Battie MC. Predictors of objectively measured walking capacity in people with degenerative lumbar spinal stenosis. *J Back Musculoskelet Rehabil.* (2013) 26:345–52. doi: 10.3233/BMR-130390
16. Ammendolia C, Côté P, Rampersaud YR, Southerst D, Budgell B, Bombardier C, et al. The boot camp program for lumbar spinal stenosis: a protocol for a randomized controlled trial. *Chiropr Man Therap.* (2016) 24:25. doi: 10.1186/s12998-016-0106-y
17. Marchand AA, Suitner M, O'Shaughnessy J, Chatillon CE, Cantin V, Descarreaux M. Feasibility of conducting an active exercise prehabilitation program in patients awaiting spinal stenosis surgery: a randomized pilot study. *Sci Rep.* (2019) 9:12257. doi: 10.1038/s41598-019-48736-7
18. Rainville J, Childs LA, Peña EB, Suri P, Limke JC, Jouve C, et al. Quantification of walking ability in subjects with neurogenic claudication from lumbar spinal stenosis–a comparative study. *Spine J.* (2012) 12:101–9. doi: 10.1016/j.spinee.2011.12.006
19. Zeifang F, Schiltenwolf M, Abel R, Moradi B. Gait analysis does not correlate with clinical and MR imaging parameters in patients with symptomatic lumbar spinal stenosis. *BMC Musculoskelet Disord.* (2008) 9:89. doi: 10.1186/1471-2474-9-89
20. Takenaka H, Sugiura H, Kamiya M, Nishihama K, Ito A, Suzuki J, et al. Predictors of walking ability after surgery for lumbar spinal canal stenosis: a prospective study. *Spine J.* (2019) 19:1824–31. doi: 10.1016/j.spinee.2019.07.002
21. Quack V, Boecker M, Mueller C, Mainz V, Geiger M, Heinemann A, et al. Psychological factors outmatched morphological markers in predicting limitations in activities of daily living and participation in patients with lumbar stenosis. *BMC Musculoskelet Disord.* (2019) 20:1–9. doi: 10.1186/s12891-019-2918-0
22. Mullen SP, McAuley E, Satariano WA, Kealey M, Prohaska TR. Physical activity and functional limitations in older adults: the influence of self-efficacy and functional performance. *J Gerontol B Psychol Sci Soc Sci.* (2012) 67:354–61. doi: 10.1093/geronb/gbs036
23. Ammendolia C, Schneider M, Williams K, Zickmund S, Hamm M, Stuber K, et al. The physical and psychological impact of neurogenic claudication: the patients' perspectives. *J Can Chiropr Assoc.* (2017) 61:18–31.
24. Peters MD, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. *Int J Evidence-Based Healthcare.* (2015) 13:141–6. doi: 10.1097/XEB.0000000000000050
25. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. *Implement Sci.* (2010) 5:69. doi: 10.1186/1748-5908-5-69
26. Downes MJ, Brennan ML, Williams HC, Dean RS. Development of a critical appraisal tool to assess the quality of cross-sectional studies (AXIS). *BMJ Open.* (2016) 6:e011458. doi: 10.1136/bmjopen-2016-011458
27. Sigmundsson FG, Kang XP, Jönsson B, Strömqvist B. Correlation between disability and MRI findings in lumbar spinal stenosis: a prospective study of 109 patients operated on by decompression. *Acta Orthopaed.* (2011) 82:204–10. doi: 10.3109/17453674.2011.566150
28. Tong HC, Haig AJ, Geisser ME, Yamakawa KS, Miner JA. Comparing pain severity and functional status of older adults without spinal symptoms, with lumbar spinal stenosis, and with axial low back pain. *Gerontology.* (2007) 53:111–5. doi: 10.1159/000096861
29. Conrad BP, Shokat MS, Abbasi AZ, Vincent HK, Seay A, Kennedy DJ. Associations of self-report measures with gait, range of motion and proprioception in patients with lumbar spinal stenosis. *Gait Posture.* (2013) 38:987–92. doi: 10.1016/j.gaitpost.2013.05.010
30. Inoue H, Watanabe H, Okami H, Shiraishi Y, Kimura A, Takeshita K. Handgrip strength correlates with walking in lumbar spinal stenosis. *Eur Spine J.* (2020) 29:2198–204. doi: 10.1007/s00586-020-06525-1
31. Ishimoto Y, Yoshimura N, Muraki S, Yamada H, Nagata K, Hashizume H, et al. Prevalence of symptomatic lumbar spinal stenosis and its association with physical performance in a population-based cohort in Japan: the Wakayama Spine Study. *Osteoarthritis Cartilage.* (2012) 20:1103–8. doi: 10.1016/j.joca.2012.06.018
32. Kim H-J, Chun H-J, Han C-D, Moon S-H, Kang K-T, Kim H-S, et al. The risk assessment of a fall in patients with lumbar spinal stenosis. *Spine.* (2011) 36:E588–E92. doi: 10.1097/BRS.0b013e3181f92d8e
33. Kuittinen P, Sipola P, Aalto TJ, Määttä S, Parviainen A, Saari T, et al. Correlation of lateral stenosis in MRI with symptoms, walking capacity and EMG findings in patients with surgically confirmed lateral lumbar spinal canal stenosis. *BMC Musculoskelet Disord.* (2014) 15:247. doi: 10.1186/1471-2474-15-247
34. Kuwahara W, Kurumadani H, Tanaka N, Nakanishi K, Nakamura H, Ishii Y, et al. Correlation between spinal and pelvic movements during gait and aggravation of low back pain by gait loading in lumbar spinal stenosis patients. *J Orthopaed Sci.* (2019) 24:207–13. doi: 10.1016/j.jos.2018.09.002
35. Minetama M, Kawakami M, Teraguchi M, Kagotani R, Mera Y, Sumiya T, et al. Associations between psychological factors and daily step count in patients with lumbar spinal stenosis. *Physiother Theory Pract.* (2020). doi: 10.1080/09593985.2020.1855685. [Epub ahead of print].
36. Nagai K, Aoyama T, Yamada M, Izeki M, Fujibayashi S, Takemoto M, et al. Quantification of changes in gait characteristics associated with intermittent claudication in patients with lumbar spinal stenosis. *J Spinal Disord Tech.* (2014) 27:E136–42. doi: 10.1097/BSD.0b013e3182a2656b
37. Özdemir E, Paker N, Bugdayci D, Tekdos DD. Quality of life and related factors in degenerative lumbar spinal stenosis: a controlled study. *J Back Musculoskelet Rehabil.* (2015) 28:749–53. doi: 10.3233/BMR-140578

38. Pryce R, Johnson M, Goytan M, Passmore S, Berrington N, Kriellaars D. Relationship between ambulatory performance and self-rated disability in patients with lumbar spinal stenosis. *Spine.* (2012) 37:1316–23. doi: 10.1097/BRS.0b013e31824a8314
39. Schmidt CT, Ward RE, Suri P, Kiely DK, Ni P, Anderson DE, et al. Association of neuromuscular attributes with performance-based mobility among community-dwelling older adults with symptomatic lumbar spinal stenosis. *Arch Phys Med Rehabil.* (2017) 98:1400–6. doi: 10.1016/j.apmr.2017.02.028
40. Conway J, Tomkins CC, Haig AJ. Walking assessment in people with lumbar spinal stenosis: capacity, performance, and self-report measures. *Spine J.* (2011) 11:816–23. doi: 10.1016/j.spinee.2010.10.019
41. Drury T, Ames SE, Costi K, Beynnon B, Hall J. Degenerative spondylolisthesis in patients with neurogenic claudication effects functional performance and self-reported quality of life. *Spine.* (2009) 34:2812–7. doi: 10.1097/BRS.0b013e3181b4836e
42. Fujita N, Sakurai A, Miyamoto A, Michikawa T, Otaka Y, Suzuki S, et al. Stride length of elderly patients with lumbar spinal stenosis: multi-center study using the Two-Step test. *J Orthopaed Sci.* (2019) 24:787–92. doi: 10.1016/j.jos.2019.01.006
43. Garbelotti SA Jr, Lucareli PRG, Ramalho A Jr, de Godoy W, Bernal M, Greve JMDA. An investigation of the value of tridimensional kinematic analysis in functional diagnosis of lumbar spinal stenosis. *Gait Posture.* (2014) 40:150–3. doi: 10.1016/j.gaitpost.2014.03.013
44. Grelat M, Gouteron A, Casillas J-M, Orliac B, Beaurain J, Fournel I, et al. Walking speed as an alternative measure of functional status in patients with lumbar spinal stenosis. *World Neurosurg.* (2019) 122:e591–e7. doi: 10.1016/j.wneu.2018.10.109
45. Igawa T, Katsuhira J, Hosaka A, Uchikoshi K, Ishihara S, Matsudaira K. Kinetic and kinematic variables affecting trunk flexion during level walking in patients with lumbar spinal stenosis. *PLoS ONE.* (2018) 13:e0197228. doi: 10.1371/journal.pone.0197228
46. Thornes E, Robinson HS, Vøllestad NK. Degenerative lumbar spinal stenosis and physical functioning: an exploration of associations between self-reported measures and physical performance tests. *Disabil Rehabil.* (2018) 40:232–7. doi: 10.1080/09638288.2016.1250123
47. Thornes E, Robinson HS, Vøllestad NK. Dynamic balance in patients with degenerative lumbar spinal stenosis; a cross-sectional study. *BMC Musculoskelet Disord.* (2018) 19:192. doi: 10.1186/s12891-018-2111-x
48. Chamberlin ME, Fulwider BD, Sanders SL, Medeiros JM. Does fear of falling influence spatial and temporal gait parameters in elderly persons beyond changes associated with normal aging? *J Gerontol A Biol Sci Med Sci.* (2005) 60:1163–7. doi: 10.1093/gerona/60.9.1163
49. Hébert JJ, Abraham E, Wedderkopp N, Bigney E, Richardson E, Darling M, et al. Preoperative factors predict postoperative trajectories of pain and disability following surgery for degenerative lumbar spinal stenosis. *Spine.* (2020) 45:E1421–30. doi: 10.1097/BRS.0000000000003587

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

frontiers in Human Neuroscience

ORIGINAL RESEARCH
published: 09 September 2021
doi: 10.3389/fnhum.2021.678302

Effect of Seat Backrest Inclination on the Muscular Pattern and Biomechanical Parameters of the Sit-to-Stand

*Nadège Tebbache and Alain Hamaoui**

Laboratoire CIAMS, Université Paris-Saclay, Saint Aubin, France

Objectives: The sit-to-stand (STS) transfer mobilizes an extended part of the kinematic chain throughout a postural phase characterized by a flexion of the trunk and a focal phase consisting of a whole-body extension. The aim of this study was to analyze the variations of the global muscular pattern and the biomechanical parameters in both phases, in relation with seat backrest inclination.

Methods: Fifteen participants were asked to stand up from a seat with 5 backrest inclination settings and at 2 execution speeds. The ground reaction forces and the activity levels of fifteen muscles of the trunk and lower limbs were investigated.

Results: Backrest-induced modifications were mainly observed in the postural phase: inclining the backrest backward increased the phase duration and the activity level of the sternocleidomastoideus and the rectus abdominis, while it reduced the activity of the tibialis anterior. It also allowed for an increased maximal anteroposterior velocity of the body center of mass. Higher execution speed led to increased and earlier muscular activities of many trunk and lower limbs muscles, predominantly in the postural phase.

Discussion: Taken together, these results suggest that a greater backrest inclination increases the demand in the postural phase due to the increase of the upper body gravity torque about the ischial tuberosities, and requires an adaptation of muscular activity levels and timing, but with the same overall pattern. The kinetic energy gained during the longer excursion of the trunk may also require less activation of the lower limbs muscles involved in the generation of propulsive forces of the body.

Keywords: sit-to-stand, backrest inclination, speed, ground reaction forces, electromyography, anticipatory postural adjustments

OPEN ACCESS

Edited by:
Teddy Caderby, Université de La Réunion, France

Reviewed by:
Romain Tisserand, University of British Columbia, Canada
Lars Janshen, Humboldt University of Berlin, Germany

***Correspondence:**
Alain Hamaoui
alain.hamaoui@universite-paris-saclay.fr

Specialty section:
This article was submitted to Motor Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *09 March 2021*
Accepted: *23 July 2021*
Published: *09 September 2021*

Citation:
Tebbache N and Hamaoui A (2021) Effect of Seat Backrest Inclination on the Muscular Pattern and Biomechanical Parameters of the Sit-to-Stand. Front. Hum. Neurosci. 15:678302. doi: 10.3389/fnhum.2021.678302

INTRODUCTION

The sit-to-stand (STS) is the demanding and frequent transfer from the seated posture to the standing posture. From a kinematic point of view, the STS consists of a trunk flexion phase followed by an extension of the trunk and lower limbs initiated after seat unloading (Kelley et al., 1976; Nuzik et al., 1986; Rodosky et al., 1989; Hirschfeld et al., 1999; Boukadida et al., 2015). Integrating kinetics, Schenkman et al. (1990) assumed that trunk flexion moves the body center of mass forward but

above all increases the upper body forward momentum. This momentum is then transferred into a whole-body vertical momentum once the seat is unloaded, allowing for whole-body extension.

The STS, a demanding task, requires the activation of a large number of muscles with appropriate coordination. Some common components of this muscular pattern can be extracted from electromyographic studies. The first muscle to be activated during the STS task is the tibialis anterior (TA) (Doorenbosch et al., 1994; Roebroeck et al., 1994; Vander Linden et al., 1994; Gross et al., 1998; Khemlani et al., 1999; Rodrigues-de-Paula-Goulart and Valls-Solé, 1999; Tebbache and Hamaoui, 2020). Its activity is associated with foot stabilization during trunk flexion (Doorenbosch et al., 1994; Roebroeck et al., 1994; Vander Linden et al., 1994; Gross et al., 1998; Khemlani et al., 1999). As in many others forward oriented tasks, it is also involved in the backward shift of the center of pressure in STS initiation, together with the inhibition of the soleus muscle (Sol) (Crenna and Frigo, 1991). Head (sternocleidomastoid) and trunk (abdominal muscles) flexors are recruited to perform the forward tilt of the trunk (Rodrigues-de-Paula-Goulart and Valls-Solé, 1999). Quadriceps, together with hamstrings, are then activated for seat unloading and lower limb extension, with head (upper trapezius) and spinal extensors guiding the verticalization of the whole body (Munton et al., 1984; Roebroeck et al., 1994; Vander Linden et al., 1994; Rodrigues-de-Paula-Goulart and Valls-Solé, 1999; Bouchouras et al., 2015; Chorin et al., 2016). Several studies reported that quadriceps, hamstrings and trunk extensors are the main driving forces of the sit-to-stand and are activated once the vertical projection of the center of mass has been brought closer to the feet or its speed is sufficient (Pai and Rogers, 1990; Vander Linden et al., 1994; Rodrigues-de-Paula-Goulart and Valls-Solé, 1999; Hof et al., 2005). Posterior lower leg muscles control the horizontal momentum and stabilize the posture at the end of the STS (Doorenbosch et al., 1994; Khemlani et al., 1999; Rodrigues-de-Paula-Goulart and Valls-Solé, 1999; Cuesta-Vargas and Gonzalez Sanchez, 2013). In addition, a recent study exploring the effect of backrest inclination on muscular activity showed an increase in the activity level of upper body flexors (abdominal muscles and SCOM) and ST, together with a decrease in TA activity before seat unloading (Tebbache and Hamaoui, 2020).

According to Gelfand revisiting Bernstein's ideas (Bernstein, 1967), voluntary movements include a postural component related to stability and a focal component related to the voluntary movement itself. Postural activity happens during and after the focal movement, but mainly beforehand (Belenkii et al., 1967; Bouisset and Zattara, 1981; Cordo and Nashner, 1982) with Anticipatory Postural Adjustments (APAs). APAs precede the focal movement, and their assumed goals include compensation of the forthcoming perturbation associated with the focal movement (Bouisset and Zattara, 1987) as well as the generation of propulsive forces when the movement involves a change of support base (Herman et al., 1973; Breniere and Do, 1986; Brenière and Do, 1991; Stapley et al., 1998). For the STS task, APAs occurring during the postural phase are rather used for the latter purpose.

Two main phases can thus be distinguished during the STS task: one called postural phase, during which the trunk is flexed forward, which acts as a preparation for the other phase, when body extension takes place and seat unloading occurs, namely the focal phase (Diakhaté et al., 2013; Alamini-Rodrigues and Hamaoui, 2017; Hamaoui and Alamini-Rodrigues, 2017). In between those 2 phases is the seat-off, when seat unloading occurs.

It has been shown that APAs are motor-task specific and are organized according to a well-defined sequence. They adapt to initial conditions, execution conditions (including speed) and to the functional state of the system (Bouisset and Do, 2008). Therefore, the characteristics of the seat, which are a key factor in seated posture ergonomics, might induce APAs adaptations when performing the STS task. Several studies explored those determinants biomechanically, mainly seat height (Rodosky et al., 1989; Schenkman et al., 1996; Gillette and Stevermer, 2012; An et al., 2013; Yoshioka et al., 2014) and feet position (Shepherd and Koh, 1996; Khemlani et al., 1999; Kawagoe et al., 2000; Gillette and Stevermer, 2012; Ng et al., 2015). It was shown that lowering seat height and putting the feet forward resulted in greater joint constraints (Burdett et al., 1985; Rodosky et al., 1989; Arborelius et al., 1992). A lower seat led to increased trunk maximal angular velocity to increase upper body momentum generation (Hughes et al., 1994; Schenkman et al., 1996) or to failure in the case of elderly subjects unable to use the momentum transfer strategy (Hughes et al., 1994).

However, the influence of seat backrest inclination in terms of biomechanics remains to our knowledge understudied, although most resting and transportation seats have an inclined backrest. In this setting, trunk flexion is initiated against the force of gravity, instead of benefitting from it when the trunk is initially upright (Millington et al., 1992). It also extends the trajectory of the center of mass during STS, offering opportunity for the generation of a greater horizontal momentum in the postural phase, which is a fundamental component of the postural phase and of the STS strategy (Schenkman et al., 1990; Pai et al., 1994).

Consequently, the question arises as to how the motor pattern of the postural and focal phases of the STS is adjusted to seat backrest inclination. The first option might be a simple adaptation of muscular activity levels, while the other would involve an in-depth reorganization of the program with a new set of muscles being active at a different timing. Given the importance of momentum control during the STS task, and in order to analyze this task when maximal performance is sought, a special interest was also given to the execution speed parameter. It was expected that performing the STS at maximum speed would exacerbate and make more visible the adaptation of the motor program to backrest inclination.

Part of a similar question was addressed in a previous paper (Tebbache and Hamaoui, 2020), which gave a first indication of muscular variations in the postural phase. This paper aims to further deepen that analysis by an additional kinetics analysis of the STS task. The main hypothesis was that inclined backrest requires a higher level of muscular activity during the postural phase, but induces an increased horizontal momentum which may ease the focal phase.

MATERIALS AND METHODS

Participants

Fifteen healthy subjects (7 males—8 females; age: 22.9 ± 3 years; weight: 65.8 ± 9.7 kg; height: 171.6 ± 7.4 cm, BMI: 22.2 ± 1.9 kg/m^2), took part in this study. It was carried out in accordance with the recommendations of the local "Ethics Committee for Movement Analysis (CERAM), INU Champollion," which has approved this study. All subjects gave written informed consent prior to the testing, in accordance with the Declaration of Helsinki. Due to a technical issue, one subject was then excluded from the results analysis.

Experimental Set-Up

Customized Adjustable Seat

A specifically designed modular airline seat (part of a 2-seat row) was used in this study. It was made adjustable by ARTEC Aerospace company (Seilh, France) by modifying a regular airline seat to allow for the investigation of the influence of specific parameters. The backrest inclination, defined as the angle between the backrest and the seatpan, was adjustable in the range 90°–130° continuously.

Force Platform

A 1 m × 2 m 6-channel custom-made force platform (Bertec, Columbus, United States), on which the adjustable seat was screwed, was used to record forces and moments in the three orthogonal directions (**Figure 1**) with a sampling frequency of 1,000 Hz.

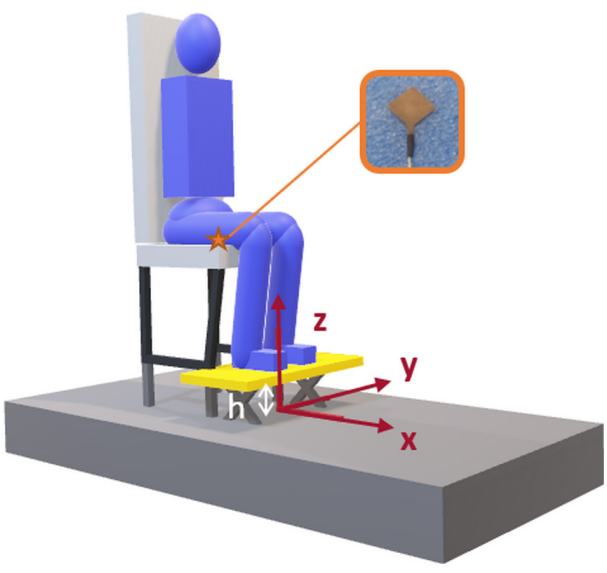

FIGURE 1 | Seat on the force platform. Axes were as follows: *x*-axis is along the anteroposterior direction and points forward, *y*-axis along the mediolateral axis, pointing to the left, and *z*-axis follows the vertical direction, pointing upward.

Pressure Sensor

A 25-mm^2 capacitive pressure sensor (C500 sensor PPS, Los Angeles, United States) was inserted under the seatpan cushion, at mid-thigh level (**Figure 1**) and used to detect the onset of seat unloading.

Electromyography

A 16-channel wireless surface EMG device (Zero Wire Model, Aurion, Milan, Italy) was used. The signal was sampled at 1,000 Hz, amplified with a gain of 1,000, the bandwidth was 10–500 Hz, and the common mode rejection ratio 90 dB.

Surface EMG was collected on the dominant side of the subject (as told by the subject), on 12 muscles: Upper trapezius (TraS), sternocleidomastoideus (SCOM), neck extensors (NE), rectus abdominis (RA), erector spinae in the thoracic region (ES T6), erector spinae in the lumbar region (ES L3), rectus femoris (RF), vastus medialis (VM), semitendinosus (ST), gastrocnemius medialis (GM), tibialis anterior (TA), and soleus (Sol). Electromyograms were obtained using Ag/AgCl pre-gelled disposable electrodes positioned 2 cm apart over the muscle belly, in line with muscle fibers direction and on prepared skin. All electrode placements were confirmed using palpation and manual resistance tests, following SENIAM recommendations (Hermens et al., 2000).

Maximal voluntary contraction (MVC) electromyograms against manual resistance were recorded for amplitude normalization purposes, with two trials of 3 s for each muscle.

Procedure

The experimental parameters were backrest inclination angle (90°–100°–110°–120°–130°) and execution speed [comfortable (CS)—maximal (MS)]. To standardize experimental conditions, the participants were barefoot and in their underwear. They first adopted a comfortable position on the seat, with their back resting against the backrest. Floor height was adjusted beforehand so that their thighs were horizontal, their feet flat on the floor, and their lower legs vertical. Feet placement was at a self-selected width, but the anterior-posterior position was imposed with the back of the heel at the rear end of the adjustable foot platform. Participants were asked to cross their arms loosely over their chest, then to stand up in response to a verbal signal, at the speed specified beforehand, namely comfortable or maximal. The comfortable speed was described as the natural self-selected speed used in daily life; the maximal speed was described as "as fast as possible." They were instructed to perform an STS task shortly after a verbal signal was given, at a self-selected moment in time. Once in the standing posture, subjects had to keep still until an audio signal indicated the end of the trial. For each combination of the five backrest inclination levels and two execution speeds, five 6-s trials were performed, with a rest time of 10 s between trials and 120 s between series. Two training trials were implemented at each change of condition for the subjects to familiarize with the task of standing at the relevant speed and with a given backrest inclination.

Execution speed was randomized, but backrest inclination was performed in a systematic ascending order from 90° to 130°. Since the system of worm screw with crank used to

set the backrest inclination at a precise level was very slow, randomization would have excessively lengthened the duration of the experiment.

Data Analysis

Electromyography

EMG signals were full-wave rectified, filtered with a band-pass Butterworth filter (10–450 Hz) and smoothed (sliding window of 51 ms) (Conforto et al., 1999).

Muscle onset was detected using an algorithm based on the work of Lidierth (1986). The muscle was considered active when the mean amplitude of the EMG signal across the 50 following samples exceeded the baseline mean by 2 baseline standard deviations for more than 90 ms, without going below it for more than 15 ms. Baseline parameters were calculated on the 50 ms before the verbal signal was given. Movement start time, described below, was considered as the time origin and subtracted from the onset times obtained.

Activity levels were calculated as the average rectified values (ARV) of the EMG signal for each phase, normalized by the ARV of the 3-s MVC signal. Each muscle was thus characterized by a mean activity level for each phase, both expressed in percent of the MVC (A_{PP} and A_{FP}).

Force Plate and Pressure Sensor Data

Center of Pressure (CoP)

The anteroposterior position of the center of pressure (CoP) was calculated from Equation 1, considering that the forces in the anteroposterior directions were applied at the height of the platform beneath the feet (h) (**Figure 1**), above the force platform. This simplification is addressed in the limitations section.

$$x_p = \frac{hF_x - M_y}{F_z} \quad (1)$$

Considering

- x_p as the anteroposterior position of the CoP,
- h as the height of the adjustable platform beneath the feet,
- F_x as the total ground reaction force in the anteroposterior direction,
- F_z as the total ground reaction force in the vertical direction,
- M_y as the external moment along the mediolateral axis calculated at the center of the force platform.

Time Markers

Start time, end time, and seat-off time were measured to calculate the duration of the postural phase (dPP), the focal phase (dFP) and the entire STS (dSTS).

Start Time. The STS transfer start time was associated with CoP backward displacement initiation. It was the first time when all the values of a 200-ms window were lower than the mean value calculated in the preceding 400-ms sliding baseline window minus two standard deviations on this window (**Figure 2**). Start time was associated with the first value of the 200-ms window.

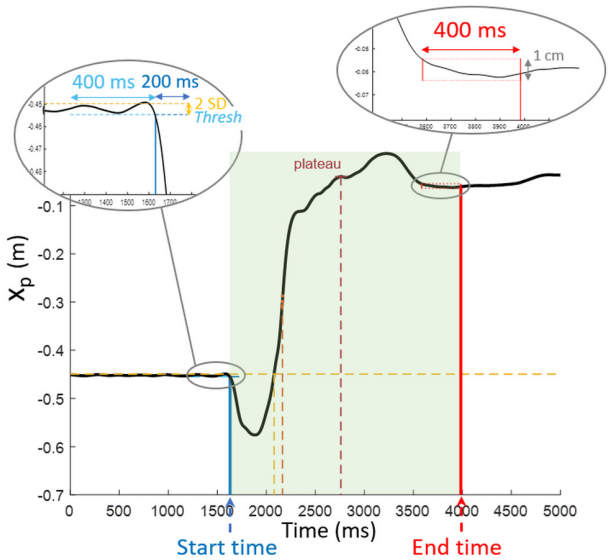

FIGURE 2 | Detection of start and end times. Start time corresponded to the fall of x_p below the threshold calculated from the preceding 400 ms baseline for at least 200 ms. Concerning end time, the detection area was reduced to the time interval following the first plateau after feet loading, and end time preceded the first 400 ms where peak-to-peak CoP anteroposterior displacement did not exceed 1 cm.

End Time. End time was detected based on CoP displacement as well. The algorithm included successive steps to determine the onset of the plateau following unloading, from which the CoP peak-to-peak amplitude on a 400 ms sliding window was calculated. When this value did not exceed 1 cm, the algorithm was stopped, and the end time was associated with the last sample of the window under consideration (**Figure 2**).

Seat-Off Time. Seat-off time was detected by means of the pressure sensor inside the seatpan structure under the cushion. The algorithm detected the time associated with the steepest negative slope, and then moved back to detect the time when this slope changed sign and stayed positive for at least 10 ms, indicating the seat-off (**Figure 3**).

STS Indicators

The STS was characterized by means of time, amplitude and velocity parameters:

- Anticipatory postural adjustments duration (dPP): time between start time and seat-off
- Focal phase duration (dFP): time between seat-off and end time
- Total STS duration (dSTS): time between start time and end time
- Anticipatory postural adjustments amplitude (Δx_p): difference between the initial and the minimal anteroposterior position of the CoP during the postural phase.
- Maximal CoG speeds in the anteroposterior (x'_G max) and vertical (z'_G max) directions: peak of CoG speed

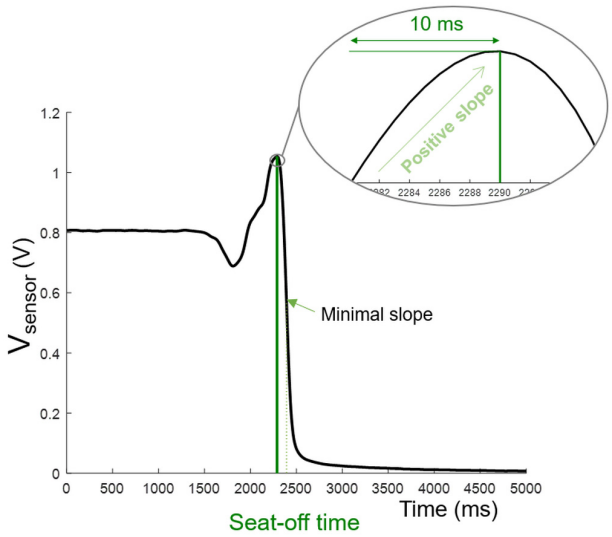

FIGURE 3 | Seat-off detection. Starting from the time of occurrence of the steepest negative slope, the signal was analyzed backwards to identify the time when the slope changed sign and remained positive for at least 10 ms.

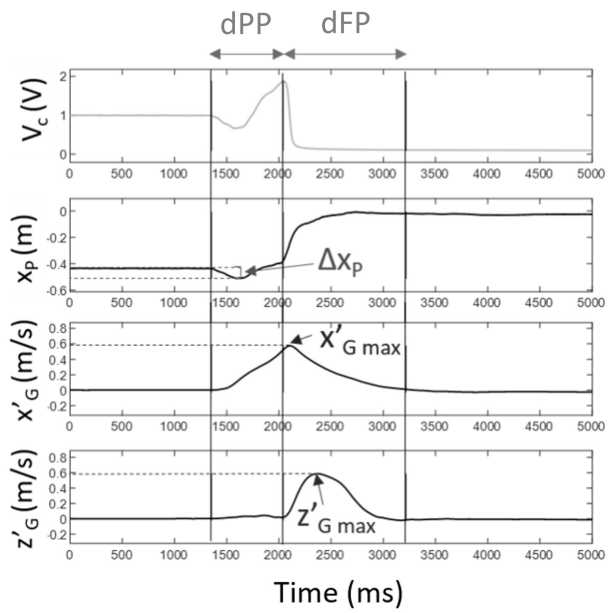

FIGURE 4 | STS indicators. V_{sensor} represents the pressure sensor beneath the seat; x_p the position of the CoP, x'_G the anterioposterior velocity of the CoG; z'_G the CoG vertical velocity.

signals obtained by integrating accelerations with null initial conditions (**Figure 4**).

Shorter times to perform the STS and higher maximal speeds were considered as indicators of a better performance, according to existing literature (Bouisset and Do, 2008; Diakhaté et al., 2013; Hamaoui and Alamini-Rodrigues, 2017).

Statistical Analysis

A 2-factor repeated-measures ANOVA was conducted for each dependent variable, with backrest inclination (5 modalities) and execution speed (2 modalities) as within-subjects factors, and the level of significance set at 0.05. When statistical significance was reached, simple contrasts were analyzed, by comparing each backrest inclination setting above 90° to the 90° setting.

RESULTS

Our results are presented in tables, completed by figures for the most relevant variations. The structure of the tables varies in order to highlight the significant results. When no significant interaction effect was found between the two independent variables, namely backrest inclination and velocity, a different table was made for each of these variables containing values averaged over the different modalities of the other variable.

Electromyography

Onset Times

Most muscles investigated were firstly activated during the postural phase, with VM, RF, ST, and GM being activated close to the beginning of the focal phase. A significant effect of backrest inclination was observed on the onset times of 4 muscles, angles higher than 90° being associated with delayed onsets for VM ($p < 0.001$), and TA ($p < 0.05$), and TraS ($p < 0.01$ but with no significant contrast compared to 90°), and earlier onset of ES L3 ($p < 0.01$) (**Table 1**).

When comparing the 2 speed conditions, performing at maximal speed significantly reduced the onset times of all muscles investigated except SCOM and RA.

Furthermore, the ANOVA revealed a significant interaction effect between backrest inclination × speed for ST ($p < 0.01$), with a significant simple main effect of backrest inclination only at comfortable speed ($p < 0.05$) but a significant effect of speed for each backrest inclination ($p < = 0.01$).

Activity Levels

When considering the mean activity levels, the most active muscles during the postural phase, showing values higher than 25%, were mainly located in the trunk (RA, ES L3, ES T6) and neck (NE, TraS) (**Table 2**). In the focal phase, these muscles were in contrast located in the lower limbs (VM, TA, Sol, GM), with decreased values for trunk and neck muscles (**Table 3**).

Increasing backrest inclination resulted in significant variations of activity levels during the postural phase, with higher values for SCOM ($p < 0.001$) and RA ($p < 0.001$), and lower for TA ($p < 0.05$) (**Table 2** and **Figure 5**). For this muscle, a significant decrease in activity was observed only from 120° on.

In the focal phase, increasing backrest inclination only led to lower activity levels for RF ($p < 0.05$) and Sol ($p < 0.05$) (**Table 3**).

Execution speed significantly increased activity levels in the postural phase of all muscles investigated except for TA and ES T6, although their mean activity level still increased in condition MS (**Table 4**).

TABLE 1 | Mean (SD) muscle onset times, in ms, for the 5 inclination conditions and for the 2 execution speeds, and *p*-values for effects of inclination (i), speed (V), and their interaction (i*V).

Muscle	V	90°	100°	110°	120°	130°	*p(i)*	*p(V)*	*p(i*V)*
NE	CS	358.9 (220)	335.1 (269.3)	310.2 (344.1)	321.8 (292.3)	355.6 (382.6)	NS	***	NS
	MS	114.6 (155.1)	76.8 (167.4)	118.5 (216.9)	111.9 (238)	65.5 (174.9)			
TraS	CS	168.9 (215.2)	123.7 (143.9)	140.6 (233.9)	126.3 (189.3)	163.1 (316.0)	**	NS	NS
	MS	9.4 (71.8)	26.3 (114.4)	15.7 (76.6)	18.9 (84.7)	9.1 (70.5)			
	/90°		***NS***	***NS***	***NS***	***NS***			
SCOM	CS	58.5 (443.8)	30.9 (379.3)	–46.7 (163.2)	–89.4 (39.4)	–121.1 (63.5)	NS	NS	NS
	MS	–45.8 (28.6)	55.9 (376.3)	–57.5 (25.8)	–66.7 (22.9)	–68 (30.2)			
RA	CS	105.1 (310.7)	–29.6 (76.8)	–60.7 (42)	–72.5 (55.3)	–17.2 (76.5)	NS	NS	NS
	MS	–16.3 (130.6)	–49.9 (32.1)	–53.7 (35.8)	–6.9 (119)	–34.9 (47.9)			
VM	CS	665.9 (205.3)	688.3 (163.5)	778.4 (201.4)	810.3 (185.7)	953.9 (257.9)	***	***	NS
	MS	293.2 (103.7)	315.8 (109.4)	332 (140.4)	398.2 (142.2)	477.3 (184.8)			
	/90°		***NS***	**	***	***			
RF	CS	569.8 (352.4)	520.1 (312.4)	590.1 (384.3)	462.8 (298.4)	610.8 (365)	NS	***	NS
	MS	225.3 (165)	197.1 (189)	206.6 (217)	190.7 (162.1)	256.9 (198.5)			
TA	CS	51.3 (100.7)	4.2 (48.4)	19.2 (55.1)	39.5 (29.3)	82.6 (127.3)	*	**	NS
	MS	26.8 (76.5)	–30.3 (12.3)	–27 (19.9)	1.2 (57.9)	0.7 (23.1)			
	/90°		**	*	***NS***	***NS***			
Sol	CS	480.8 (341.2)	443.3 (432.4)	576.6 (485.7)	523.7 (497.4)	667 (511)	NS	***	NS
	MS	153.8 (166.3)	172.3 (182.1)	163.1 (250.4)	122.7 (169.3)	199.3 (245.9)			
GM	CS	634.8 (331.9)	638.9 (268.3)	691.3 (349.5)	748.2 (474.8)	719.8 (472.9)	NS	***	NS
	MS	160.6 (101.6)	203.6 (160.7)	207.3 (196.8)	192.1 (218.5)	227 (234.4)			
ST	CS	655.9 (159.9)	726.5 (192)	822.7 (265.7)	787.3 (318)	893.6 (399.3)	*		**
	/90°		***NS***	*	***NS***	***			
	MS	272.1 (141)	302.3 (156.3)	340.5 (182.1)	323.8 (245.7)	280.1 (264.4)	NS		
ES T6	CS	280 (180.5)	273.9 (139.6)	273.9 (183.1)	267.4 (220.4)	253.6 (188.7)	NS	***	NS
	MS	150 (77.9)	124.9 (90.1)	112.8 (88)	100.7 (93.5)	105.6 (114.5)			
ES L3	CS	462.1 (182.6)	396.6 (111)	414 (225.4)	354.9 (145.1)	310.1 (142.7)	**	***	NS
	MS	148.9 (81.6)	131.5 (89.9)	113.3 (110.1)	93.7 (97.7)	81.5 (93)			
	/90°		***NS***	***NS***	**	***			

*When the global effect of inclination is significant, the contrasts for each inclination compared to i0 is also shown (/90°). Symbols for the p-values are as follows: *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$; NS: $p \geq 0.05$.*

During the focal phase, only half of the muscles investigated showed any significant variation according to execution speed, with a systematically higher activity in MS condition: RA ($p < 0.05$), RF ($p < 0.001$), VM ($p < 0.001$), Sol ($p < 0.05$), GM ($p < 0.01$), and ST ($p < 0.01$) (**Table 4**).

No statistically significant effect of the interaction between execution speed and backrest inclination was found.

STS Indicators

Durations

The total duration of the STS increased with backrest inclination ($p < 0.01$) and decreased with execution speed ($p < 0.001$) (**Table 5**), but some variations were also specific to each phase of the STS.

When considering the focal phase, its duration was shortened at maximum speed ($p < 0.01$), with no effect resulting from backrest inclination. When focusing on the postural phase, an interaction was found between the 2 factors (inclination × speed) ($p < 0.01$), requiring a specific analysis of the simple main effect of each variable for each different setting. Backrest inclination significantly lengthened postural phase duration under both speed conditions ($p < 0.001$), and maximal speed produced the reverse effect for all inclination levels ($p < 0.001$) (**Table 5**).

CoP Maximal Backward Displacement (Δx_P)

An interaction effect inclination × speed was evidenced by the ANOVA ($p < 0.001$) (**Figure 6**), requiring that each simple main effect be analyzed separately.

Backrest inclination had a significant effect only in the condition MS ($p < 0.001$), with CoP maximal backward displacement decreasing with backrest inclination at 120° inclination and 130° inclination compared to the 90° level (**Figure 6** and **Table 6**).

The effects of backrest inclination on CoP parameters could be observed in the raw data presented in **Figure 7**, with smaller and earlier excursion of CoP traces associated with increased inclination.

Execution speed had a significant effect at each inclination level with greater CoP maximal backward displacement at MS ($p < 0.001$) (**Table 6**).

TABLE 2 | Mean (SD) muscle activity levels in the postural phase (A_{PP}), in % MVC, for the 5 inclination conditions, calculated for both execution speeds.

A_{PP}	90°	100°	110°	120°	130°	*p(i)*
NE	35.03 (16.64)	36.97 (17.31)	37.86 (19.66)	39.06 (20.92)	38.13 (19.42)	NS
p(/90°)		–	–	–	–	
TraS	33.22 (23.75)	31.03 (22.39)	24.91 (13.77)	24.6 (14.15)	22.99 (13.61)	NS
p(/90°)		–	–	–	–	
SCOM	14.64 (13.53)	16.19 (13.75)	19.33 (14.3)	21.38 (14.16)	24.21 (13.89)	***
p(/90°)		NS	**	***	***	
RA	25.11 (20.86)	39.57 (37.31)	44.5 (29.94)	52.28 (38.53)	54.88 (36.49)	***
p(/90°)		**	***	***	***	
VM	3.84 (2.56)	3.86 (2.55)	3.96 (2.55)	3.95 (2.48)	4.82 (6.02)	NS
p(/90°)		–	–	–	–	
RF	5.45 (4.4)	6.07 (4.48)	5.97 (4.31)	6.04 (3.56)	5.45 (3.51)	NS
p(/90°)		–	–	–	–	
TA	22.31 (17.24)	21.09 (19.96)	20.15 (15.92)	19.25 (15.76)	16.9 (13)	**
p(/90°)		NS	NS	**	***	
Sol	19.04 (14.05)	16.41 (11.01)	19.01 18.17)	18.19 (12.49)	18.2 (12.69)	NS
p(/90°)		–	–	–	–	
GM	16.25 (19.44)	14.82 (16.95)	14.74 (16.09)	16.95 (16.02)	15.7 (15.61)	NS
p(/90°)		–	–	–	–	
ST	3.35 (2.59)	3.02 (2.1)	2.99 (1.89)	4.04 (3.05)	4.7 (4.82)	NS
p(/90°)		–	–	–	–	
ES T6	29.82 (43.78)	30.68 (51.41)	34.35 (60)	28.74 (34.18)	25.98 (30.47)	NS
p(/90°)		–	–	–	–	
ES L3	47.57 (57.32)	54.32 (56.65)	56.42 (62.69)	64.11 62.27)	69.26 (79.11)	NS
p(/90°)		–	–	–	–	

*Symbols for the p-values are as follows: **$p < 0.01$; ***$p < 0.001$; NS: $p \geq 0.05$. A dash ("–") indicates that no statistically significant global effect was found, and therefore no further analysis was made.*

Δx_P decrease with backrest inclination at maximal speed can be observed in **Table 6** and from the raw data in **Figure 7**.

CoG Maximal Forward Velocity

Maximal CoG forward velocity (x'_{Gmax}), reached around seat-off, significantly increased with backrest inclination ($p < 0.001$) (**Table 5**) and with execution speed ($p < 0.001$). The contrast analysis showed that all backrest inclination levels higher than 90° caused significantly higher x'_{Gmax} compared to the 90° level.

CoG Maximal Vertical Velocity

CoG maximal vertical velocity (z'_{Gmax}), which was reached during the focal phase, was affected by speed conditions ($p < 0.001$), with larger values at MS (853 ± 159 mm/s at MS vs. 561 ± 85 mm/s at CS) (**Table 5**). However, no variation was observed according to backrest inclination.

DISCUSSION

Effects of Backrest Inclination

Results calculated from EMG and force plate signals revealed that the increase in backrest inclination levels caused significant variations of both muscular activity and biomechanical parameters during the STS.

TABLE 3 | Mean (SD) muscle activity levels in the focal phase (A_{FP}), in % MVC, for the 5 inclination conditions, calculated for both execution speeds.

A_{FP}	90°	100°	110°	120°	130°	*p(i)*
NE	22.57 (12.45)	22.44 (11.84)	26.16 (19.37)	27.41 (22.17)	27.86 (21.72)	NS
p(/90°)		–	–	–	–	
TraS	10.42 (7.49)	9.62 (6.63)	9.08 (5.77)	8.98 (6.13)	9.55 (7.37)	NS
p(/90°)		–	–	–	–	
SCOM	3.25 (1.93)	3.18 (1.82)	3.78 (2.23)	3.52 (2.03)	3.55 (2.24)	NS
p(/90°)		–	–	–	–	
RA	5.61 (6.28)	5.82 (6.15)	5.63 (6.06)	5.73 (6.19)	5.85 (6.6)	NS
p(/90°)		–	–	–	–	
VM	33.15 (10.64)	30.62 (9.78)	31.49 (11.01)	30.10 (11.17)	30.34 (10.92)	NS
p(/90°)		–	–	–	–	
RF	16.51 (8.06)	15.04 (7.47)	15.98 (8.24)	15.45 (7.51)	15.97 (8.28)	*
p(/90°)		**	NS	*	NS	
TA	28.19 (21.63)	26.57 (20.19)	26.18 (17.88)	25.57 (18.92)	26.84 (22.01)	NS
p(/90°)		–	–	–	–	
Sol	34.72 (16.25)	32.4 (14.93)	31.35 (15.48)	30.22 (13.88)	32.85 (18.26)	*
p(/90°)		NS	*	**	NS	
GM	26.41 (22.46)	27.96 (26.65)	25.51 (23.60)	27.63 (23.94)	28.11 (24.48)	NS
p(/90°)		–	–	–	–	
ST	24.67 (18.13)	20.18 (12.32)	23.79 (18.44)	22.61 (18.00)	21.27 (14.87)	NS
p(/90°)		–	–	–	–	
ES T6	15.5 (9.28)	15.61 (9.01)	16.09 (9.40)	15.38 (7.95)	15.87 (8.70)	NS
p(/90°)		–	–	–	–	
ES L3	32.10 (11.45)	30.51 (10.26)	30.61 (12.18)	28.58 (8.18)	29.53 (8.81)	NS
p(/90°)		–	–	–	–	

*Symbols for the p-values are as follows: *$p < 0.05$; **$p < 0.01$; NS: $p \geq 0.05$. A dash ("–") indicates that no statistically significant global effect was found, and therefore no further analysis was made.*

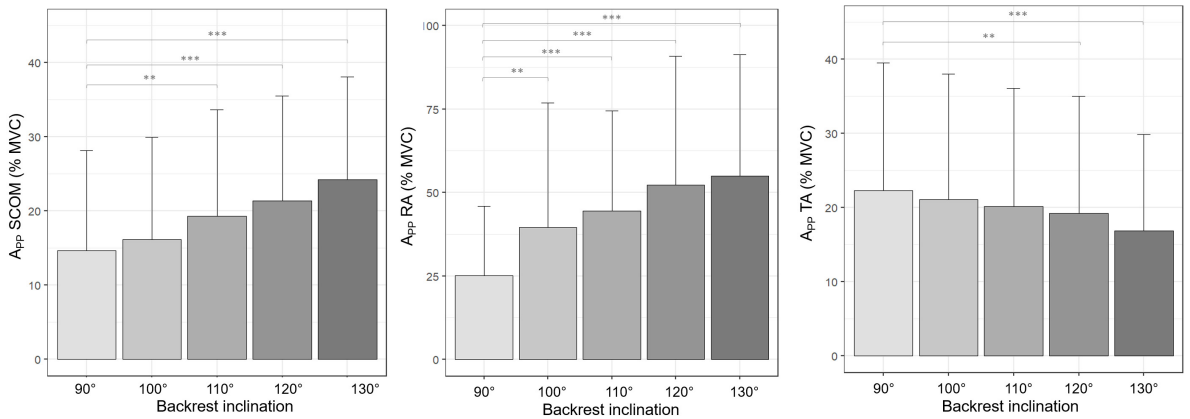

FIGURE 5 | Mean (SD) muscle activity levels in the postural phase (APP), in % MVC, for the 5 inclination conditions calculated for both execution speeds. Symbols for the *p*-values are as follows: $^{**}p < 0.01$; $^{***}p < 0.001$.

With a reclined backrest, the duration of the postural phase increased. This phenomenon can be related to the increased range of motion of the trunk when it is initially more extended, under the hypothesis of a limited variation of movement velocity. Consistently, onset times were also delayed with backrest inclination for VM and ST, which are part of the prime movers of body extension (Roebroeck et al., 1994; Vander Linden et al., 1994; Rodrigues-de-Paula-Goulart and Valls-Solé, 1999).

In accordance with a recent study (Tebbache and Hamaoui, 2020), differences in mean muscular activity levels were mainly observed during the postural phase, with higher values for two trunk (RA) and neck (SCOM) muscles when the trunk was more inclined backward.

These variations might be explained by a larger initial torque of the force of gravity about the ischial tuberosities, as the lever arm of upper body weight is larger when the trunk is further extended, and therefore a higher level of muscular activity is required to perform trunk flexion. Moreover, the onset time of ES L3 was shorter when the backrest was more inclined, suggesting earlier involvement of the lower back muscles in order to generate forces at the lumbar level to counteract gravity.

This increased muscular demand during the postural phase led to a larger x'_{Gmax}, which took place shortly after the seat-off. Smaller APAs amplitude and TA activity level could be related to this higher momentum gained during the extended course of trunk flexion.

More specifically, these results suggest that with increased trunk range of motion and velocity, the role played by TA is taken over by trunk muscles (specifically flexors, SCOM and RA) and becomes less essential for STS success.

Indeed, as observed in our previous study (Tebbache and Hamaoui, 2020), TA activity level was reduced with backrest inclination in the postural phase, with no variation during the focal phase. Its activation was also delayed when the backrest was inclined, suggesting a lower participation in the STS task, as observed by various authors when the initial geometrical configuration deviated from the standard one (Doorenbosch et al., 1994; Vander Linden et al., 1994; Khemlani et al., 1999; Rodrigues-de-Paula-Goulart and Valls-Solé, 1999). Indeed, TA is involved in the backward shift of the center of pressure at STS initiation, occurring together with the inhibition of the soleus

TABLE 4 | Mean (SD) muscle activity levels in the postural phase (A_{PP}) and in the focal phase (A_{FP}) in % MVC for the 2 speed conditions: comfortable speed (CS) and maximal speed (MS), calculated for the 5 backrest inclination levels.

	A_{PP}			A_{FP}		
	CS	**MS**	***p(V)***	**CS**	**MS**	***p(V)***
NE	27.20	47.62	***	24.91	25.66	–
	(14.00)	(16.99)		(15.75)	(19.99)	
TraS	19.62	35.08	***	10.01	9.05	–
	(10.39)	(21.07)		(6.72)	(6.54)	
SCOM	10.24	28.06	***	3.11	3.8	–
	(6.49)	(14.10)		(1.66)	(2.32)	
RA	27.11	59.43	**	5.29	6.16	*
	(18.85)	(38.58)		(6.19)	(6.1)	
VM	3.31	4.86	*	28.49	33.79	***
	(3.94)	(2.79)		(9.73)	(10.88)	
RF	4.28	7.31	***	14.16	17.42	***
	(2.9)	(4.42)		(7.33)	(8.01)	
TA	18.65	21.23	–	25.71	27.63	–
	(15.08)	(16.35)		(20.98)	(18.89)	
Sol	11.67	24.67	**	28.99	35.63	*
	(6.7)	(15.79)		(12.96)	(17.46)	
GM	8.25	23.14	***	20.39	33.87	**
	(7.91)	(19.59)		(17.45)	(27.52)	
ST	2.66	4.59	**	17.35	27.65	**
	(1.76)	(3.8)		(10.12)	(19.59)	
ES T6	17.5	42.32	–	16.27	15.11	–
	(16.24)	(58.75)		(9.5)	(7.97)	
ES L3	33.36	83.31	***	28.98	31.55	–
	(34.07)	(75.74)		(7.75)	(12.1)	

*Symbols for the p-values are as follows: *p < 0.05; **p < 0.01; ***p < 0.001; NS: p ≥ 0.05. A dash ("–") indicates that no statistically significant global effect was found, and therefore no further analysis was made.*

TABLE 5 | Mean (SD) total durations of the STS (dSTS), duration of the postural phase (dPP), maximal CoG anteroposterior velocity (x'_{Gmax}), for the 5 inclination conditions and for the 2 speed conditions: comfortable speed (CS) and maximal speed (MS).

	dSTS (ms)	dPP (ms)		dFP (ms)	x'_{Gmax} (mm/s)	z'_{Gmax} (mm/s)
		CS	MS			
90°	2,267 (436)	738 (154)	374 (71)	1,711 (276)	578 (118)	706 (217)
100°	2,393 (379)	775 (149)	407 (97)	1,802 (316)	601 (111)	693 (194)
110°	2,342 (477)	851 (175)	463 (98)	1,685 (292)	612 (112)	706 (186)
120°	2,487 (430)	939 (150)	525 (110)	1,755 (304)	626 (108)	721 (196)
130°	2,553 (476)	1,080 (163)	610 (124)	1,707 (313)	630 (14)	709 (190)
p(i)	**	***	***	NS	***	NS
p(100°/90°)	NS	NS	*	–	*	–
p(110°/100°)	NS	***	***	–	***	–
p(120°/110°)	**	***	***	–	***	–
p(130°/120°)	***	***	***	–	***	–
p(V)	***	***		**	***	***
*p(i*V)*	NS	**		NS	NS	NS

*For dPP, speed conditions were considered separately as the interaction effect i x V was significant. Symbols for the p-values are as follows: *p < 0.05; **p < 0.01; ***p < 0.001; NS: p ≥ 0.05. A dash ("–") indicates that no statistically significant global effect was found, and therefore no further analysis was made.*

TABLE 6 | Δx_P values for the 5 inclination conditions and for in the 2 speed conditions: comfortable speed (CS) and maximal speed (MS).

	Δx_P (mm)	
	CS	MS
90°	55 (25)	210 (72)
100°	60 (22)	212 (71)
110°	62 (23)	194 (65)
120°	67 (26)	178 (58)
130°	65 (24)	157 (50)
p(i)	**NS**	***
p(100°/90°)	–	NS
p(110°/100°)	–	NS
p(120°/110°)	–	***
p(130°/120°)	–	***
p(V)	***	
p(i*V)	***	

*Symbols for the p-values are as follows: ***p < 0.001; NS: p ≥ 0.05. A dash ("–") indicates that no statistically significant global effect was found, and therefore no further analysis was made.*

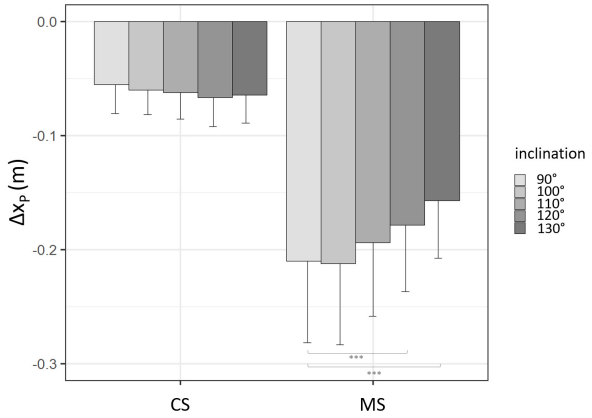

FIGURE 6 | Maximal CoP backward displacement as a function of speed and backrest inclination. Mean and standard deviations are presented for the 2 speed conditions and the 5 backrest inclination levels. ***$p < 0.001$.

muscle (Sol) (Crenna and Frigo, 1991). This functional unit thus results in a larger lever arm of the ground reaction force about the ankle joint, creating an angular external moment which facilitates the propulsion of the body by breaking the rotation equilibrium in whole-body movements such as the STS task, gait initiation or pushing ramp efforts (Breniere and Do, 1986; Crenna and Frigo, 1991). The analysis of CoP trajectory showed that the initial backward shift (Δx_P), which is considered as an indicator of APAs amplitude (Bouisset and Do, 2008; Diakhaté et al., 2013; Hamaoui and Alamini-Rodrigues, 2017), had smaller values when the backrest was more inclined, but only in MS condition.

This tends to further confirm the reduced necessity to generate those APAs, because they would have been less efficient given the initial segmental configuration and would even be counterproductive for fast hip flexion.

The compensation by the increased horizontal momentum should be enhanced at maximal speed, as the momentum gained is larger.

Furthermore, these results can be analyzed in light of the three mechanisms by which balance of a standing human can be maintained (Hof, 2007): displacing the CoP with respect to the vertical projection of the CoG (first mechanism), rotating a body segment with respect to the CoG (second mechanism) and applying an external force other than the ground reaction force (third mechanism) (Hof, 2007). Those three mechanisms contribute to modifying CoG acceleration. In the present study, it was observed that counter-rotating the trunk around the CoG (thus using the second mechanism) reduced the need for larger displacement of the CoP within the base of support (first mechanism).

The adjustments taking place during the postural phase and leading to a larger horizontal velocity allow for the maintenance of a globally unaltered focal phase, as suggested by its unchanged duration and CoG maximal vertical velocity.

Indeed, in contrast with x'_{Gmax}, z'_{Gmax}, which was reached later during the focal phase, was unaffected by backrest inclination, probably because the main effect of trunk flexion occurred along the anterior-posterior axis. Although the momentum transfer strategy suggests a transfer of the horizontal

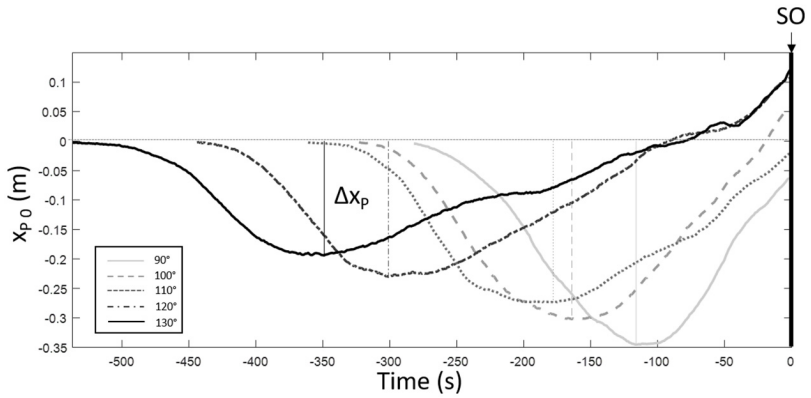

FIGURE 7 | Displacement of x_P during the postural phase (until SO, seat-off time) as a function of time for one subject for the 5 backrest inclinations.

momentum to the vertical momentum (Schenkman et al., 1990), it seemed not to be entirely so in this study.

These results rather suggest a separate programming of the two phases although they are biomechanically interdependent.

It must be noted that the increase of postural phase duration in conditions of more inclined backrest does not necessarily represents a reorganization of the postural adjustments, as the course of trunk flexion is larger, and then automatically longer for a same execution speed.

Effects of Execution Speed

The speed factor was initially selected to highlight the effects of backrest inclination, but speed effects were also studied thoroughly. Results showed that all muscles, except TA and SCOM, which were the first to be activated, presented a reduced onset time at maximal speed. Higher levels were observed for 10 muscles out of 12 during the postural phase, and for 6 out of 12 during the focal phase, suggesting a predominant effect in the former, as observed in previous work (Tebbache and Hamaoui, 2020). These variations in the muscular pattern resulted in a shorter duration of both postural and focal phases, with an increase of Δx_P, x'_{Gmax} and z'_{Gmax} values. This way, earlier and higher muscular activity allowed for larger anticipatory postural adjustments and a better performance along the anterior-posterior and vertical axes. In contrast with the existing literature, which has depicted a more pronounced variation of vertical linear momenta compared to horizontal momenta (Pai and Rogers, 1988, 1990; Pai et al., 1994; Gross et al., 1998), our data showed the same levels of variation between CoP velocity peaks. Hence, the theory according to which horizontal momentum is limited due to balance constraints requiring the subject to stand straight at the end of the movement (Pai and Rogers, 1990) cannot be extended to conditions where the trunk was initially inclined backward.

Adaptability of STS Parameters

Taken together, results from EMG and force plate data showed an adaptation of the STS strategy driven by the new biomechanical demand related to backrest inclination and execution speed.

A more extended initial position of the trunk was associated with increased muscular activity which led to increased kinetic energy gained through a wider range of trunk flexion, lowering the need of APAs.

A similar analysis could be made in respect of execution speed, showing an increased activity of all recorded muscles during the postural phase, and an increase in APAs magnitude and CoG velocity peaks.

These adaptations to biomechanical factors, rather than an in-depth reprogramming of the task, are in line with existing literature, which showed that an increase in ischiofemoral contact area with the seat (Diakhaté et al., 2013), a reduction in cervical (Hamaoui and Alamini-Rodrigues, 2017) or lumbar mobility (Alamini-Rodrigues and Hamaoui, 2017) led to modifications in APAs amplitude or duration and to lower motor performance. An insight of this result was observed in our previous study (Tebbache and Hamaoui, 2020), with muscular variations concordant with the initial geometrical configuration and mainly confined to the muscles active in the postural phase.

However, it must be noted that the increase of postural phase duration in conditions of more inclined backrest does not necessarily represents a reorganization of the postural adjustments, as the course of trunk flexion is larger, which naturally extends the duration of the postural phase for a same execution velocity.

From a more conceptual point of view, our findings also support the key principles that postural adjustments are task-specific, adaptable and under the control of the central nervous system (Bouisset and Do, 2008). Such ability requires an internal representation of the biomechanical parameters of the human body and their integration in motor programming.

Practical Implications

Reclining the backrest, which increases static comfort due to a better distribution of the pressure across the soft tissue in contact with the seat (Hertzberg, 1972; Andersson et al., 1975; Barbenel, 1992) and to a decreased component of the gravity force on the spine (Andersson et al., 1979), has implications regarding the completion of the STS. It concerns the postural phase, with a need

for higher activity of neck and trunk flexors (SCOM and RA) that could be a limiting factor for older people or patients presenting a weakness in these muscles. As a consequence, one can question the interest of bringing the backrest at 90° before performing the task, especially for people suffering a limited function of trunk and neck muscles. However, setting backrest inclination must then be easy to perform and much secure (slow velocity, no accidental triggering. . .), which is a challenging objective.

When considering the increase of kinetic energy for higher ranges of trunk flexion, which are associated with a lower need of TA and RF activity, it might in theory be beneficial to patients suffering lower limbs disorders, but only if trunk and neck muscles function is preserved.

LIMITATIONS

The main limitation of the study design was the absence of kinematical data, which did not allow for a segmental analysis of osteo-articular mobility and its association with the muscular pattern. The sample size was also relatively small, but the population was homogeneous in terms of age and BMI. Regarding data analysis, the method was oversimplified and approximations were made in calculating the position of the CoP and the CoG, but the consequences can be considered as negligible because the system was at postural equilibrium prior to movement initiation.

Another limitation might be the order of the tasks which was partly randomized (execution speed but not the backrest inclination angle) due to the technical constraints of the customed seat. However, the 120 s rest time between series and the repeated stimulation of the subject all along the experiment should have minimized this side effect.

It must also be noted that the postural phase is longer and probably more conscious in the STS than in many other tasks exploring the postural adjustments (rising on tip toes, pointing, gait initiation. . .). As a consequence, one can question the possibility that the variations of the postural phase observed in maximum velocity condition might rather represent the compliance to the experiment instructions than a postural adjustment supporting the focal phase. However, the participants were asked to reach the standing posture as fast as possible, and not to perform the two phases quicker. With the focus on the goal, they were given the freedom to adapt postural phase parameters to the focal phase.

CONCLUSION

This study revealed that the variations in STS programming associated with inclined backrest mainly consist in a simple and direct adaptation to the new biomechanical demand, with no in-depth reprogramming. It mainly raised the activity level of trunk and neck flexors due to the augmented torque of gravity about the ischial tuberosities center, but it also lowered the recruitment of some lower limbs muscles (TA, RF) thanks to the increased kinetic energy gained during the longer trunk flexion. Hence reclining the backrest should make the task more demanding at trunk level but less demanding for the lower limbs.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee for Movement Analysis (CERAM), INU Champollion. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

AH wrote the initial research project. NT and AH contributed to conception and design of the study. NT organized the database. Both authors contributed to manuscript revision, read, and approved the submitted version.

FUNDING

This work has been funded by the Region Occitanie (France) and the European Regional Development Fund (FEDER). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

REFERENCES

Alamini-Rodrigues, C., and Hamaoui, A. (2017). Effect of three different lumbar splints on posturokinetic capacity when performing the sit-to-stand task. *Ann. Phys. Rehabil. Med.* 60, 406–409. doi: 10.1016/j.rehab.2016.09.003

An, Q., Ishikawa, Y., Nakagawa, J., Oka, H., Yamakawa, H., Yamashita, A., et al. (2013). "Muscle synergy analysis of human standing-up motion with different chair heights and different motion speeds," in *Proceedings of the 2013 IEEE International Conference on Systems, Man, and Cybernetics*, (Manchester: IEEE), 3579–3584.

Andersson, B. J., Ortengren, R., Nachemson, A. L., Elfström, G., and Broman, H. (1975). The sitting posture: an electromyographic and discometric study. *Orthop. Clin. North Am.* 6, 105–120. doi: 10.1016/s0030-5898(20)31205-0

Andersson, G. B., Murphy, R. W., Ortengren, R., and Nachemson, A. L. (1979). The influence of backrest inclination and lumbar support on lumbar lordosis. *Spine* 4, 52–58. doi: 10.1097/00007632-197901000-00009

Arborelius, U. P., Wretenberg, P., and Lindberg, F. (1992). The effects of armrests and high seat heights on lower-limb joint load and muscular activity during sitting and rising. *Ergonomics* 35, 1377–1391. doi: 10.1080/00140139208967399

Barbenel, J. (1992). Pressure management. *Prosthet. Orthot. Int.* 15, 225–231.

Belenkii, V. E., Gurfinkel, V. S., and Paltsev, E. I. (1967). [Control elements of voluntary movements]. *Biofizika* 12, 135–141.

Bernstein, N. (1967). *The Co-Ordination and Regulation of Movements*. Oxford: Pergamon-Press, 236.

Bouchouras, G., Patsika, G., Hatzitaki, V., and Kellis, E. (2015). Kinematics and knee muscle activation during sit-to-stand movement in women with knee osteoarthritis. *Clin. Biomech.* 30, 599–607. doi: 10.1016/j.clinbiomech.2015.03.025

Bouisset, S., and Do, M.-C. (2008). Posture, dynamic stability, and voluntary movement. *Neurophysiol. Clin.* 38, 345–362. doi: 10.1016/j.neucli.2008.10.001

Bouisset, S., and Zattara, M. (1981). A sequence of postural movements precedes voluntary movement. *Neurosci. Lett.* 22, 263–270. doi: 10.1016/0304-3940(81)90117-8

Bouisset, S., and Zattara, M. (1987). Biomechanical study of the programming of anticipatory postural adjustments associated with voluntary movement. *J. Biomech.* 20, 735–742. doi: 10.1016/0021-9290(87)90052-2

Boukadida, A., Piotte, F., Dehail, P., and Nadeau, S. (2015). Determinants of sit-to-stand tasks in individuals with hemiparesis post stroke: a review. *Ann. Phys. Rehabil. Med.* 58, 167–172. doi: 10.1016/j.rehab.2015.04.007

Breniere, Y., and Do, M. C. (1986). When and how does steady state gait movement induced from upright posture begin? *J. Biomech.* 19, 1035–1040. doi: 10.1016/0021-9290(86)90120-x

Brenière, Y., and Do, M. C. (1991). Control of gait initiation. *J. Mot. Behav.* 23, 235–240.

Burdett, R. G., Habasevich, R., Pisciotta, J., and Simon, S. R. (1985). Biomechanical comparison of rising from two types of chairs. *Phys. Ther.* 65, 1177–1183. doi: 10.1093/ptj/65.8.1177

Chorin, F., Cornu, C., Beaune, B., Frère, J., and Rahmani, A. (2016). Sit to stand in elderly fallers vs non-fallers: new insights from force platform and electromyography data. *Aging Clin. Exp. Res.* 28, 871–879. doi: 10.1007/s40520-015-0486-1

Conforto, S., D'Alessio, T., and Pignatelli, S. (1999). Optimal rejection of movement artefacts from myoelectric signals by means of a wavelet filtering procedure. *J. Electromyogr. Kinesiol.* 9, 47–57. doi: 10.1016/s1050-6411(98)00023-6

Cordo, P. J., and Nashner, L. M. (1982). Properties of postural adjustments associated with rapid arm movements. *J. Neurophysiol.* 47, 287–302. doi: 10.1152/jn.1982.47.2.287

Crenna, P., and Frigo, C. (1991). A motor programme for the initiation of forward-oriented movements in humans. *J. Physiol.* 437, 635–653. doi: 10.1113/jphysiol.1991.sp018616

Cuesta-Vargas, A. I., and Gonzalez Sanchez, M. (2013). Differences in muscle activation patterns during sit to stand task among subjects with and without intellectual disability. *Biomed Res. Int.* 2013:e173148.

Diakhaté, D. G., Do, M. C., and Le Bozec, S. (2013). Effects of seat-thigh contact on kinematics performance in sit-to-stand and trunk flexion tasks. *J. Biomech.* 46, 879–882. doi: 10.1016/j.jbiomech.2012.12.022

Doorenbosch, C. A., Harlaar, J., Roebroeck, M. E., and Lankhorst, G. J. (1994). Two strategies of transferring from sit-to-stand; the activation of monoarticular and biarticular muscles. *J. Biomech.* 27, 1299–1307. doi: 10.1016/0021-9290(94)90039-6

Gillette, J. C., and Stevermer, C. A. (2012). The effects of symmetric and asymmetric foot placements on sit-to-stand joint moments. *Gait Posture* 35, 78–82. doi: 10.1016/j.gaitpost.2011.08.010

Gross, M. M., Stevenson, P. J., Charette, S. L., Pyka, G., and Marcus, R. (1998). Effect of muscle strength and movement speed on the biomechanics of rising from a chair in healthy elderly and young women. *Gait Posture* 8, 175–185. doi: 10.1016/s0966-6362(98)00033-2

Hamaoui, A., and Alamini-Rodrigues, C. (2017). Influence of cervical spine mobility on the focal and postural components of the sit-to-stand task. *Front. Hum. Neurosci.* 11:129. doi: 10.3389/fnhum.2017.00129

Herman, R., Cook, T., Cozzens, B., and Freedman, W. (1973). "Control of postural reactions in man: the initiation of gait," in *Control of Posture and Locomotion. Advances in Behavioral Biology*, eds R. B. Stein, K. G. Pearson, R. S. Smith, and J. B. Redford (Boston, MA: Springer US), 363–388. doi: 10.1007/978-1-4613-4547-3_28

Hermens, H. J., Freriks, B., Disselhorst-Klug, C., and Rau, G. (2000). Development of recommendations for SEMG sensors and sensor placement procedures. *J. Electromyogr. Kinesiol.* 10, 361–374. doi: 10.1016/s1050-6411(00)00027-4

Hertzberg, H. T. E. (1972). *The Human Buttocks in Sitting: Pressures, Patterns, and Palliatives*. SAE Technical Paper No. 72005. New York, NY: SAE Inc.

Hirschfeld, H., Thorsteinsdottir, M., and Olsson, E. (1999). Coordinated ground forces exerted by buttocks and feet are adequately programmed for weight transfer during sit-to-stand. *J. Neurophysiol.* 82, 3021–3029. doi: 10.1152/jn.1999.82.6.3021

Hof, A., Gazendam, M. G. J., and Sinke, W. E. (2005). The condition for dynamic stability. *J. Biomech.* 38, 1–8. doi: 10.1016/j.jbiomech.2004.03.025

Hof, A. L. (2007). The equations of motion for a standing human reveal three mechanisms for balance. *J. Biomech.* 40, 451–457. doi: 10.1016/j.jbiomech.2005.12.016

Hughes, M. A., Weiner, D. K., Schenkman, M. L., Long, R. M., and Studenski, S. A. (1994). Chair rise strategies in the elderly. *Clin. Biomech.* 9, 187–192. doi: 10.1016/0268-0033(94)90020-5

Kawagoe, S., Tajima, N., and Chosa, E. (2000). Biomechanical analysis of effects of foot placement with varying chair height on the motion of standing up. *J. Orthop. Sci.* 5, 124–133. doi: 10.1007/s007760050139

Kelley, D. L., Dainis, A., Wood, G. K. (1976). "Mecanics and muscular dynamics of rising from a seated position," in *Proceedings of the 5th International Congress of Biomechanics, Jyväskylä, Finland. Biomechanics, V-B*, Vol. 1B, ed. P. V. Komi (Baltimore, MD: University Park Press), 127-134.

Khemlani, M. M., Carr, J. H., and Crosbie, W. J. (1999). Muscle synergies and joint linkages in sit-to-stand under two initial foot positions. *Clin. Biomech.* 14, 236–246. doi: 10.1016/s0268-0033(98)00072-2

Lidierth, M. (1986). A computer based method for automated measurement of the periods of muscular activity from an EMG and its application to locomotor EMGs. *Electroencephalogr. Clin. Neurophysiol.* 64, 378–380. doi: 10.1016/0013-4694(86)90163-x

Millington, P. J., Myklebust, B. M., and Shambes, G. M. (1992). Biomechanical analysis of the sit-to-stand motion in elderly persons. *Arch. Phys. Med. Rehabil.* 73, 609–617.

Munton, J. S., Ellis, M. I., and Wright, V. (1984). Use of electromyography to study leg muscle activity in patients with arthritis and in normal subjects during rising from a chair. *Ann. Rheum. Dis.* 43, 63–65. doi: 10.1136/ard.43.1.63

Ng, S. S. M., Kwong, P. W. H., Chau, M. S. P., Luk, I. C. Y., Wan, S. S., and Fong, S. S. M. (2015). Effect of arm position and foot placement on the five times sit-to-stand test completion times of female adults older than 50 years of age. *J. Phys. Ther. Sci.* 27, 1755–1759. doi: 10.1589/jpts.27.1755

Nuzik, S., Lamb, R., VanSant, A., and Hirt, S. (1986). Sit-to-stand movement pattern. A kinematic study. *Phys. Ther.* 66, 1708–1713. doi: 10.1093/ptj/66.11.1708

Pai, Y.-C. C., Naughton, B., Chang, R., and Rogers, M. (1994). Control of body centre of mass momentum during sit-to-stand among young and elderly adults. *Gait Posture* 2, 109–116. doi: 10.1016/0966-6362(94)90100-7

Pai, Y.-C. C., and Rogers, M. W. (1988). Dependence of weight transfer patterns on the speed of ascent during sit-to-stand. *J. Biomech.* 21:863. doi: 10.1016/0021-9290(88)90054-1

Pai, Y.-C. C., and Rogers, M. W. (1990). Control of body mass transfer as a function of speed of ascent in sit-to-stand. *Med. Sci. Sports Exerc.* 22, 378–384.

Rodosky, M. W., Andriacchi, T. P., and Andersson, G. B. (1989). The influence of chair height on lower limb mechanics during rising. *J. Orthop. Res.* 7, 266–271. doi: 10.1002/jor.1100070215

Rodrigues-de-Paula-Goulart, F., and Valls-Solé, J. (1999). Patterned electromyographic activity in the sit-to-stand movement. *Clin. Neurophysiol.* 110, 1634–1640. doi: 10.1016/s1388-2457(99)00109-1

Roebroeck, M. E., Doorenbosch, C. A., Harlaar, J., Jacobs, R., and Lankhorst, G. J. (1994). Biomechanics and muscular activity during sit-to-stand transfer. *Clin. Biomech.* 9, 235–244. doi: 10.1016/0268-0033(94)90004-3

Schenkman, M., Berger, R. A., Riley, P. O., Mann, R. W., and Hodge, W. A. (1990). Whole-body movements during rising to standing from sitting. *Phys. Ther.* 70, 638–648; discussion648–651.

Schenkman, M., Riley, P., and Pieper, C. (1996). Sit to stand from progressively lower seat heights — alterations in angular velocity. *Clin. Biomech.* 11, 153–158. doi: 10.1016/0268-0033(95)00060-7

Shepherd, R. B., and Koh, H. P. (1996). Some biomechanical consequences of varying foot placement in sit-to-stand in young women. *Scand. J. Rehabil. Med.* 28, 79–88.

Stapley, P., Pozzo, T., and Grishin, A. (1998). The role of anticipatory postural adjustments during whole body forward reaching movements. *Neuroreport* 9, 395–401. doi: 10.1097/00001756-199802160-00007

Tebbache, N., and Hamaoui, A. (2020). Sit-to-stand muscular activity for different seat backrest inclination levels and execution speeds. *Motor Control* 24, 527–542. doi: 10.1123/mc.2020-0014

Vander Linden, D. W., Brunt, D., and McCulloch, M. U. (1994). Variant and invariant characteristics of the sit-to-stand task in healthy elderly adults. *Arch. Phys. Med. Rehabil.* 75, 653–660. doi: 10.1016/0003-9993(94)90188-0

Yoshioka, S., Nagano, A., Hay, D. C., and Fukashiro, S. (2014). Peak hip and knee joint moments during a sit-to-stand movement are invariant to the change of seat height within the range of low to normal seat height. *Biomed. Eng. Online* 13:27. doi: 10.1186/1475-925x-13-27

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Human Neuroscience

ORIGINAL RESEARCH
published: 10 September 2021
doi: 10.3389/fnhum.2021.719502

Vibration of the Whole Foot Soles Surface Using an Inexpensive Portable Device to Investigate Age-Related Alterations of Postural Control

*Lydiane Lauzier[1], Mohamed Abdelhafid Kadri[1], Emilie Bouchard[1], Kevin Bouchard[2], Sébastien Gaboury[2], Jean-Michel Gagnon[1], Marie-Pier Girard[1], Andréanne Larouche[1], Roxane Robert[1], Patrick Lapointe[2], Rubens A. da Silva[1,3] and Louis-David Beaulieu[1]**

[1] Laboratoire de Recherche Biomécanique & Neurophysiologique en Réadaptation Neuro-Musculo-Squelettique (Lab BioNR), Centre Intersectoriel en Santé Durable, Université du Québec à Chicoutimi, Chicoutimi, QC, Canada, [2] Laboratoire d'Intelligence Ambiante pour la Reconnaissance d'Activités (LIARA), Centre Intersectoriel en Santé Durable, Université du Québec à Chicoutimi, Chicoutimi, QC, Canada, [3] Centre Intégré de Santé et Services Sociaux du Saguenay-Lac-Saint-Jean (CIUSSS SLSJ), Hôpital de La Baie, Saguenay, QC, Canada

OPEN ACCESS

Edited by:
Paolo Cavallari,
University of Milan, Italy

Reviewed by:
Paolo Bernardis,
University of Trieste, Italy
Renato Moraes,
University of São Paulo, Brazil

***Correspondence:**
Louis-David Beaulieu
louis-david_Beaulieu@uqac.ca

Specialty section:
This article was submitted to Motor Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: 02 June 2021
Accepted: 18 August 2021
Published: 10 September 2021

Citation:
Lauzier L, Kadri MA, Bouchard E, Bouchard K, Gaboury S, Gagnon J-M, Girard M-P, Larouche A, Robert R, Lapointe P, da Silva RA and Beaulieu L-D (2021) Vibration of the Whole Foot Soles Surface Using an Inexpensive Portable Device to Investigate Age-Related Alterations of Postural Control. Front. Hum. Neurosci. 15:719502. doi: 10.3389/fnhum.2021.719502

Background: Standing on a foam surface is used to investigate how aging affect the ability to keep balance when somatosensory inputs from feet soles become unreliable. However, since standing on foam also affects the efficacy of postural adjustments, the respective contributions of sensory and motor components are impossible to separate. This study tested the hypothesis that these components can be untangled by comparing changes of center of pressure (CoP) parameters induced by standing on a foam pad vs. a novel vibration (VIB) platform developed by our team and targeting feet soles' mechanoreceptors.

Methods: Bipedal postural control of young (n = 20) and healthy elders (n = 20) was assessed while standing barefoot on a force platform through 3 randomized conditions: (1) Baseline (BL); (2) VIB; and (3) Foam. CoP Amplitude and Velocity in the antero-posterior/medio-lateral (AP/ML) directions and COP Surface were compared between conditions and groups.

Findings: Both VIB and Foam increased CoP parameters compared to BL, but Foam had a significantly greater impact than VIB for both groups. Young and Old participants significantly differed for all three Conditions. However, when correcting for BL levels of postural performance, VIB-related increase of COP parameters was no longer different between groups, conversely to Foam.

Interpretation: Although both VIB and Foam highlighted age-related differences of postural control, their combined use revealed that "motor" and "sensory" components are differently affected by aging, the latter being relatively unaltered, at least in healthy/active elders. The combined used of these methods could provide relevant knowledge to better understand and manage postural impairments in the aging population.

Keywords: aging, cutaneous vibration, exteroception, foam surface, postural control, proprioception running title

INTRODUCTION

Aging results in structural and functional deteriorations of sensory receptors, as well as less effective neural processing of sensory afferents for motor and postural control (Perry, 2006; Atchison et al., 2008; Goble et al., 2009; Kwan et al., 2010; Seidler et al., 2010; Owsley, 2011). These changes play a key role in the increased risk of postural imbalance and falls in older adults (>65 years) (Vellas et al., 1997; Viseux, 2020), which have dreadful consequences both in human lives and healthcare costs[1]. Cutaneous mechanoreceptors located under the feet progressively lose their sensitivity with advancing age [i.e., reduced number of sensory receptors, decreased skin elasticity and a lower conduction time in the nervous system (Shaffer and Harrison, 2007; Kwan et al., 2010; Roberts and Allen, 2016; Viseux, 2020). Reduced sensitivity to cutaneous stimuli is in fact one of the earliest signs of peripheral neuropathy that develops with advancing age and in the presence of various diseases such as diabetes (Sacco et al., 2015). As a direct physical link with the ground, the foot sole is particularly well positioned to provide the postural control system with crucial sensory information about the ongoing state of balance (Viseux, 2020). Testing the integrity of feet mechanoreceptors and their contribution to postural control is thus highly relevant for an early detection of balance disorders and risk of falls in older peoples (Magnusson et al., 1990; Aboutorabi et al., 2018). However, most of the available evidence tested foot soles sensitivity with the participant lying down or seated, hence limiting our understanding of how foot sole receptors are actively engaged during postural tasks (Patel et al., 2011; Mildren et al., 2016).

Previous attempts to isolate the contribution of the foot sole during upright stance used various neuro-inhibitory methods targeting cutaneous receptors (e.g., cryotherapy, pharmacology or ischemia) (Magnusson et al., 1990; Meyer et al., 2004; Patel et al., 2011; Machado et al., 2017). However, these methods can be time-consuming, invasive and painful, and are therefore less suited for identifying sensory and postural control impairments in clinical settings. Instead, clinicians often ask patients to stand barefoot with their eyes closed on a compliant surface such as a foam mat (Cohen et al., 1993; Chiang and Wu, 1997; Patel et al., 2008; Khattar and Hathiram, 2012). The use of a soft surface intends to reduce the quality of skin mechanoreceptors' input from the feet soles due to the decreased strength of the ground reaction force compared to a firm surface (Chiang and Wu, 1997). As a result, postural sway increases and discharge patterns from feet mechanoreceptors decrease because the postural control system re-weighted the sensory gains to rely more on the other available inputs (e.g., proprioceptive afferents from the ankles joint and muscles, vestibular system) (Fransson et al., 2007; Baltich et al., 2015). Therefore, the use of a foam mat helps clinicians interpreting the risk of falls and postural control impairments from a proprioceptive and exteroceptive standpoint. However, because the patient stands on a surface having particular viscoelastic properties, postural adjustments are also less efficient (Patel et al., 2011). Standing on a foam thus represents a more challenging environment for both sensory and motor aspects of postural control, and their distinctive impact on the global increase of body sway is inextricable.

In research, stimulation of the plantar surface of the foot by the use of focal vibration motors could offer an alternative solution to investigate the specific role of feet mechanoreceptors and sensory re-weighting mechanisms for postural control (Kavounoudias et al., 1998; Maurer et al., 2001; Thompson et al., 2011; Viseux et al., 2019). Our team recently developed the PortVIBplate, a simplified, portable and inexpensive tool to test the contribution of cutaneous mechanoreceptors to postural control (Lafontaine et al., 2020). The device exploits 40 vibration motors analogically. The software to control the platform, the 3D schematics and important information are made openly available to be reproduced by technological savvy persons (Lafontaine et al., 2020). Vibration (VIB) of feet soles with such a system has the advantage of reducing the quality of sensory inputs from mechanoreceptors without impacting the effectiveness of postural adjustments because the person is standing on a firm surface. The strong suprathreshold stimulation of the whole foot by the synchronous activation of VIB motors across the whole foot soles results in a constant bombardment of sensory receptors (Kavounoudias et al., 1998; Maurer et al., 2001; Thompson et al., 2011). By directly increasing their firing rate, foot soles mechanoreceptors are therefore less able to track and correct the course of the ongoing body sway. Contrasting the effects between VIB and foam could provide an unprecedented way for discriminating the contributions of sensory (vibration) vs. sensory + motor (foam) aspects of postural control allowing clinicians to better detect and manage sensory impairments and consequently reduce the risk of falls in older adults (>65 years).

The aim of this study was to compare the effects of vibrating the feet soles vs. standing on a foam mat on postural control in young adults and older adults (>65 years). Based on the available evidence, we hypothesized that (i) old adults will generally present higher postural imbalances compared to young adults; (ii) both the foam mat and feet vibration will increase postural oscillations compared to control condition (i.e., standing on a firm surface), but the impact will be greater for the foam because it challenges both sensory and motor aspects of postural control.

MATERIALS AND METHODS

Participants

Forty male and women aged from 22 to 87 years old were recruited to participate in the experiment. They were divided into 2 groups, young (n = 20) and old (n = 20) based on their age (i.e., young group: 18–30 years; old group: >65 years). Age, morphological characteristics and details about the level of their physical activity are presented in **Table 1**. Based on the inclusion criteria, the recruited participants were in good general health, community-dwelling and able to walk independently without a walking-aid. Exclusion criteria included any functional impairment related to cognitive, neurological, musculoskeletal,

[1] www.who.int/mediacentre/factsheets/fs344/fr/

TABLE 1 | Participant's characteristics.

	Young *N* = 20	Old *N* = 20	Significant difference between groups
Characteristics			
Age (years):			
Mean ± SD	24.85 ± 2.37	73.8 ± 5.72	$p = 0.00$
Gender (*n* = women/male)	9/11	9/11	$p = 0.62$
Height (cm):			
Mean ± SD	171.41 ± 9.43	166.68 ± 9.1	$p = 0.11$
Weight (lbs):			
Mean ± SD	162.5 ± 35.33	157.35 ± 29.39	$p = 0.61$
Physical activity level (min/week):			
Mean ± SD	374.2 ± 297.08	147.4 ± 65.81	$p = 0.00$

vestibular disorders, cardiovascular diseases and ankle, knee and hip injuries in the past 2 years. Research ethical approval was obtained prior to recruitment and participants gave their written informed consent in accordance with the Declaration of Helsinki and the local Ethics Committee.

Experimental Procedure

Anthropometric measures were taken during the first session and the Global Physical Activity ($GPAQ_{v2}$) questionnaire (Bull et al., 2009) was self-administered to collect information regarding the level of physical activity at work and in leisure time. The experimental session (60 min) assessed postural control in bipedal stance in three randomized conditions (10 s/condition; 5 trials/condition): (i) Baseline (standing on the vibration platform but without stimulation), (ii) VIB (cutaneous vibration applied to the whole surface of both feet), (iii) Foam (standing on a $20'' \times 16'' \times 2.5''$ balance pad, Airex Compagny, Switzerland). Duration of the postural measures in all conditions is established according to the duration of vibratory stimulation which, in a similar context (i.e., disruption of muscle spindles by tenon vibration), presents a good reliability for the CoP-based postural parameters (Kadri et al., 2020). Vibration was delivered at 50 Hz by the 40 vibrators (20/foot) of the portable vibration platform (*PortVIBplate*—see Lafontaine et al. (2020)). For all conditions, participants were asked to stand barefoot with eyes blindfolded and the arms along the body, and the feet position was standardized using marks on the *PortVIBplate* and Foam mat. The *PortVIBplate* and the foam mat were placed on a force platform (BIOMEC400, EMG System do Brazil, Ltda., SP) [for the characteristics see Kadri et al. (2020)], to measure variables of postural control based on linear parameters of the center of pressure (CoP). Brief rest period of 1 min between each trial and each condition allowed participants to rest and remove the blindfold. An investigator stood close to the participant to ensure its security during the tests. To control for potentially disruptive sounds and other distractions, the experimenters and participants were instructed to avoid conversations and make abrupt movements.

Data Analysis

The vertical ground reaction force data from the force platform was sampled at 100 Hz. All force signals were filtered with a Butterworth second order low-pass 35 Hz filter (Kadri et al., 2020). Data was converted into stabilometric analyses using the BIOMEC software combined with MATLAB routines (The Mathworks, Natick, MA, United States). The Amplitude (the absolute distance between the max and min center of pressure displacement, in cm), Velocity (sum of the cumulated CoP displacement divided by the total time, in cm s^{-1}) in the anteroposterior (AP) and mediolateral (ML) directions of movement and Surface (90% confidence ellipse, in cm^2) were calculated from CoP data.

Statistical Analysis

Data normality and the absence of outliers were confirmed with the Shapiro–Wilk test and visual screening of box-and-whisker plots. Participant's characteristics were compared with the Unpaired *T*-Test (age, height, weight, and physical activity level) and the Chi-square test (gender). A repeated measures ANOVA model was applied with factors *Group* (young; old) and *Conditions* (BL, VIB, and Foam). In cases of a significant interaction between factors, pair-wise Bonferroni tests adjusted for multiple comparisons were realized. Statistical analysis was done using the SPSS version 20 program (Armonk, NY, United States) with a significant alpha risk below 0.05.

RESULTS

The young and old groups did not differ in terms of gender, height and weight, but were significantly different in their age and level of physical activity (young participants being more active than older—cf. **Table 1**).

Effects of Groups and Experimental Conditions

The analysis of variance found significant interactions between factors *Groups* and *Conditions* for all CoP parameters: AP Amplitude [$F_{(2;76)} = 7.68$; $P = 0.01$]; ML Amplitude [$F_{(2;76)} = 18.65$; $P < 0.000$]; AP Velocity [$F_{(2;76)} = 4.91$; $P = 0.01$]; ML Velocity [$F_{(2;76)} = 22.22$; $P < 0.000$]; CoP Surface [$F_{(2;76)} = 21.43$; $P < 0.000$]. As shown in **Table 2**, *post hoc* comparisons found that all CoP parameters were significantly higher (p values < 0.01) for old compared to young participants across the three experimental conditions (BL, VIB, and Foam). Also, both groups showed significantly higher CoP parameters (P values < 0.01) with mostly large (>0.80) effect sizes (Cohen's D, G*Power 3.1 Software) for Foam vs. BL, VIB vs. BL and Foam vs. VIB (**Table 3**).

Since Young and Old groups differed at BL, a supplementary analysis was realized to compare the impact of VIB and Foam between groups when correcting for BL levels of CoP parameters. Specifically, CoP parameters obtained during VIB and Foam conditions were expressed as ratios of BL level (i.e., VIB BL; Foam BL) and Young and Old groups were compared using Unpaired *T*-Tests. The analysis revealed that the following Foam/BL ratios

TABLE 2 | Postural parameters expressed in mean ± standard deviation for each group and experimental conditions.

	Groups					
	Young			Old		
	Conditions					
Postural parameters	**Baseline**	**VIB**	**Foam**	**Baseline**	**VIB**	**Foam**
Amplitude AP (cm)	1.20 ± 0.33	1.41 ± 0.39[a]	2.79 ± 0.64[a,b]	1.40 ± 0.43	1.72 ± 0.54[a]	3.76 ± 1.16[a,b]
Amplitude ML (cm)	1.49 ± 0.43	2.10 ± 0.62[a]	3.41 ± 0.63[a,b]	1.88 ± 0.47	2.46 ± 0.74[a]	5.03 ± 1.01[a,b]
Velocity AP (cm/s)	1.07 ± 0.17	1.20 ± 0.18[a]	1.85 ± 0.49[a,b]	1.28 ± 0.33	1.38 ± 0.29[a]	2.43 ± 0.73[a,b]
Velocity ML (cm/s)	1.02 ± 0.32	1.55 ± 0.43[a]	2.19 ± 0.53[a,b]	1.38 ± 0.44	1.99 ± 0.69[a]	3.77 ± 1.06[a,b]
Surface (cm^2)	1.66 ± 0.84	2.63 ± 1.63[a]	8.70 ± 3.53[a,b]	2.42 ± 1.28	3.72 ± 2.05[a]	16.75 ± 6.72[a,b]

All conditions are statistically different between Young and Old groups ($p < 0.01$). [a]denotes significant difference with Baseline ($p < 0.01$). [b]denotes significant difference between Foam and VIB conditions ($p < 0.01$). VIB, Cutaneous vibration with the PortVIBplate.

were significantly higher for Old vs. Young participants: ML Velocity ($p = 0.002$); CoP Surface ($p = 0.014$). No significant differences between groups were found for VIB/BL ratios.

DISCUSSION

The present study compared the postural responses resulting from two different techniques aiming at altering the sensitivity of plantar mechanoreceptors in healthy young and old participants. Our results confirmed that significant but distinctive effects were found between these two techniques, suggesting different underlying mechanisms of sensorimotor integration and postural control. Using both vibratory and foam approaches in clinical practice could provide rich and complementary knowledge for better managing postural impairments and risk of falls in the older adults (>65 years).

We are not the first to use plantar cutaneous vibration to investigate mechanisms of postural control. However, previous studies vibrated restricted zones of the foot, such as the forefoot or the heels (Kavounoudias et al., 1998, 1999, 2001; Roll et al., 2002). Vibrating the forefoot soles mimics a forward change in the CoP position under the feet. This false proprioceptive signal is interpreted as a fall, and a rapid backward postural reaction occurs to maintain balance. In 1999, Kavounoudias et al. (1999) did test the impact of co-vibrating the two heels and two forefoot zones in nine young adults. They reported a slight but non-significant increase of COP parameters compared to baseline value without VIB. Conversely, our study found significant increases of all COP parameters when applying VIB, even in the youngest participants. Discrepancies between our respective results could be ascribed to the different methods used and sample size, especially VIB duration which was longer in the present work [10 vs. 2.5 s in Kavounoudias et al. (1999)]. Also, they employed 4 VIB motors covering restricted parts of the foot (heels and metatarsal heads), whereas our 40 vibrators essentially covered the whole foot soles, even the toes which have the highest density of cutaneous mechanoreceptors (Viseux et al., 2019). In addition, to the best of our knowledge no study used VIB of the whole foot to compare postural effects between young and older populations. A few studies did use other vibration techniques, such as tendinous vibration of ankle muscles (Hay et al., 1996; Teasdale and Simoneau, 2001; Abrahamova et al., 2009). It was found that these proprioceptive-to-motor postural reactions were greater in healthy older vs. younger adults, suggesting that age does not significantly impact the interpretation of proprioceptive feedback, but instead limits the ability to adapt to the disruptive sensory signal and reach a new "stabilized" posture during VIB stimulation (Abrahamova et al., 2009).

Conversely, we rather used vibration as a "directionless" increase in mechanoreception firing of the whole sole surface, and found that the determinants of postural stability (i.e., the Amplitude of CoP), postural control (the Velocity of CoP) and postural performance (i.e., the Surface of CoP) (Paillard and Noe, 2015) were markedly increased for both groups. This finding confirms that the spatial and temporal information about the pressure variations exerted under the feet were significantly altered by vibration (Kavounoudias et al., 1998, 1999), highlighting the privileged position of the feet soles as the only physical link between the body and the ground (Viseux, 2020). Plantar skin mechanoreceptors play a key role in regulating mechanisms of postural control by transmitting crucial information about the body's relation with the environment (Patel et al., 2008; Viseux, 2020). The fact that mechanical vibration increased postural oscillations for both young and older adults support the relevance and effectiveness of this approach to study sensory processing and re-weighting

TABLE 3 | Effect sizes (Cohen's D) between different conditions for each group in all postural parameters.

	Baseline vs VIB		Baseline vs Foam		VIB vs Foam	
	Young group	**Old group**	**Young group**	**Old group**	**Young group**	**Old group**
Postural parameters						
Amplitude AP (cm)	0.57	0.64	2.86	2.32	2.47	2.02
Amplitude ML (cm)	1.10	0.89	3.44	3.59	2.09	2.83
Velocity AP (cm/s)	0.74	0.32	1.81	1.81	1.51	1.64
Velocity ML (cm/s)	1.36	1.00	2.53	2.59	1.31	1.91
Surface (cm2)	0.68	0.72	1.36	2.31	1.23	2.18

mechanisms. Sensory re-weighting can be observed in the presence of an altered sensory signal (like it is the case when vibrating skin mechanoreceptors) and consists of dynamic inhibitory/excitatory mechanisms resulting in a decreased gain from the altered signal and increased reliance on the other unaltered sensory systems (Mahboobin et al., 2009).

As expected, our results showed a greater increase in all CoP postural parameters while standing on a foam surface in both young and old people (**Table 2**). These results are consistent with previous studies having found a decreased performance of postural control when standing with eyes closed on a foam surface vs. on a solid surface (Cohen et al., 1993; Chiang and Wu, 1997; Patel et al., 2008, 2011). Because our results found a significantly higher impact of foam vs. feet vibration for both groups (**Table 2**), it can be hypothesized that the relative contribution of "motor" disturbances caused by standing on an unsteady environment adds a significant impact to the reduced reliability of somatosensory information from the feet. Instead of VIB, Patel et al. (2011) applied a cooling technique targeting fast-adapting mechanoreceptors of foot soles and also concluded that foam-induced effect on postural control involves different mechanisms that remains to be elucidated. Therefore, we highly recommend that observations from the foam condition consider both the sensory and motor disturbances as a whole, because only cutaneous-specific methods such as VIB offer a restricted mean of altering mechanoreceptors' function. However, by being more challenging the foam mat might serves as a better screening tool for ruling out postural control impairments than the vibratory platform. Overall, the use of both approaches (Foam and VIB with the *PortVIBplate*) in clinical practice could provide a more in-depth evaluation of sensory vs. motor impairments in an individual presenting with postural imbalance.

Another interesting finding concerns group comparisons between young and older participants. During baseline condition, postural parameters were significantly higher in the old group compared to the young group, which is in line with the literature having described a progressive deterioration of postural control with age (Lord et al., 2018). Aging has been shown to cause a decreased sensitivity of somatosensory receptors, lower conduction times within the nervous system, altered efficacy of sensorimotor processing mechanisms and delayed/weaker postural adjustments (Shaffer and Harrison, 2007; Viseux, 2020). In particular, Pacini's corpuscles exhibit a reduction in their number and a decrease in their sensitivity to cutaneous vibration and other mechanical stimuli (Shaffer and Harrison, 2007). These age-related changes could in part explain the different performances at baseline between young and old groups. However, the significant increase in postural sway caused by vibration underlines that cutaneous afferents from the feet are still contributing significantly to maintain balance, at least in healthy and physically active older adults (>65 years) (Vellas et al., 1997; Kristinsdottir et al., 2001). Interestingly, when correcting for BL differences with the use of Foam/BL and VIB/BL ratios, we found that only Foam resulted in significantly higher postural disturbances for Old vs. Young participants. Because VIB had no such age-related contrast, it can be argued that mechanisms involved in re-weighting of sensory gains toward more reliable inputs (e.g., proprioceptive afferents from the ankles joint and muscles, vestibular systems) (Fransson et al., 2007; Baltich et al., 2015) are relatively unaffected in healthy elders. Instead, postural impairments observed when sanding on the foam pad are probably resulting to a greater extend to less effective motor adjustments (ex: appropriate strength and timing of leg muscle contractions).

As mentioned above, this new knowledge brought by our work enables an improved analysis of the specific contribution of somatosensory afferents to postural control. This is highly relevant for both research and clinical purposes, for instance to foster our understanding of sensory reweighting mechanisms and how there are affected by peripheral neuropathy and other age-related changes within the nervous system. For example, if no change of postural sway is observed when vibrating the feet soles it can be hypothesized that mechanoreceptors are severely impaired. Then, depending on the performances at baseline (and also with the foam mat), it can be concluded that the postural control system was able to rely on other sensory systems, or not. Future studies could also investigate whether postural oscillations are progressively re-stabilizing when applying a prolonged vibration, which would signify that the postural control network can undergo plastic adaptation and motor learning in the presence of a challenging / unreliable sensory environment. Future studies should investigate similar mechanisms but in persons presenting with balance and sensorimotor disorders, and in other postural tasks such as the semi-tandem or unipedal stance. Interestingly, recent publications highlighted the potential clinical interest of using skin vibration as a novel neurostimulation therapy for sensory and postural control retraining (Zhou et al., 2016; Viseux et al., 2019). Our vibration system could therefore serve both to identify individuals with altered foot sole / sensory-reweighting functions and provide therapeutic options to reduce the risk of fall in elders and other populations suffering from peripheral neuropathy.

Our results are mainly limited by the use of an inexpensive vibration platform, the PortVIBplate designed to be clinical-friendly (Lafontaine et al., 2020). VIB frequency in the present study was set at 50 Hz according to the technical charts provided by the manufacturer's motors. Since the rotational movement of motors can be altered by several factors (e.g., technical quality of the motor, compliance of the surface in contact with the motor, variation in the electrical current which is separated into 40 motors, amount/modulation of pressure exerted by the foot), the actual frequency transmitted to the subject's skin during weight-bearing was impossible to verify. During pilot tests realized when developing the PortVIBplate, we found random variations in the observed frequency which sometimes peaked at $\pm$ 20 Hz around the targeted 50 Hz. Even though we were able to find significant effects with our VIB parameters, it is impossible to know whether different findings could have been obtained if using different parameters (i.e., frequency or duration), knowing for instance that higher frequencies tend to induce greater postural effects (Kavounoudias et al., 1999, 2001). The impact of better controlling and modulating VIB parameters should be investigated further in the future. There is a clear need for developing closed-loop control systems able to measure

and possibly apply online corrections of VIB parameters to ensure the methodological robustness of VIB research. Also, we recruited healthy and physically active older adults (>65 years) that are not representative of the general population, hence potentially underestimating the impact of age and comorbidities on the postural control system. Finally, guidelines about CoP measurements recommend at least 10 s for unipedal balance (Lin et al., 2008), and 10–20 s and more for the bipodal stance like in our study for reaching high reliability indices of CoP data (Parreira et al., 2013), but we preferred to restrict vibration to 10 s to replicate published protocols in the field of VIB-induced postural effects (Kadri et al., 2020). Future works should consider trying different vibration durations in order to determine the protocol offering the best balance between reliability, time-consumption and fatigue build-up.

In conclusion, our study provided the first evidence of a contrasting effect between two postural tests of sensory-reweighting (Foam, cutaneous VIB). While both approaches induced significant postural imbalances and were able to highlight age-related differences, we argue that only VIB of the whole plantar surface can specifically alter the sensory feedback from plantar soles mechanoreceptor. Using this specificity of VIB, we found that "motor" rather than "sensory" components involved postural control was primarily affected by aging. The foam mat might better serve as a screening tool, as the postural imbalances likely encompass both sensory and motor disturbances related to standing on an unsteady environment. Using the two methods in clinical practice appear highly complementary, for instance to investigate the integrity of proprioception coding in the presence of diabetic peripheral neuropathy (VIB), or to evaluate the risk of fall in unsteady environment such as snowy/sandy grounds (Foam).

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Comité d'Éthique à la Recherche Avec des Êtres Humains—Université du Québec à Chicoutimi. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

LL, J-MG, M-PG, AL, and RR contributed to the conception and design of the study, realized the experiments, and statistical analysis. LL wrote the first draft of the manuscript. MK and EB helped in the experiments, statistical analysis, and redaction of the manuscript. PL, KB, and SG developed the PortVIBplate technology tested in the study and contributed to the redaction. RS and L-DB trained and supervised the students involved throughout the study. As senior author and PI of this project, L-DB oversaw all aspects of the study. All authors contributed to manuscript revision, read, and approved the submitted version.

FUNDING

This research received financial support from the Centre intersectoriel en santé durable (Université du Québec à Chicoutimi).

ACKNOWLEDGMENTS

The authors would like to thank all the participants who took part in our study. This research received financial support from the *Centre Intersectoriel en Santé Durable* (*Université du Québec à Chicoutimi*).

REFERENCES

Aboutorabi, A., Arazpour, M., Bahramizadeh, M., Farahmand, F., and Fadayevatan, R. (2018). Effect of vibration on postural control and gait of elderly subjects: a systematic review. *Aging Clin. Exp. Res.* 30, 713–726. doi: 10.1007/s40520-017-0831-7

Abrahamova, D., Mancini, M., Hlavacka, F., and Chiari, L. (2009). The age-related changes of trunk responses to Achilles tendon vibration. *Neurosci. Lett.* 467, 220–224. doi: 10.1016/j.neulet.2009.10.041

Atchison, D. A., Markwell, E. L., Kasthurirangan, S., Pope, J. M., Smith, G., and Swann, P. G. (2008). Age-related changes in optical and biometric characteristics of emmetropic eyes. *J. Vis.* 8:29. doi: 10.1167/8.4.29

Baltich, J., von Tscharner, V., and Nigg, B. M. (2015). Degradation of postural control with aging. *Proc. Inst. Mech. Eng. H* 229, 638–644.

Bull, F. C., Maslin, T. S., and Armstrong, T. (2009). Global physical activity questionnaire (GPAQ): nine country reliability and validity study. *J. Phys. Act. Health* 6, 790–804. doi: 10.1123/jpah.6.6.790

Chiang, J. H., and Wu, G. (1997). The influence of foam surfaces on biomechanical variables contributing to postural control. *Gait Posture* 13, 35–40.

Cohen, H., Blatchly, C. A., and Gombash, L. L. (1993). A study of the clinical test of sensory interaction and balance. *Phys. Ther.* 73, 346–351. discussion 51-4., doi: 10.1093/ptj/73.6.346

Fransson, P. A., Gomez, S., Patel, M., and Johansson, L. (2007). Changes in multi-segmented body movements and EMG activity while standing on firm and foam support surfaces. *Eur. J. Appl. Physiol.* 101, 81–89. doi: 10.1007/s00421-007-0476-x

Goble, D. J., Coxon, J. P., Wenderoth, N., Van Impe, A., and Swinnen, S. P. (2009). Proprioceptive sensibility in the elderly: degeneration, functional consequences and plastic-adaptive processes. *Neurosci. Biobehav. Rev.* 33, 271–278. doi: 10.1016/j.neubiorev.2008.08.012

Hay, L., Bard, C., Fleury, M., and Teasdale, N. (1996). Availability of visual and proprioceptive afferent messages and postural control in elderly adults. *Exp. Brain Res.* 108, 129–139.

Kadri, M. A., Chevalier, G., Mecheri, H., Ngomo, S., Lavalliere, M., da Silva, R. A., et al. (2020). Time course and variability of tendinous vibration-induced postural reactions in forward and backward directions. *J. Electromyogr. Kinesiol.* 51:102386. doi: 10.1016/j.jelekin.2020.102386

Kavounoudias, A., Roll, R., and Roll, J. P. (1998). The plantar sole is a 'dynamometric map' for human balance control. *Neuroreport* 9, 3247–3252. doi: 10.1097/00001756-199810050-00021

Kavounoudias, A., Roll, R., and Roll, J. P. (1999). Specific whole-body shifts induced by frequency-modulated vibrations of human plantar soles. *Neurosci. Lett.* 266, 181–184. doi: 10.1016/s0304-3940(99)00302-x

Kavounoudias, A., Roll, R., and Roll, J. P. (2001). Foot sole and ankle muscle inputs contribute jointly to human erect posture regulation. *J. Physiol.* 532(Pt 3), 869–878. doi: 10.1111/j.1469-7793.2001.0869e.x

Khattar, V. S., and Hathiram, B. T. (2012). The clinical test for the sensory interaction of balance. *Int. J. Otorhinolaryngol. Clin.* 4, 41–45. doi: 10.5005/jp-journals-10003-1086

Kristinsdottir, E. K., Fransson, P. A., and Magnusson, M. (2001). Changes in postural control in healthy elderly subjects are related to vibration sensation, vision and vestibular asymmetry. *Acta Otolaryngol.* 121, 700–706. doi: 10.1080/00016480152583647

Kwan, R. L., Zheng, Y. P., and Cheing, G. L. (2010). The effect of aging on the biomechanical properties of plantar soft tissues. *Clin. Biomech. (Bristol, Avon)* 25, 601–605. doi: 10.1016/j.clinbiomech.2010.04.003

Lafontaine, V., Bouchard, K., Lapointe, P., Gagnon, J. M., Dallaire, M., Gaboury, S., et al. (2020). An open vibration and pressure platform for falls prevention with a reinforcement learning agent. *Pers. Ubiquit. Comput.* 25, 7–19. doi: 10.1007/s00779-020-1416-0

Lin, D., Seol, H., Nussbaum, M. A., and Madigan, M. L. (2008). Reliability of COP-based postural sway measures and age-related differences. *Gait Posture.* 28, 337–342. doi: 10.1016/j.gaitpost.2008.01.005

Lord, S. R., Delbaere, K., and Sturnieks, D. L. (2018). Aging. *Handb. Clin. Neurol.* 159, 157–171.

Machado, A. S., da Silva, C. B., da Rocha, E. S., and Carpes, F. P. (2017). Effects of plantar foot sensitivity manipulation on postural control of young adult and elderly. *Rev. Bras. Reumatol. Engl. Ed.* 57, 30–36. doi: 10.1016/j.rbre.2016.03.007

Magnusson, M., Enbom, H., Johansson, R., and Pyykko, I. (1990). Significance of pressor input from the human feet in anterior-posterior postural control. The effect of hypothermia on vibration-induced body-sway. *Acta Otolaryngol.* 110, 182–188. doi: 10.3109/00016489009122535

Mahboobin, A., Loughlin, P., Atkeson, C., and Redfern, M. (2009). A mechanism for sensory re-weighting in postural control. *Med. Biol. Eng. Comput.* 47, 921–929. doi: 10.1007/s11517-009-0477-5

Maurer, C., Mergner, T., Bolha, B., and Hlavacka, F. (2001). Human balance control during cutaneous stimulation of the plantar soles. *Neurosci. Lett.* 302, 45–48. doi: 10.1016/s0304-3940(01)01655-x

Meyer, P. F., Oddsson, L. I., and De Luca, C. J. (2004). The role of plantar cutaneous sensation in unperturbed stance. *Exp. Brain Res.* 156, 505–512.

Mildren, R. L., Strzalkowski, N. D., and Bent, L. R. (2016). Foot sole skin vibration perceptual thresholds are elevated in a standing posture compared to sitting. *Gait Posture* 43, 87–92. doi: 10.1016/j.gaitpost.2015.10.027

Owsley, C. (2011). Aging and vision. *Vision Res.* 51, 1610–1622. doi: 10.1016/j.visres.2010.10.020

Paillard, T., and Noe, F. (2015). Techniques and methods for testing the postural function in healthy and pathological subjects. *Biomed. Res. Int.* 2015:891390.

Parreira, R. B., Boer, M. C., Rabello, L., Costa Vde, S., de Oliveira, E. Jr., and da Silva, R. A. Jr. (2013). Age-related differences in center of pressure measures during one-leg stance are time dependent. *J. Appl. Biomech.* 29, 312–316. doi: 10.1123/jab.29.3.312

Patel, M., Fransson, P. A., Johansson, R., and Magnusson, M. (2011). Foam posturography: standing on foam is not equivalent to standing with decreased rapidly adapting mechanoreceptive sensation. *Exp. Brain Res.* 208, 519–527. doi: 10.1007/s00221-010-2498-6

Patel, M., Fransson, P. A., Lush, D., Petersen, H., Magnusson, M., Johansson, R., et al. (2008). The effects of foam surface properties on standing body movement. *Acta Otolaryngol.* 128, 952–960. doi: 10.1080/00016480701827517

Perry, S. D. (2006). Evaluation of age-related plantar-surface insensitivity and onset age of advanced insensitivity in older adults using vibratory and touch sensation tests. *Neurosci. Lett.* 392, 62–67. doi: 10.1016/j.neulet.2005.08.060

Roberts, K. L., and Allen, H. A. (2016). Perception and cognition in the ageing brain: a brief review of the short- and long-term links between perceptual and cognitive decline. *Front. Aging Neurosci.* 8:39. doi: 10.3389/fnagi.2016.00039

Roll, R., Kavounoudias, A., and Roll, J. P. (2002). Cutaneous afferents from human plantar sole contribute to body posture awareness. *Neuroreport* 13, 1957–1961. doi: 10.1097/00001756-200210280-00025

Sacco, I. C., Suda, E. Y., Vigneron, V., and Sartor, C. D. (2015). An 'importance' map of signs and symptoms to classify diabetic polyneuropathy: an exploratory data analysis. *PLoS One* 10:e0129763. doi: 10.1371/journal.pone.0129763

Seidler, R. D., Bernard, J. A., Burutolu, T. B., Fling, B. W., Gordon, M. T., Gwin, J. T., et al. (2010). Motor control and aging: links to age-related brain structural, functional, and biochemical effects. *Neurosci. Biobehav. Rev.* 34, 721–733. doi: 10.1016/j.neubiorev.2009.10.005

Shaffer, S. W., and Harrison, A. L. (2007). Aging of the somatosensory system: a translational perspective. *Phys. Ther.* 87, 193–207. doi: 10.2522/ptj.20060083

Teasdale, N., and Simoneau, M. (2001). Attentional demands for postural control: the effects of aging and sensory reintegration. *Gait Posture* 14, 203–210. doi: 10.1016/s0966-6362(01)00134-5

Thompson, C., Belanger, M., and Fung, J. (2011). Effects of plantar cutaneomuscular and tendon vibration on posture and balance during quiet and perturbed stance. *Hum. Mov. Sci.* 30, 153–171. doi: 10.1016/j.humov.2010.04.002

Vellas, B. J., Wayne, S. J., Romero, L., Baumgartner, R. N., Rubenstein, L. Z., and Garry, P. J. (1997). One-leg balance is an important predictor of injurious falls in older persons. *J. Am. Geriatr. Soc.* 45, 735–738. doi: 10.1111/j.1532-5415.1997.tb01479.x

Viseux, F., Lemaire, A., Barbier, F., Charpentier, P., Leteneur, S., and Villeneuve, P. (2019). How can the stimulation of plantar cutaneous receptors improve postural control? Review and clinical commentary. *Neurophysiol. Clin.* 49, 263–268. doi: 10.1016/j.neucli.2018.12.006

Viseux, F. J. F. (2020). The sensory role of the sole of the foot: review and update on clinical perspectives. *Neurophysiol. Clin.* 50, 55–68. doi: 10.1016/j.neucli.2019.12.003

Zhou, J., Lipsitz, L., Habtemariam, D., and Manor, B. (2016). Sub-sensory vibratory noise augments the physiologic complexity of postural control in older adults. *J. Neuroeng. Rehabil.* 13:44.

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

frontiers in Neurology

CLINICAL TRIAL
published: 13 October 2021
doi: 10.3389/fneur.2021.719305

Effects of Robot-Aided Rehabilitation on the Ankle Joint Properties and Balance Function in Stroke Survivors: A Randomized Controlled Trial

Xiaoxue Zhai[1,2], *Qiong Wu*[1], *Xin Li*[1], *Quan Xu*[1], *Yanlin Zhang*[1], *Senchao Fan*[1], *Li-Qun Zhang*[3,4,5]* and *Yu Pan*[1,2]*

[1] Department of Rehabilitation, Beijing Tsinghua Changgung Hospital, Beijing, China, [2] School of Clinical Medicine, Tsinghua University, Beijing, China, [3] Department of Physical Therapy and Rehabilitation Science, University of Maryland, Baltimore, MD, United States, [4] Department of Orthopaedics, University of Maryland, Baltimore, MD, United States, [5] Department of Bioengineering, University of Maryland, College Park, MD, United States

OPEN ACCESS

Edited by:
Eric Yiou,
Université Paris-Saclay, France

Reviewed by:
Arnaud Lardon,
Institut Franco-Européen de Chiropraxie (IFEC), France
Arnaud Gouelle,
ProtoKinetics LLC, United States
Arnaud Delafontaine,
CIAMS, Univ. Paris-Sud., Université Paris-Saclay, France
Clint Hansen,
University of Kiel, Germany

***Correspondence:**
Li-Qun Zhang
l-zhang@som.umaryland.edu
Yu Pan
panyu@btch.edu.cn

Specialty section:
This article was submitted to Neurorehabilitation, a section of the journal Frontiers in Neurology

Received: 02 June 2021
Accepted: 09 September 2021
Published: 13 October 2021

Citation:
Zhai X, Wu Q, Li X, Xu Q, Zhang Y, Fan S, Zhang L-Q and Pan Y (2021) Effects of Robot-Aided Rehabilitation on the Ankle Joint Properties and Balance Function in Stroke Survivors: A Randomized Controlled Trial. Front. Neurol. 12:719305. doi: 10.3389/fneur.2021.719305

Background: Stroke survivors with impaired control of the ankle due to stiff plantarflexors often experience abnormal posture control, which affects balance and locomotion. Forceful stretching may decrease ankle stiffness and improve balance. Recently, a robot-aided stretching device was developed to decrease ankle stiffness of patient post-stroke, however, their benefits compared to manual stretching exercises have not been done in a randomized controlled trial, and the correlations between the ankle joint biomechanical properties and balance are unclear.

Objective: To compare the effects of robot-aided to manual ankle stretching training in stroke survivors with the spastic ankle on the ankle joint properties and balance function post-stroke, and further explore the correlations between the ankle stiffness and balance.

Methods: Twenty inpatients post-stroke with ankle spasticity received 20 minutes of stretching training daily over two weeks. The experimental group used a robot-aided stretching device, and the control group received manual stretching. Outcome measures were evaluated before and after training. The primary outcome measure was ankle stiffness. The secondary outcome measures were passive dorsiflexion ranges of motion, dorsiflexor muscle strength, Modified Ashworth Scale (MAS), Fugl-Meyer Motor Assessment of Lower Extremity (FMA-LE), Berg Balance Scale (BBS), Modified Barthel Index (MBI), and the Pro-Kin balance test.

Results: After training, two groups showed significantly within-group improvements in dorsiflexor muscle strength, FMA-LE, BBS, MBI ($P < 0.05$). The between-group comparison showed no significant differences in all outcome measures ($P > 0.0025$). The experimental group significantly improved in the stiffness and passive range of motion of dorsiflexion, MAS. In the Pro-Kin test, the experimental group improved significantly with eyes closed and open ($P < 0.05$), but significant improvements were found in the control group only with eyes open ($P < 0.05$). Dorsiflexion stiffness was positively correlated with the Pro-Kin test results with eyes open and the MAS ($P < 0.05$).

Conclusions: The robot-aided and manual ankle stretching training provided similar significant improvements in the ankle properties and balance post-stroke. However, only the robot-aided stretching training improved spasticity and stiffness of dorsiflexion significantly. Ankle dorsiflexion stiffness was correlated with balance function.

Clinical Trial Registration: www.chictr.org.cn ChiCTR2000030108.

Keywords: stroke, ankle, spasticity, stiffness, balance, robot

INTRODUCTION

Stroke is a leading cause of mortality, and approximately 2.5 million people experience a stroke annually in China (1). Stroke survivors have abnormal balance function due to spasticity, muscle weakness, sensory loss, and/or motor dysfunction (2–4). Structural changes of muscle fibers and connective tissue in stroke patients may result in a reduction in joint range of motion (ROM) and a clinical contracture for lacking mobilization and serious spasticity (5–9). Previous studies have demonstrated that stroke patients with impaired ankle control due to stiff plantarflexors and weak dorsiflexors often have a high fall rate (4, 10) because the ankle is crucial to control the location of the body's base of support and assist in controlling balance (11). Maintaining balance relies on well-controlled contraction of dorsiflexors and plantarflexors and specific ankle ROM (4, 12). Therefore, alleviating ankle muscle stiffness, and improving the muscles' soft-tissue extensibility and viscoelastic properties are important rehabilitation goals for stroke survivors in reestablishing balance function (13).

Many treatments to improve balance ability in stroke survivors are aimed at improving the posture control of the trunk and lower limbs including the use of strengthening exercises, functional neuromuscular stimulation, and visual feedback balance training (14–16). Ankle stretching exercises are also widely utilized to prevent and treat limited ankle ROM post-stroke to improve balance ability. Previous studies have demonstrated that higher resistance torque, increased joint stiffness, and decreased ankle ROM characterized by stroke survivors improved after completing passive stretching exercises (17–21). The aims of stretching exercises are to increase soft-tissue extensibility, normalize muscle tone, improve function and reduce pain (17, 22, 23). Passive ankle stretching can be manually applied by physical therapists or by using a stretching board, or by robotic systems (20, 23–26). Some of the factors that have limited clinic therapeutic regimens including cost, labor-intensive manual provision, availability of physical therapists, and limited access to clinical facilities. In practice, there are differences among therapies in the actual effects of manual stretching training, such as subjective judgment about the severity of spasticity, intensity, frequency, and duration of the manual stretching exercises.

Recently, an intelligent robot-aided stretching device was developed to decrease ankle stiffness of patients with neurological impairment due to stroke, spinal cord injury, multiple sclerosis, or cerebral palsy. Significant improvements were found in the ROM, maximum voluntary contraction, ankle stiffness, and comfortable walking speed (20, 27–29). The stretching velocity of this device decreases as resistance increasing, and will hold the ankle joint at the extreme position for a while to let stress relaxation occur when the predefined resistance torque is reached. By using this control strategy, the stretching device moves quickly in the middle (non-spastic) ROM and slows down in the stiffer part of the ROM, while never exceeding predefined stretching torques (19). Robotic adaptive stretching may be a quantitative stretching alternative therapy (30).

At present, there is a lack of RCT comparing the effects of robot-aided to manual ankle stretching training on the ankle joint properties and balance function post-stroke. The primary aim of this study was to evaluate the effects of the intelligent robot-aided stretching and manual stretching therapies on the ankle properties and balance function post-stroke. A secondary aim was to study how ankle stretching affects balance. We hypothesized ankle stretching would improve balance function for changing the neural and musculoskeletal characteristics of the ankle joint, and there may be different mechanisms between manual and intelligent stretching. A third aim was to investigate the relationship between ankle stiffness and balance function post-stroke.

METHODS

Trial Design

This is an assessor-blinded, randomized controlled trial. The aim was to compare the effects of robot-aided to manual ankle stretching training in stroke survivors with the spastic ankle on the ankle properties and balance function post-stroke, and further explore the correlations between the stiffness of the ankle and balance. The study was conducted according to the tenets of the Declaration of Helsinki, the guidelines for Good Clinical Practice, and the Consolidated Standards of Reporting Trials (CONSORT), approved by the local Ethics Committee "Beijing Tsinghua Chang Gung Hospital Medical Ethics" (18172-0-01), and registered at clinical trial (ChiCTR2000030108).

Abbreviations: ROM, Range of Motion; COP, Center of Pressure; MAS, Modified Ashworth Scale; DF dorsiflexion; PF, plantarflexion; FM-LE, Fugl-Meyer Motor Assessment of Lower Extremity; BBS, Berg Balance Scale; MBI, Modified Barthel Index; ADL, Activities of daily living; OE, Opened eyes; CE, Closed eyes; SD, Standard deviation; AS, Average speed; M/L, Medial/Lateral; F/B, Forward/Backward; BMI, Body Mass Index; M, male; F, female; DSP, Digital signal processor; CI, Confidence interval.

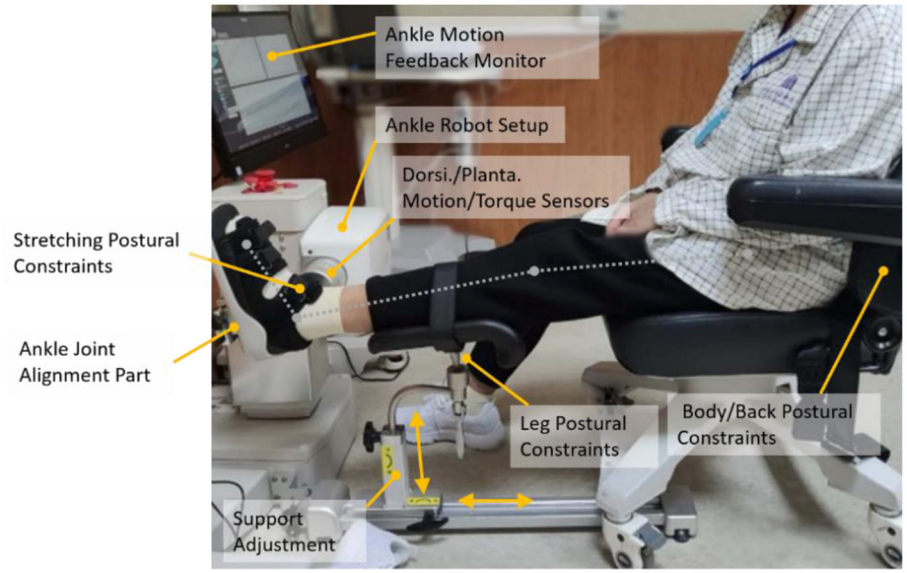

FIGURE 1 | A subject seated in the ankle rehabilitation robot device.

Participants

This RCT was conducted at the Beijing Tsinghua Chang Gung Hospital in China. Inpatients with stroke in the rehabilitation department of the hospital were recruited between May 2019 and November 2019. The inclusion criteria were: (1) ages between 18 and 75 years; (2) first-ever stroke with less than 6 months duration of spasticity of the affected ankle (Modified Ashworth Scale, MAS: 1-3 points); (3) medically stable; and (4) ability to stand independently without aids for at least 1 minute. Exclusion criteria were: communication problems, dementia based on clinical diagnosis, comorbidities affecting motor performance such as orthopedic, arthritic, inflammatory conditions that could influence balance, and limited ankle movement.

Interventions

Subjects in the experimental and control group had 10-session stretching training using the intelligent robot-aided stretching or manual stretching respectively (five times a week over 2 weeks, 20 minutes/session). During the 2-week period, both groups continued movement exercises for ankle mobility and strength.

Experimental Setup

An ankle rehabilitation robot (Beijing LTK Science and Technology Co., Ltd., Beijing, China) was used for intervention and outcome evaluations. While the subject was comfortably seated, the leg of the subject was strapped to leg support with the knee at 30° flexion and the foot was strapped onto a footplate with ankle dorsiflexion (DF) at 0°. The foot was secured to a footplate at the dorsal side and the heel using adjustable straps. The footplate was fixed to the motor shaft, and a torque sensor was aligned with the motor shaft to measure the ankle joint torque (**Figure 1**). The ankle stretching device was clamped to the chair to avoid movement of the device during stretching (18).

Stretching Protocol

The ankle rehabilitation robot was driven by a servomotor controlled by a digital signal processor (20). Briefly, the stretching velocity was inversely proportional to the joint resistance torque, with the control adjusted at 2,000 Hz. The maximum stretching velocity was set at 12°/s (31). Typical stretching parameters were 15 to 20 Nm peak resistance torque in dorsiflexion, 5 to 10 Nm peak resistance torque in plantarflexion, and a 5-second holding period at the extreme positions. An experienced physiotherapist adjusted the peak resistance torque for each session based on manual stretching and feedback from the subject during the stretching therapy. When receiving the intelligent stretching exercises, the subjects were required to look at the display screen where an "ankle joint" moves from dorsiflexion to plantarflexion as the real dynamic stretching simultaneously and try to feel the ankle movement. The control group received stretching sessions in a clinic by the appointed physiotherapist. The positive range of motion (PROM) of the ankle was measured using a goniometer to ensure the safety of manual stretching before manual stretching exercises. Subjects remained as relaxed as possible while the physiotherapist stretching the paretic ankle from plantar to dorsiflexion in the sagittal plane slowly, and a 5-second holding period at the extreme dorsiflexion positions. There is no break in the process of manual or intelligent stretching training.

Outcomes

Clinical and demographic data were collected at enrollment. Subjects were evaluated before and after the interventions by a designated physiotherapist blinded to the group assignment. The primary outcome of the study was the change of stiffness of the ankle after the training, due to its relevance in physiologic control of the ankle. The secondary outcomes of the study were divided into three categories: biomechanical evaluations,

clinical evaluations, and the Pro-Kin balance test (Pro-Kin254P, TecnoBody Company, Italy). The assessments included pre-assessment (baseline, before the first exercise session), post-assessment (after the tenth exercise session). The assessment sessions were done at the same time of the day with the assessments in the same order.

Biomechanical Evaluations

Evaluations included the DF PROM (passive ranges of motion measured in dorsiflexion direction movement), DF and PF stiffness (stiffness measured in dorsiflexion and plantarflexion direction movement), and dorsiflexor muscle strength. ROM and muscle strength were measured using the HogganMicroFET3 portable device (Hoggan Health Industries, Inc. Salt Lake City, USA). The Stiffness is defined as the ratio of ground reaction moment to angular deflection of the specific joint. Ankle stiffness measured in DF or PF passive movement was assessed as $K = \Delta T/\Delta\theta$, where K (Nm/°) was the quasi-static stiffness and ΔT was the passive torque increment during a certain amount of ankle angular movement ($\Delta\theta$). As $\Delta\theta$ becomes infinitely small, the quasi-static stiffness approaches the slope of a tangential line of the torque-angle curve at a specific ankle position (32, 33). The peak stretching velocity in this study was set at 5°/s to avoid inducing reflex responses (21). The biomechanical evaluations using the ankle robot have been used and validated in several previous studies (34, 35). Quasi-static stiffness of the ankle plantarflexor (DF stiffness) was evaluated at 10° of DF and that of the ankle dorsiflexor (stiffness measured in PF direction movement, PF stiffness) at 30° of PF for the PROM of the subjects in the two groups all meet this criterion.

Clinical Evaluations

Each subject completed the following functional assessments during clinical evaluation sessions. MAS (0–5 points, with higher scores indicating worse spasticity) was used to measure the calf muscle hypertonia (36). Fugl-Meyer Motor Assessment of Lower Extremity (FMA-LE) (0–34 points) was used to evaluate the sensorimotor function of the lower limbs (37). The Berg Balance Scale (BBS) (0–56 points) was used to evaluate the balance function (38). The Modified Barthel Index (MBI) (0–100 points) was used to measure the activities of daily living (ADL) (39).

Balancing Test

This study also used a Balancing Instrument (Pro-Kin254P, TecnoBody Company, Italy) to assess balance function, based on the instantaneous data of postural sway using the force platform from movements of the center of pressure (COP) (16) (**Figure 2**). The COP is a weighted average of all the pressures over the surface area in contact with the ground. This is a valid and reliable device that measures static and dynamic balance function (40, 41). The force platform consists of multiple strain gauges placed under a circular surface of 50 cm of diameter at 120° to each other and has a 20 Hz sampling frequency (42). When subjects were standing on the platform, the COP sway was documented. The COP measures demonstrate where a subject's pressure is located in both the x- and y-axes. An increase in COP in either the F/B or M/L direction is indicative of postural disturbance. Subjects were required to stand statically on the force platform, and maintain visual focus on an "X mark" placed on an eye-level screen from their face. The position of the feet on the platform was standardized using a V-shaped frame. Each subject performed two standing tests lasting 30 seconds each: One test with eyes open (EO) and one with eyes closed (EC). There were six outcome variables: trajectory lengths (measured in mm), elliptical trajectory (measured in mm^2), standard deviation medial/lateral (M/L SD measured in mm), standard deviation forward/backward (F/B SD measured in mm), average speed medial/lateral (M/L AS measured in m/s), and average speed forward/backward (F/B AS measured in m/s). Smaller values of the six parameters indicated the subject had a better balance function (43).

FIGURE 2 | Static Balance Assessed by the Pro-Kin System.

Sample Size

The sample size calculation was conducted using G*Power 3.1.7 (http://www.gpower.hhu.de/). The effect size was estimated using our pilot data regarding decreases in DF stiffness after training (experimental group vs control group: 0.61 ± 0.21 vs. 0.31 ± 0.27) would be able to reveal a large effect size of Cohen's d = 1.24, at a power of 0.8 and an α level of 0.05 assuming a non-directional hypothesis. Thus, in the current study, a large effect size f = 0.4 was assumed in the Mann–Whitney U test model, with an α value of 0.05, power of 0.8, and an attrition rate of 10%, the minimum required sample size was estimated to be 18 subjects for this study.

Randomization and Blinding

After recruited subjects presented written informed consent, they were randomly assigned into the experimental group or control group in 1:1 ratio by drawing lots. The lots were designated as "experimental" or "control" by stratified randomization with random numbers generated from statistical software and presented in sealed opaque envelopes. Each subject received a sealed envelope that indicated the group they were assigned to.

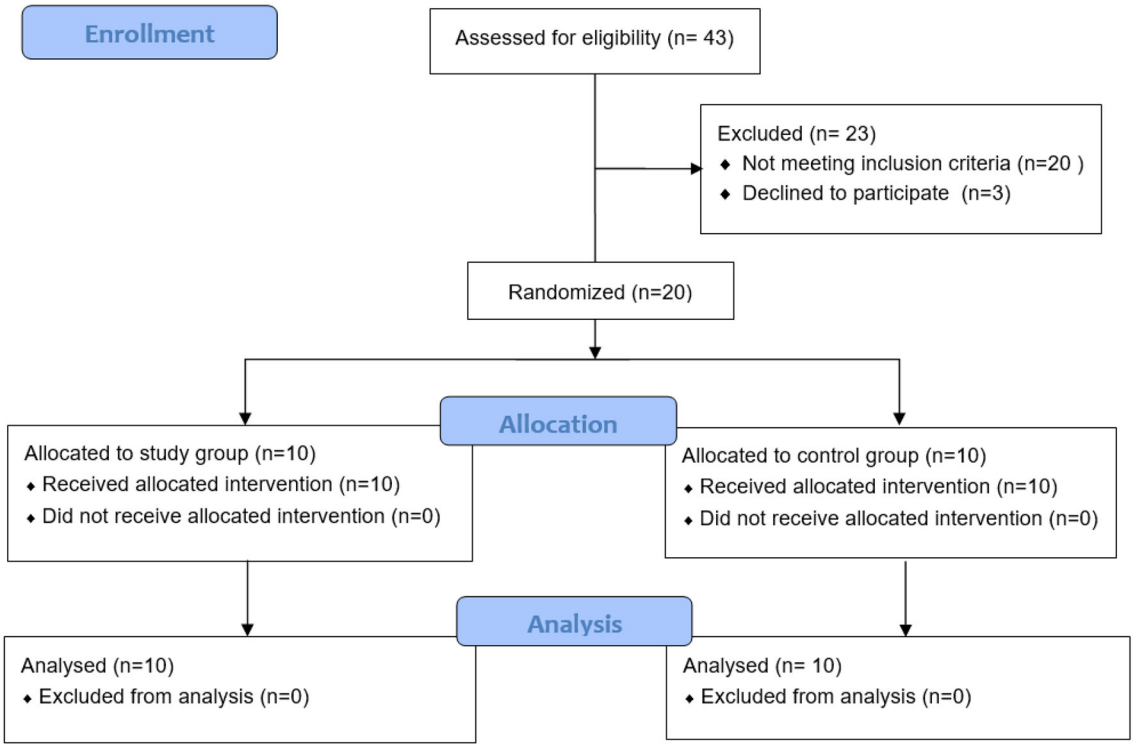

FIGURE 3 | CONSORT patient flow throughout the study.

The researchers in charge of recruitment and randomization procedures were different, and the designated therapist was responsible for the assessment was kept blinded to the group allocation throughout the trial.

Statistical Analysis

Baseline characteristics were compared between the two groups by using Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous and ordinal variables. The continuous variables were tested using the Shapiro-Wilk test to verify whether they met the normal distribution and using the homogeneity of variance test. Change with each intervention and during an observation period of two weeks were examined between the groups with a Mann-Whitney U test. Bonferroni corrections were applied to account for multiple comparisons ($\alpha = 0.0025$) to reduce the probability of Type-I error. The Wilcoxon Signed Rank test was used to compare pre-and post-intervention measurements in each group. Furthermore, to more deeply understand the effects of ankle stiffness on balance function, the Spearman correlation analysis was performed for testing the association between stiffness and the Pro-Kin test, and the Kendall rank correlation coefficient (τ) for the correlation between MAS and ankle stiffness (effects were considered significant if $P < 0.05$). Under a small sample size, T-distribution was used to compute a 95% confidence interval (95% CI). All statistical analyses were performed with SPSS version 21.0. (IBM Corporation, Armonk, NY, USA).

RESULTS

The Flow of the Trial and Baseline Characteristics of Subjects

From May 2019 to November 2019, all inpatients in the rehabilitation department were screened. Of these, 43 stroke patients with ankle spasticity were eligible for evaluation. Among these subjects, 20 subjects did not meet the inclusion criteria, and 3 subjects declined to participate in this study (see **Figure 3** for more details). A total of 20 subjects were recruited to the study, including 10 subjects randomized to the experimental group, and 10 subjects randomized to the control group. All enrolled subjects completed the 2-week training, and there were no dropouts or adverse events. There were no significant differences in subjects' characteristics between the two groups (**Table 1**).

Biomechanical Evaluations: DF PROM, DF Muscle Strength and Joint Stiffness

Before training, there were no significant differences in DF PROM, DF muscle strength, or DF and PF stiffness between the two groups. The DF muscle strength increased significantly after the 2-week training period in the control group and experimental group ($P = 0.005$, and 0.005, respectively). Besides, significant decreases in DF stiffness and improvements in DF PROM were found for subjects in the experimental group ($P = 0.008$, and 0.041, respectively), but not in the control group ($P = 0.139$, and 0.157, respectively). No significant differences in biomechanical

TABLE 1 | Baseline Characteristics of the Subjects[a].

Parameters	Experimental group ($n = 10$)	Control group ($n = 10$)	*P*
Age (year)	61.90 ± 9.62	60.00 ± 6.62	0.288[c]
Duration post-stroke (day)	54.20 ± 33.85	58.10 ± 50.20	0.650[c]
Sex (M/F)	9/1	9/1	1.00[b]
Cerebral infarction/cerebral hemorrhage (case)	10/0	10/0	1.00[b]
Side of lesion (right/left, case)	7/3	7/3	1.00[b]
Height (*m*)	1.68 ± 0.05	1.69 ± 0.04	0.568[c]
Weight (*kg*)	74.70 ± 9.71	70.40 ± 5.40	0.120[c]
BMI (kg/m^2)	26.33 ± 3.65	24.45 ± 1.72	0.082[c]

BMI, Body Mass Index; M, male; F, female. [a]Values are mean ± standard deviation, or number. [b]Fisher's exact test. [c]Mann–Whitney U tests between groups for baseline values. There were no significant differences between groups at baseline for clinical characteristics.

TABLE 2 | Biomechanical Properties at pre- and post-training between two groups.

Variable	Experimental group			Control group			Between-Group Difference in Change
	Pre	Post[a]	Change	Pre	Post[a]	Change	*P*[b]
	Mean ± SD	Mean ± SD	Mean (LB; UB) 95%CI	Mean ± SD	Mean ± SD	Mean (LB; UB) 95%CI	
DF PROM (°)	15.50 ± 2.17	16.70 ± 1.42*	1.20 (−0.14; 2.54)	17.00 ± 1.15	17.20 ± 1.23	0.20 (−0.10; 0.50)	0.108
DF Strength (N)	102.50 ± 44.54	132.82 ± 43.44**	30.32 (10.73; 49.91)	101.4 ± 59.71	123.80 ± 58.55**	22.46 (6.55; 38.37)	0.596
DF Stiffness (Nm/deg)	1.62 ± 0.24	1.19 ± 0.24**	−0.43 (−0.61; −0.24)	1.32 ± 0.41	1.10 ± 0.42	−0.22 (−0.53; 0.08)	0.472
PF Stiffness (Nm/deg)	0.21 ± 0.04	0.19 ± 0.03	−0.02 (−0.05; 0.02)	0.21 ± 0.07	0.24 ± 0.09	0.03 (−0.05; 0.10)	0.622

*SD, standard deviation; CI, confidence interval. DF or PF stiffness is stiffness measured in dorsiflexion or plantarflexion passive movement. [a]Comparison between pre- and post-training values in each group with Wilcoxon signed rank test: *P < 0.05, **P < 0.01. [b]P values indicate significance level of between-group differences in change with Mann-Whitney U test: according to the Bonferroni correction, ***P < 0.0025.*

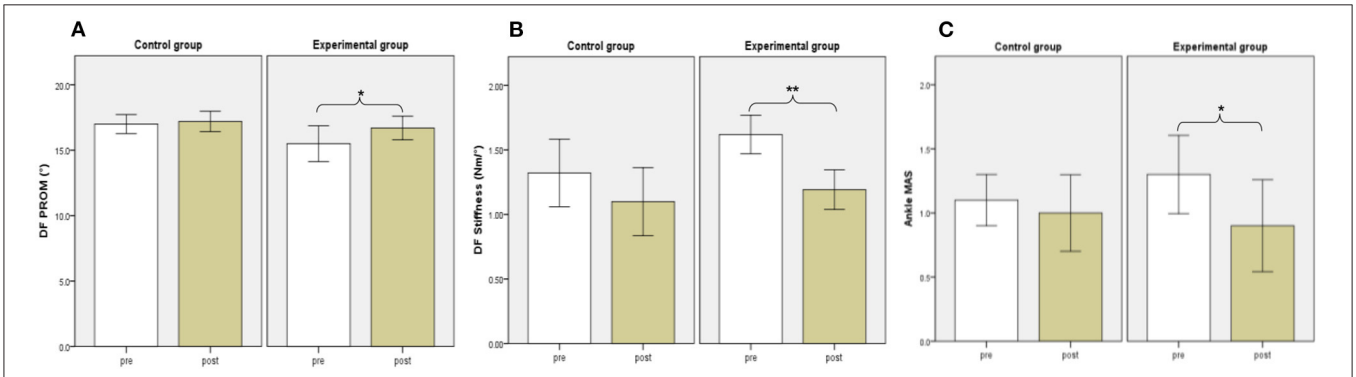

FIGURE 4 | Biomechanical and Clinical evaluations between groups. DF PROM **(A)**, DF Stiffness **(B)**, Ankle MAS **(C)**. White and brown bars indicate pre-, and post-assessment. Error bars indicate standard error of the corresponding average (*$p < 0.05$ and **$P < 0.01$). DF, dorsiflexion; PROM, positive range of motion; MAS, Modified Ashworth Scale.

evaluations were found between the two groups after training ($P > 0.0025$) (**Table 2**) (**Figure 4**).

Clinical Evaluations

There were no significant differences in MAS, FMA-LE, BBS, or MBI before training between the two groups. The FMA-LE, BBS, and MBI increased significantly after the 2-week training period in the control group ($P = 0.005$, 0.007, and 0.041, respectively). We also found significant improvement in FMA-LE, BBS, and MBI in the experimental group ($P = 0.007$, 0.012, and 0.007, respectively). Besides, significant decreases were found in MAS for subjects in the experimental group ($P = 0.046$) but not in the control group ($P = 0.317$). No significant differences in clinical evaluations were found

TABLE 3 | Clinical evaluations at pre- and post-training between two groups.

Variable	Experimental group			Control group			Between-Group Difference in Change
	Pre	Post[a]	Change	Pre	Post[a]	Change	P^b
	Mean ± SD	Mean ± SD	Mean (LB; UB) 95%CI	Mean ± SD	Mean ± SD	Mean (LB; UB) 95%CI	
MAS	1.30 ± 0.48	0.90 ± 0.57*	−0.4 (−0.77; −0.03)	1.10 ± 0.32	1.00 ± 0.47	−0.10 (−0.33; 0.13)	0.131
FM-LE	26.50 ± 5.36	29.30 ± 4.42**	2.8 (1.50; 4.10)	24.80 ± 7.25	27.60 ± 6.31**	2.80 (1.02; 4.58)	0.587
BBS	41.40 ± 13.74	45.00 ± 13.87*	3.60 (0.28; 6.93)	43.40 ± 10.23	46.70 ± 9.93**	3.30 (1.33; 5.27)	0.644
MBI	59.50 ± 15.89	75.00 ± 14.14**	15.50 (8.06; 22.93)	75.50 ± 19.21	80.00 ± 17.95*	4.50 (0.56; 8.44)	0.015

*SD, standard deviation; CI, confidence interval; MAS, Modified Ashworth Scale; FMA-LE, Fugl-Meyer Motor Assessment of Lower Extremity; BBS, Berg Balance Scale; PASS, Postural Assessment Scale for Stroke Patients; 6 MWT, 6-minute walk test; MBI, Modified Barthel. [a]Comparison between pre- and post-training values in each group with Wilcoxon signed rank test: *P < 0.05, **P < 0.01. [b]P values indicate significance level of between-group differences in change with Mann-Whitney U test: according to the Bonferroni correction, ***P < 0.0025.*

between the two groups after training ($P > 0.0025$) (**Table 3**) (**Figure 4**).

Balancing Test Results

There was no significant difference between the two groups in the Pro-Kin balance test before training. The ellipse area, trajectory length, M/L SD, and F/B AS with closed eyes and F/B SD with opened eyes decreased significantly after the 2-week training period in the experimental group ($P = 0.005$, 0.013, 0.012, 0.005, and 0.041, respectively). The trajectory length and M/L AS with opened eyes decreased significantly after the 2-week training period in the control group ($P = 0.022$, and 0.042, respectively). No significant difference in the Pro-Kin balance test results was found between the two groups after training ($P > 0.0025$) (**Table 4**).

Correlations Between the Stiffness of the Ankle and the Balance Function

Regarding the two groups as a whole, we further explore the correlations between ankle stiffness and balance. The DF stiffness was significantly correlated with the results of the Pro-kin balance test with opened eyes, including the trajectory length, M/L SD, F/B AS, M/L AS ($\gamma = 0.464$, $P = 0.003$; $\gamma = 0.313$, P = 0.049; $\gamma = 0.386$, P=0.014; $\gamma = 0.466$, $P = 0.002$, respectively). The DF stiffness was also significantly correlated with MAS ($\tau = 0.265$, $P = 0.041$) (**Table 5**) (**Figure 5**).

DISCUSSION

The RCT showed significant within-group improvements in DF muscle strength, motor function of lower limbs, balance function, and activities of daily living after a 10-session training in two groups. However, the experimental group showed additional improvements in the DF stiffness, DF PROM, and MAS. Between-group comparisons represented no differences in all outcome measures. We believe the intelligent stretching robot could be an effective and safe alternative to manual stretching for therapists. Also, the intelligent stretching robot has the potential to use in stretching the ankle with spasticity and/or contracture regularly without the daily involvement of clinicians or physiotherapists.

Several studies have already been shown that continuous passive stretching can effectively reduce ankle stiffness (18, 20, 44). Another study further demonstrated that the repeated passive stretching can decrease spasticity through a combination of reflexive and mechanical factors for stroke survivors (45). Previous studies have shown that the change in mechanical properties of tendons depends on the stretching protocol (46). Stretching exercise under intelligent control has been effectively used to decrease ankle contracture and/or spasticity in stroke survivors (18, 20, 47). The intelligent stretching device was driven by a servomotor controlled by a digital signal processor (20). Briefly, the stretching velocity was inversely proportional to the joint resistance torque. The torque limits of plantar and dorsiflexion were preset before the stretching exercises. Once reaching the predefined resistance torque peak, the joint will be held at the extreme position for stress relaxation in a preset period (18, 32). This method may overcome potential viscoelastic responses and alter the muscle-tendon properties (48). Since the outcome of manual stretching might depend on the ability of the therapist to measure the limits of the ROM or "end feel" (19), which could not provide lasting and effective stretching. In addition, high-intensity stretching can induce a physiological response within the muscle-tendon unit and enhance neuroplasticity (49–52). Thus, the intelligent stretching robot can offer ideal exercise intensity, frequency, and duration (53, 54), while it is not feasible for the limited availability of physical therapists to deliver laborious manual therapy. This study demonstrated that improvements after the intelligent stretching of the spastic ankles post-stroke were consistent with previous research, including increased ROM and muscle strength, decreased ankle stiffness and spasticity (19, 55).

In this study, the Pro-Kin was used to quantitatively evaluate the static balance of subjects, excluding the influences of the hip and stride strategy, and further explore the role of ankle strategy in posture control independently (56). The experimental group had significant improvements in balance tests with eyes open and closed, while the control group only improved with eyes open,

TABLE 4 | Pro-Kin balance test results at pre- and post-training between two groups.

Variable	Experimental group			Control group			Between-Group Difference in Change
	Pre	Post[a]	Change	Pre	Post[a]	Change	P[b]
	Mean ± SD	Mean ± SD	Mean (LB; UB) 95%CI	Mean ± SD	Mean ± SD	Mean (LB; UB) 95%CI	
Eyes Closed							
Ellipse Area mm^2	1,396.10 ± 1,085.48	847.70 ± 486.15**	−548.40(−1024.58; −72.22)	2,431.50 ± 2,569.09	1,371.00 ± 1,236.41	−1,059.50(−2,748.31; 629.31)	1.000
Trajectory Length *mm*	962.40 ± 344.94	820.80 ± 280.43*	−141.60(−254.13; −29.07)	1,141.30 ± 6,13.22	918.00 ± 522.08	−223.30(−705.04; 258.44)	0.821
F/B SD	7.40 ± 1.90	6.80 ± 2.53	−0.60(−2.19; 0.99)	10.20 ± 4.76	7.60 ± 2.72	−2.60(−5.87; 0.67)	0.340
L/M SD	10.10 ± 5.34	6.10 ± 2.77*	−4.00(−7.05; −0.95)	10.50 ± 6.00	9.10 ± 4.79	−1.40(−6.04; 3.24)	0.068
F/B AS mm/sec	22.30 ± 8.37	18.60 ± 7.11**	−3.70(−5.49; −1.91)	23.50 ± 14.87	19.30 ± 14.12	−4.20(−13.77; 5.37)	0.381
L/M AS mm/sec	18.90 ± 7.94	17.50 ± 7.86	−1.40(−6.21; 3.41)	19.50 ± 13.30	15.40 ± 11.11	−4.10(−15.70; 7.50)	0.909
Eyes Open							
Ellipse Area mm^2	755.50 ± 659.29	518.90 ± 224.25	−236.60(−654.05; 180.85)	713.20 ± 450.40	533.40 ± 201.92	−179.80(−478.82; 119.22)	0.734
Trajectory Length *mm*	585.30 ± 188.54	458.70 ± 122.65	−126.60(−277.81; 24.61)	539.30 ± 182.93	459.40 ± 126.06*	−79.90(−169.86; 10.06)	0.705
F/B SD	5.80 ± 2.15	4.50 ± 0.85*	−1.30(−2.47; −0.13)	5.80 ± 1.75	5.10 ± 0.88	−0.70(−1.92; 0.52)	0.301
L/M SD	7.10 ± 4.38	6.10 ± 1.73	−1.00(−3.92; 1.92)	6.10 ± 2.08	5.90 ± 2.13	−0.20(−1.78; 1.38)	0.817
F/B AS mm/sec	13.60 ± 5.46	10.80 ± 2.62	−2.8(−7.59; 1.99)	11.30 ± 5.06	10.20 ± 3.97	−1.10(−3.25; 1.05)	0.939
L/M AS mm/sec	11.00 ± 2.91	9.10 ± 4.31	−1.90(−5.07; 1.27)	11.10 ± 4.12	9.00 ± 2.00*	−2.10(−4.40; 0.20)	0.539

*SD, standard deviation; CI, confidence interval; AS, Average speed; F/B, Forward/Backward; M/L, Medial/Lateral direction. [a]Comparison between pre- and post-training values in each group with Wilcoxon signed rank test: *P < 0.05, **P < 0.01. [b]P values indicate significance level of between-group differences in change with Mann-Whitney U test: according to the Bonferroni correction, ***P < 0.0025.*

which suggested that two kinds of stretching models might take different mechanisms to improve balance function.

Balance disorders of stroke survivors have various causes, such as muscle weakness, limited range of motion, spasticity, sensory changes, loss of coordination, and impaired central integration.

TABLE 5 | Correlations Between stiffness and Pro-Kin balance test results when open eyes.

	DF stiffness	P	PF stiffness	P
MAS	0.265	0.041*	−0.133	0.317
Ellipse Area	0.262	0.102	−0.285	0.074
Trajectory Length	0.464	0.464	−0.308	0.053
F/B SD	0.155	0.339	−0.228	0.157
M/L SD	0.313	0.049*	−0.277	0.084
F/B AS	0.386	0.014*	−0.206	0.202
M/L AS	0.466	0.002**	−0.264	0.100

*Spearman's coefficient (γ) was used to estimate the correlation between stiffness (K) and the Pro-Kin system results, and the Kendall rank correlation coefficient (τ) was used to estimate the correlation between stiffness (K) and MAS. Values are γ or τ. *P < 0.05, **P < 0.01.*

In particular, stiff plantar flexors and weak dorsiflexors on the affected side increasing the risk to cause the muscular imbalance of the ankle (57). In our study, M/L SD in the experimental group and M/L AS in the control group decreased significantly. We assumed that two kinds of stretching exercises could change the ankle properties, and can improve balance in the M/L direction, for improving the symmetry of weight-loading on the lower limbs by increasing the contribution of the paretic limb in stroke survivors. The intelligent stretching could forcefully, safely, and repeatedly stretch the ankle to its extreme positions in the sagittal plane resulting in structural changes in the viscoelastic properties of the muscles and connective tissues. This method can further reduce ankle stiffness and increasing ROM and improving the stability of the ankle joint (19–21), therefore the movement of COP decreased significantly in sagittal planes with eyes closed and opened in our experimental group. Adequate balance relies on an accurate perception of physical input from the visual, proprioceptive, and vestibular systems (58). Stroke survivors exhibited obvious decreased postural stability, especially without visual feedback. Proprioception around the ankle joint resulting from sensory inputs (e.g., from cutaneous receptors, muscle-spindle receptors, and Golgi tendon organ located in muscles,

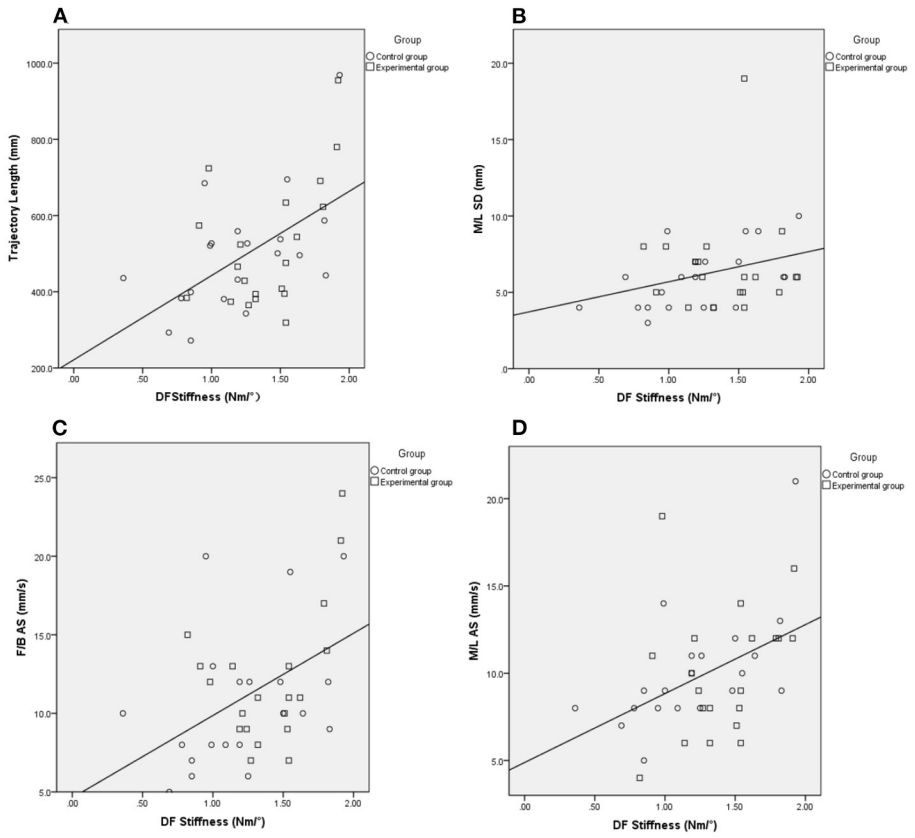

FIGURE 5 | The Spearman correlation analysis between DF stiffness and outcomes of the Pro-Kin test with eyes open. Trajectory length **(A)**, M/L SD **(B)**, F/B AS **(C)**, M/L AS **(D)**, Circle and Square indicate control, and experimental group. EO, Eye Open; F/B, Forward/Backward; M/L, Medial/Lateral; AS, Average Speed; SD, Standard Deviation.

tendons, and ligaments) is damaged post-stroke, which impairs the ankle strategy (59). In this study, the M/L SD and F/B AS decreased significantly in the experimental group with eyes closed. We hypothesized the robot-aided cyclic stretching could enhance proprioception of ankle joints effectively, and the balance of patients with eyes closed is also improved even in the visual feedback removal (60). While the control group did not have significant improvements in balance function with eyes closed. Compared with manual stretching exercises, the intelligent stretching device can provide feedback for patients. The strength of stretching force and range of motion of the ankle were displayed in the interface accompanied by a real-time ankle animation. This visual feedback might provoke the recovery of the damaged central nervous system (CNS) (61). Besides, this system contains different user-friendly modes, such as the evaluation of biomechanical properties, and the training mode. Those user-friendly features might attract patients to participate in the training and accelerate the recovery of balance function.

An ankle strategy is typically used on a solid base supporting a small amount of body sway (56, 62). This study further explored the correlation between ankle stiffness and the Pro-Kin balance test results with opened eyes. The findings showed that the stiffness of dorsiflexion was positively related to trajectory length, M/L SD, F/B AS, and M/L AS when opened eyes. However, those tests showed no significant correlation between PF stiffness and the Pro-Kin balance test results due to the mechanism was unclear. We suppose the possible mechanisms of how the ankle stiffness affected balance function are as follows.

The central controller uses sensory information to generate descending commands that produce corrective muscle forces to stabilize the body (63). The central nervous system (CNS) injuries post-stroke leads to muscle weakness and spasticity of the affected limb(s) post-stroke, often accompanied with drop and varus foot (64, 65), and lack of mobilization and prolonged spasticity may be accompanied by structural changes of muscle fibers and connective tissue, which may result in reductions in ROM and the contact area between the sole and the ground (66). Several studies have demonstrated that higher resistance torque, increased joint stiffness, and decreased ankle ROM characterized by stroke survivors improved after completing passive stretching exercises (18–20, 22, 67, 68). One previous study reported that the weaker inter-limb coordination in the sagittal plane (DF-PF) after stroke would cause imbalance (66). The intelligent stretching decrease ankle stiffness in the sagittal plane (DF-PF), which improved inter-limb coordination post-stroke in the F/B direction. Stroke survivors usually load more over their non-paretic limb than the paretic one when standing (69), as the re-establishment of ankle strategies, balance in M/L direction was also improved (67). After stretching, loosening of stiff muscle fascicles tendon and/or aponeuroses might facilitate force generation among fascicles and increase their overall force output, which increases the passive stability of the ankle joint by limiting ankle movement in both the frontal and sagittal planes (18, 67). Alterations in muscle-tendon unit stiffness and length induced by continuous stretching could improve the fidelity of ankle proprioception (50, 60), which might improve balance. In conclusion, we assumed that the decreased DF stiffness might improve balance by activating the muscles and increasing proprioception and ROM of the ankle joints. Further studies are necessary to verify this hypothesis. Overall, in this study, a significant correlation ($\tau = 0.265$, $P = 0.041$) was observed between MAS and DF stiffness, which is consistent with the previous studies (19). This measure of stiffness can be used to obtain a more quantitative evaluation of ankle properties in the future.

LIMITATIONS

This study had limitations in methodological. First, given the number of samples available, between-group comparisons represented no differences in the biomechanical properties or balance function. Future studies with more subjects involved might show further group differences and increase the power of the study. Second, this study lacks a quantitative assessment of proprioception of the ankle joint, which is important in exploring the mechanisms of balance control recovery after stretching exercises. Third, the long-term effects of stretching training were unknown due to the absence of a follow-up period. Besides, our study only investigated the correlations between ankle stiffness and static balance in stroke survivors. The effects of ankle properties on dynamic balance need further investigation. Furthermore, muscle activations around the ankle joint will be collected using EMG for analysis as a function of ankle ROM, balance control, etc. Another limitation is the lack of a third group treated without stretching exercises. We plan to add one group of patients without stretching exercises to eliminate the improvement of ankle joint properties and balance function due to the natural history of stroke and better evaluate the effectiveness of the stretching therapy in the future. Future studies will further address these issues.

CONCLUSIONS

The robot-aided and manual ankle stretching training provided similar significant improvements in the ankle properties, balance, motor function, and ADL post-stroke. The robot-aided stretching devices provided labor-saved, high-intensity, and well-controlled passive stretching to stroke survivors with ankle impairments, which showed additional improvements across more parameters including the spasticity and stiffness of the ankle. Findings in this study suggested that robot-aided rehabilitation may be a beneficial addition to current rehabilitation programs. As an important part of posture control, the ankle joint properties were important in keeping the upright stance. In particular, ankle stiffness was correlated with balance function post-stroke. As a biomechanical property of the ankle joint, dorsiflexion stiffness may be a sensitive indicator for evaluating the balance ability post-stroke and predicting the risk of falls in the future.

DATA AVAILABILITY STATEMENT

The datasets used and analyzed during the current study are available from the corresponding author upon appropriate request.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Medical Ethics Committee of Beijing Tsinghua Changgung Hospital (18172-0-01). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

YP and L-QZ contributed to the study design, analysis, and interpretation of data and revisions to the manuscript. QW contributed to the analysis and interpretation of data. XZ contributed to the study design, data collection, analysis, interpretation of data, and drafting of the manuscript. Data collection was performed by XZ, XL, and QX. YZ and SF performed experiments. All authors read and approved the manuscript submitted and agree to be accountable for all aspects of the work.

FUNDING

This study was supported by Beijing Municipal Natural Science Foundation (L182028) and Beijing Municipal Science and Technology Commission (Z181100009218003 and Z181100003118004). No additional external funding was received for this study. The funders had no role in study design, data collection, and analysis, decision to publish, or preparation of the manuscript.

ACKNOWLEDGMENTS

We thank Yupeng Ren's thoughtful suggestions, for Jiehua Yu's assistance for biomechanical calculations, Meizhen Huang assistance with statistical analysis, and all the subjects for participating in this study.

REFERENCES

1. Liu L, Wang D, Wong KS, Wang Y. Stroke and stroke care in China: huge burden, significant workload, and a national priority. *Stroke.* (2011) 42:3651–4. doi: 10.1161/STROKEAHA.111.635755
2. Winter DA. Human balance and posture Human balance and posture control during standing and walking. *Gait Posture.* (1995) 3:193–214. doi: 10.1016/0966-6362(96)82849-9
3. Liston RA, Brouwer BJ. Reliability and validity of measures obtained from stroke patients using the Balance Master. *Arch Phys Med Rehabil.* (1996) 77:425–30. doi: 10.1016/S0003-9993(96)90028-3
4. de Haart M, Geurts AC, Huidekoper SC, Fasotti L, van Limbeek J. Recovery of standing balance in postacute stroke patients: a rehabilitation cohort study. *Arch Phys Med Rehabil.* (2004) 85:886–95. doi: 10.1016/j.apmr.2003.05.012
5. Rymer WZ, Katz RT. Mechanisms of spastic hypertonia. *Phys Med Rehabil: State Art Rev.* (1994) 8:441–54.
6. Tabary JC, Tabary C, Tardieu C, Tardieu G, Goldspink G. Physiological and structural changes in the cat's soleus muscle due to immobilization at different lengths by plaster casts. *J Physiol.* (1972) 224:231–44. doi: 10.1113/jphysiol.1972.sp009891
7. Tabary JC, Tardieu C, Tardieu G, Tabary C. Experimental rapid sarcomere loss with concomitant hypoextensibility. *Muscle Nerve.* (1981) 4:198–203. doi: 10.1002/mus.880040305
8. Tardieu C, Tabary JC, Tabary C, Tardieu G. Adaptation of connective tissue length to immobilization in the lengthened and shortened positions in cat soleus muscle. *J Physiol (Paris).* (1982) 78:214–20.
9. Williams PE, Goldspink G. Connective tissue changes in immobilised muscle. *J Anat.* (1984) 138:343–50.
10. Hyndman D, Ashburn A, Stack E. Fall events among people with stroke living in the community: circumstances of falls and characteristics of fallers. *Arch Phys Med Rehabil.* (2002) 83:165–70. doi: 10.1053/apmr.2002.28030
11. Karakaya MG, RutbIl H, Akpinar E, Yildirim A, Karakaya IÇ. Effect of ankle proprioceptive training on static body balance. *J Phys Ther Sci.* (2015) 27:3299–302. doi: 10.1589/jpts.27.3299
12. Morasso PG, Vittorio S. Ankle muscle stiffness alone cannot stabilize balance during quiet standing. *J Neurophysiol.* (2002) 88:2157–62. doi: 10.1152/jn.2002.88.4.2157
13. Thibaut A, Chatelle C, Ziegler E, Bruno M, Laureys S, Gosseries O. Spasticity after stroke: physiology, assessment and treatment. *Brain Injury.* (2013) 27:1093–105. doi: 10.3109/02699052.2013.804202
14. Dean CM, Rissel C, Sharkey M, Sherrington C, Cumming RG, Barker RN, et al. Exercise intervention to prevent falls and enhance mobility in community dwellers after stroke: a protocol for a randomised controlled trial. *BMC Neurol.* (2009) 9:38. doi: 10.1186/1471-2377-9-38
15. Daly JJ, Roenigk K, Holcomb, PhD J, Rogers JM, Butler K, Gansen J, et al. A randomized controlled trial of functional neuromuscular stimulation in chronic stroke subjects. *Stroke.* (2006) 37:172–8. doi: 10.1161/01.STR.0000195129.95220.77
16. Srivastava A, Taly AB, Gupta A, Kumar S, Murali T. Post-stroke balance training: role of force platform with visual feedback technique. *J Neurol Sci.* (2009) 287:89–93. doi: 10.1016/j.jns.2009.08.051
17. Wu CL, Huang MH, Lee CL, Liu CW, Lin LJ, Chen CH. Effect on spasticity after performance of dynamic-repeated-passive ankle joint motion exercise in chronic stroke patients. *Kaohsiung J Med Sci.* (2006) 22:610–7. doi: 10.1016/S1607-551X(09)70361-4
18. Gao F, Ren Y, Roth EJ, Harvey R, Zhang LQ. Effects of repeated ankle stretching on calf muscle-tendon and ankle biomechanical properties in stroke survivors. *Clin Biomech.* (2011) 26:516–22. doi: 10.1016/j.clinbiomech.2010.12.003
19. Selles RW Li X, Lin F, Chung SG, Roth EJ, Zhang LQ. Feedback-controlled and programmed stretching of the ankle plantarflexors and dorsiflexors in stroke: effects of a 4-week intervention program. *Arch Phys Med Rehabil.* (2005) 86:2330–6. doi: 10.1016/j.apmr.2005.07.305
20. Zhang LQ, Chung SG, Bai Z, Xu D, Van Rey EM, Rogers MW, et al. Intelligent stretching of ankle joints with contracture/spasticity. *IEEE Trans Neural Syst Rehabil Eng.* (2002) 10:149–57. doi: 10.1109/TNSRE.2002.802857
21. Chung SG, Van Rey E, Bai Z, Roth EJ, Zhang LQ. Biomechanic changes in passive properties of hemiplegic ankles with spastic hypertonia. *Arch Phys Med Rehabil.* (2004) 85:1638–46. doi: 10.1016/j.apmr.2003.11.041
22. Winstein CJ, Stein J, Arena R, et al. Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the american heart association/american stroke association. *Stroke.* (2016) 47:e98–e169. doi: 10.1161/STR.0000000000000098
23. Smania N, Picelli A, Munari D, et al. Rehabilitation procedures in the management of spasticity. *Eur J Phys Rehabil Med.* (2010) 46:423–38.
24. Vér C, Hofgárt G, Menyhárt L, Kardos L, Csiba L. Ankle-foot continuous passive motion device for mobilization of acute stroke patients. *Open J Therapy Rehabil.* (2015) 03:23–34. doi: 10.4236/ojtr.2015.32004

25. Nakayama Y, Iijima S, Kakuda W, Abo M. Effect of home-based training using a slant board with dorsiflexed ankles on walking function in post-stroke hemiparetic patients. *J Phys Ther Sci.* (2016) 28:2353–7. doi: 10.1589/jpts.28.2353
26. Waldman G, Yang CY, Ren Y, Liu L, Guo X, Harvey RL, et al. Effects of robot-guided passive stretching and active movement training of ankle and mobility impairments in stroke. *NeuroRehabilitation.* (2013) 32:625–34. doi: 10.3233/NRE-130885
27. Wu YN, Hwang M, Ren Y, Gaebler-Spira D, Zhang LQ. Combined passive stretching and active movement rehabilitation of lower-limb impairments in children with cerebral palsy using a portable robot. *Neurorehabil Neural Repair.* (2011) 25:378–85. doi: 10.1177/1545968310388666
28. Sukal-Moulton T, Clancy T, Zhang LQ, Gaebler-Spira D. Clinical application of a robotic ankle training program for cerebral palsy compared to the research laboratory application: does it translate to practice? *Arch Phys Med Rehabil.* (2014) 95:1433–40. doi: 10.1016/j.apmr.2014.04.010
29. Forrester LW, Roy A, Krywonis A, Kehs G, Krebs HI, Macko RF. Modular ankle robotics training in early subacute stroke: a randomized controlled pilot study. *Neurorehabil Neural Repair.* (2014) 28:678–87. doi: 10.1177/1545968314521004
30. Zheng QX, Ge L, Wang CC, Ma QS, Liao YT, Huang PP, et al. Robot-assisted therapy for balance function rehabilitation after stroke: A systematic review and meta-analysis. *Int J Nurs Stud.* (2019) 95:7–18. doi: 10.1016/j.ijnurstu.2019.03.015
31. Muraoka T, Muramatsu T, Fukunaga T, Kanehisa H. Elastic properties of human Achilles tendon are correlated to muscle strength. *J Appl Physiol.* (2005) 99:665–9. doi: 10.1152/japplphysiol.00624.2004
32. Zhang LQ, Wang G. Dynamic and static control of the human knee joint in abduction-adduction. *J Biomech.* (2001) 34:1107–15. doi: 10.1016/S0021-9290(01)00080-X
33. Olmstead TG, Wevers HW, Bryant JT, Gouw GJ. Effect of muscular activity on valgus/varus laxity and stiffness of the knee. *J Biomech*. (1986) 19:565–9. doi: 10.1016/0021-9290(86)90162-4
34. Sung PS, Baek JY, Kim YH. Reliability of the intelligent stretching device for ankle stiffness measurements in healthy individuals. *Foot.* (2010) 20:126–32. doi: 10.1016/j.foot.2010.09.005
35. Magnusson SP. Passive properties of human skeletal muscle during stretch maneuvers. A review. *Scand J Med Sci Sports*. (1998) 8:65–77. doi: 10.1111/j.1600-0838.1998.tb00171.x
36. Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. *Phys Ther.* (1987) 67:206–7. doi: 10.1093/ptj/67.2.206
37. Fugl-Meyer AR, Jääskö L, Leyman I, Olsson S, Steglind S. The post-stroke hemiplegic patient 1 a method for evaluation of physical performance. *Scand J Rehabil Med.* (1975) 7:13–31.
38. Berg K, Wood-Dauphinee S, William JT, Gayton D. Measuring balance in the elderly: preliminary development of an instrument. *Physiother Can.* (1989) 41:304–11. doi: 10.3138/ptc.41.6.304
39. Granger CV, Dewis LS, Peters NC, Sherwood CC, Barrett JE. Stroke rehabilitation: analysis of repeated Barthel index measures. *Arch Phys Med Rehabil.* (1979) 60:14–7.
40. Xu H-P, Quan L-J, Qiu Z. Study on validity and reliability of PRO- KIN balance instrument for predicting fall in elderly people. *J Nanchang Univ.* (2012) 52:34–7. doi: 10.3969/j.issn.1000-2294.2012.05.009
41. Mauch M, Kalin X. Reliability of the Prokin Type B Line System (TechnoBody ^{TM}) Balance System. *Internal Project Report. Praxisklinik Rennbahn.* (2011) 1–9.
42. Cattaneo D, Jonsdottir J. Sensory impairments in quiet standing in subjects with multiple sclerosis. *Mult Scler.* (2009) 15:59–67. doi: 10.1177/1352458508096874
43. Ibrahim AI, Muaidi QI, Abdelsalam MS, Hawamdeh ZM, Alhusaini AA. Association of postural balance and isometric muscle strength in early- and middle-school-age boys. *J Manipulative Physiol Ther.* (2013) 36:633–43. doi: 10.1016/j.jmpt.2013.08.009
44. Bressel E, McNair PJ. The effect of prolonged static and cyclic stretching on ankle joint stiffness, torque relaxation, and gait in people with stroke. *Phys Ther.* (2002) 82:880–7. doi: 10.1093/ptj/82.9.880
45. Nuyens GE, De Weerdt WJ, Spaepen AJ Jr, Kiekens C, Feys HM. Reduction of spastic hypertonia during repeated passive knee movements in stroke patients. *Arch Phys Med Rehabil.* (2002) 83:930–5. doi: 10.1053/apmr.2002.33233
46. Magnusson SP, Aagaard P, Dyhre-Poulsen P, Kjaer M. Load-displacement properties of the human triceps surae aponeurosis *in vivo*. *J Physiol*. (2001) 531:277–88. doi: 10.1111/j.1469-7793.2001.0277j.x
47. Chung S, Bai Z, Rymer WZ, Zhang LQ. *Changes of reflex, non-reflex and torque generation properties of spastic ankle plantar flexors induced by intelligent stretching.* In: 2005 IEEE Engineering in Medicine and Biology 27th Annual Conference. IEEE. (2005). p. 3672–5. doi: 10.1109/IEMBS.2005.1617279
48. Yeh CY, Tsai KH, Chen JJ. Effects of prolonged muscle stretching with constant torque or constant angle on hypertonic calf muscles. *Arch Phys Med Rehabil.* (2005) 86:235–41. doi: 10.1016/j.apmr.2004.03.032
49. Freitas SR, Vilarinho D, Rocha Vaz J, Bruno PM, Costa PB, Mil-homens P. Responses to static stretching are dependent on stretch intensity and duration. *Clin Physiol Funct Imaging.* (2015) 35:478–84. doi: 10.1111/cpf.12186
50. Lecharte T, Gross R, Nordez A, Le Sant G. Effect of chronic stretching interventions on the mechanical properties of muscles in patients with stroke: a systematic review. *Ann Phys Rehabil Med.* (2020) 63:222–9. doi: 10.1016/j.rehab.2019.12.003
51. Birkenmeier RL, Prager EM, Lang CE. Translating animal doses of task-specific training to people with chronic stroke in 1-hour therapy sessions: a proof-of-concept study. *Neurorehabil Neural Repair.* (2010) 24:620–35. doi: 10.1177/1545968310361957
52. Langhorne P, Coupar F, Pollock A. Motor recovery after stroke: a systematic review. *Lancet Neurol.* (2009) 8:741–54. doi: 10.1016/S1474-4422(09)70150-4
53. Krebs HI, Volpe BT, Aisen ML, Hogan N. Increasing productivity and quality of care: robot-aided neuro-rehabilitation. *J Rehabil Res Dev.* (2000) 37:639–52. doi: 10.1067/mmt.2000.110940
54. Hussain S, Jamwal PK, Vliet PV, Brown NAT. Robot assisted ankle neuro-rehabilitation: state of the art and future challenges. *Expert Rev Neurother.* (2021) 21:111–21. doi: 10.1080/14737175.2021.1847646
55. McNair PJ, Dombroski EW, Hewson DJ, Stanley SN. Stretching at the ankle joint: viscoelastic responses to holds and continuous passive motion. *Med Sci Sports Exerc.* (2001) 33:354–8. doi: 10.1097/00005768-200103000-00003
56. Jeon SN, Choi JH. The effects of ankle joint strategy exercises with and without visual feedback on the dynamic balance of stroke patients. *J Phys Therapy Sci.* (2015) 27:2515–8. doi: 10.1589/jpts.27.2515
57. Yoo D, Kim DH, Seo KH, Lee BC. The Effects of Technology-Assisted Ankle Rehabilitation on Balance Control in Stroke Survivors. *IEEE Trans Neural Syst Rehabil Eng.* (2019) 27:1817–23. doi: 10.1109/TNSRE.2019.2934930
58. Anacker SL, Di Fabio RP. Influence of sensory inputs on standing balance in community-dwelling elders with a recent history of falling. *Phys Ther.* (1992) 72:575–84. doi: 10.1093/ptj/72.8.575
59. Han J, Anson J, Waddington G, Adams R, Liu Y. The role of ankle proprioception for balance control in relation to sports performance and injury. *Biomed Res Int.* (2015) 2015:842804. doi: 10.1155/2015/842804
60. Yoo D, Son Y, Kim DH, Seo KH, Lee BC. Technology-assisted ankle rehabilitation improves balance and gait performance in stroke survivors: a randomized controlled study with 1-month follow-up. *IEEE Trans Neural Syst Rehabil Eng.* (2018) 26:2315–23. doi: 10.1109/TNSRE.2018.2879783
61. Zhao W, You H, Jiang S, Zhang H, Yang Y, Zhang M. Effect of Pro-kin visual feedback balance training system on gait stability in patients with cerebral small vessel disease. *Medicine.* (2019) 98:e14503. doi: 10.1097/MD.0000000000014503
62. Shumway-Cook A, Woollacott M. Attentional demands and postural control: the effect of sensory context. *J Gerontol A Biol Sci Med Sci.* (2000) 55:M10–6.
63. Amiri P, Mohebbi A, Kearney R. Experimental methods to study human postural control. *J Vis Exp.* (2019) 151:e60078. doi: 10.3791/60078
64. Beyaert C, Vasa R, Frykberg GE. Gait post-stroke: pathophysiology and rehabilitation strategies. *Neurophysiol Clin.* (2015) 45:335–55. doi: 10.1016/j.neucli.2015.09.005

65. Kitatani R, Ohata K, Aga Y, Mashima Y, Hashiguchi Y, Wakida M, et al. Descending neural drives to ankle muscles during gait and their relationships with clinical functions in patients after stroke. *Clin Neurophysiol.* (2016) 127:1512–20. doi: 10.1016/j.clinph.2015.10.043
66. Wang W, Li K, Wei N, Yin C, Yue S. Evaluation of postural instability in stroke patient during quiet standing. In: 2017 39th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC). (2017). p. 2522–5. doi: 10.1109/EMBC.2017.8037370
67. Chern JS, Chang HS, Lung CW, Wu CY, Tang SF. Static ankle-foot orthosis improves static balance and gait functions in hemiplegic patients after stroke. In: 2013 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC). (2013). p. 5009–12.
68. Zeng X, Zhu G, Zhang M, Xie SQ. Reviewing clinical effectiveness of active training strategies of platform-based ankle rehabilitation robots. *J Healthc Eng.* (2018) 2018:1–12. doi: 10.1155/2018/2858294
69. Chern JS, Yang SW, Wu CY. Whole-body reaching as a measure of dynamic balance in patients with stroke. *Am J Phys Med Rehabil.* (2006) 85:201–8. doi: 10.1097/01.phm.0000200357.98448.d7

Conflict of Interest: L-QZ holds an equity position in Beijing LTK Science and Technology Co., which made the ankle rehabilitation robot used in this study.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Human Neuroscience

BRIEF RESEARCH REPORT
published: 21 October 2021
doi: 10.3389/fnhum.2021.771446

Age-Related Changes of the Anticipatory Postural Adjustments During Gait Initiation Preceded by Vibration of Lower Leg Muscles

Jana Kimijanová, Diana Bzdúšková, Zuzana Hirjaková and František Hlavačka*

Department of Behavioral Neuroscience, Institute of Normal and Pathological Physiology, Centre of Experimental Medicine, Slovak Academy of Sciences, Bratislava, Slovakia

Gait initiation (GI) challenges the balance control system, especially in the elderly. To date, however, there is no consensus about the age effect on the anticipatory postural adjustments (APAs). There is also a lack of research on APAs in older adults after proprioceptive perturbation in the sagittal plane. This study aimed to compare the ability of young and older participants to generate APAs in response to the vibratory-induced perturbation delivered immediately before GI. Twenty-two young and 22 older adults performed a series of GI trials: (1) without previous vibration; (2) preceded by the vibration of triceps surae muscles; and (3) preceded by the vibration of tibialis anterior muscles. The APAs magnitude, velocity, time-to-peak, and duration were extracted from the center of pressure displacement in the sagittal plane. Young participants significantly modified their APAs during GI, whereas older adults did not markedly change their APAs when the body vertical was shifted neither backward nor forward. Significant age-related declines in APAs were observed also regardless of the altered proprioception. The results show that young adults actively responded to the altered proprioception from lower leg muscles and sensitively scaled APAs according to the actual position of the body verticality. Contrary, older adults were unable to adjust their postural responses indicating that the challenging transition from standing to walking probably requires higher reliance on the visual input. The understanding of age-related differences in APAs may help to design training programs for the elderly specifically targeted to improve balance control in different sensory conditions, particularly during gait initiation.

Keywords: gait initiation, anticipatory postural adjustments, age, proprioception, muscle vibration

OPEN ACCESS

Edited by:
Eric Yiou,
Université Paris-Saclay, France

Reviewed by:
John Stins,
Vrije Universiteit Amsterdam, Netherlands
Charles Layne,
University of Houston, United States

****Correspondence:***
Jana Kimijanová
jana.kimijanova@savba.sk

Specialty section:
This article was submitted to Motor Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *06 September 2021*
Accepted: *27 September 2021*
Published: *21 October 2021*

Citation:
Kimijanová J, Bzdúšková D, Hirjaková Z and Hlavačka F (2021) Age-Related Changes of the Anticipatory Postural Adjustments During Gait Initiation Preceded by Vibration of Lower Leg Muscles. Front. Hum. Neurosci. 15:771446. doi: 10.3389/fnhum.2021.771446

INTRODUCTION

One of the most important requirements of successful locomotion is the ability to adapt gait to the various demands of the environment (Shumway-Cook and Woollacott, 2007). Motor adaptation, playing a significant role, can be defined as the process of making feedforward modifications or adjustments based on sensorimotor integration to already well-learned motor skills (Martin et al., 1996). The transition from standing to walking, i.e., gait initiation (GI) is known to be a highly challenging task for the balance control system involving correct sequencing of movement preparation and execution. Immediately prior to the stepping, anticipatory postural adjustments (APAs) act to accelerate the center of body mass (CoM) forward and towards the stance leg by

moving the center of pressure (CoP) backward and towards the stepping leg in order to minimize the potential imbalance at the moment of single-leg stance (Crenna and Frigo, 1991; Jian et al., 1993). APAs along the anterior-posterior (AP) axis are predictive of motor performance (Lepers and Brenière, 1995) while APAs along the medio-lateral (ML) axis are predictive of postural stability (McIlroy and Maki, 1999; Honeine et al., 2016). In addition, as older individuals are more likely to fall during common daily activities, such as walking, changing position (Tinetti et al., 1995), or initiating a step in different environments (Polcyn et al., 1998; Henriksson and Hirschfeld, 2005), it is particularly important to appropriately respond to either externally or internally generated perturbation stimuli and produce corresponding balance adjustments during these locomotor tasks. Regarding this, GI provides an ideal task to investigate age-related changes in APAs, especially when a sudden change in sensory signals occurs. During the unperturbed stepping, previous studies reported characteristic modifications of APAs in older adults, for instance, reduced initial backward CoP shift, reduced velocity of CoM at the time of first swing foot toe off (Halliday et al., 1998; Khanmohammadi et al., 2015), or significantly diminished momentum-generating capacity of CoP shift (Polcyn et al., 1998). Due to aging, a delayed onset activity of tibialis anterior (Khanmohammadi et al., 2015), more variable muscle activity (Mickelborough et al., 2004), or even lack of anticipatory activity of lower leg muscles (Henriksson and Hirschfeld, 2005) were shown. The older adults exhibited a longer unloading phase with a higher frequency of ground reaction forces peaks and an earlier maximal force rate achieved during this phase (Jonsson et al., 2007). However, other studies reported no age effect (Patchay et al., 2002; Plate et al., 2016; Lu et al., 2017) or only a partial effect of aging (Jonsson et al., 2007) on APAs. Hence, generally, there is no consensus about the age effect on APAs during GI. Moreover, despite the fact that imbalance or falls frequently occur while moving the body in the sagittal plane and position of the body verticality is compromised currently in this plane (Robinovitch et al., 2013), previous studies have investigated APAs mostly in terms of lateral weight shift. Furthermore, to our knowledge, there is a complete lack of research on APAs in older adults when the proprioceptive system was perturbed in the sagittal plane before or during GI. If there are reports which elaborate about the changes in APAs associated with balance perturbation, they have examined postural responses in the frontal plane and mostly in young subjects (Ruget et al., 2008, 2010; Mouchnino and Blouin, 2013; Mille et al., 2014). These studies indicated that young adults are able to modify their APAs when the body is subjected to an external perturbation. If this is true also for older adults, who are more vulnerable to fall in the occurrence of balance perturbation in the sagittal plane, is still unclear. There is a general agreement that proprioceptive signals from leg muscles provide the primary source of information for postural control (see review by Henry and Baudry, 2019). However, aging is associated with a decrease in sensitivity, acuity, and integration of the proprioceptive signal resulting in reduced efficiency of postural control (Deshpande et al., 2016). Therefore, we assume that the age-related impairments in detection and processing of the proprioceptive signals would influence the postural adjustments of GI preceded by the vibration of lower leg muscles.

In the present study, we dealt with this issue by comparing the ability of young and older adults to generate the appropriate APAs in response to the vibratory-induced perturbation delivered immediately before GI. To our knowledge, no study to date examined the age-related differences in APAs due to such perturbation of balance in the sagittal plane. The specific aims were: (1) to determine to what extent the proprioceptive perturbation of balance affects APAs in young and older adults, and (2) to examine whether such an effect is dependent on age. We hypothesized that altered proprioception from lower leg muscles resulting in a modified representation of the body verticality would significantly affect APAs and this would manifest as a change of the APAs magnitude, velocity, and timing in young adults. In contrast, we further hypothesized that older adults would show decreased ability to appropriately respond to the perturbation due to postural and physiological declines associated with aging.

MATERIALS AND METHODS

Participants

Twenty-two young and 22 older adults (**Table 1**) free of musculoskeletal and neurological disorders that could influence balance control participated in the study. They had no medical history of falls, no pain, numbness, tingling, or weakness at the time of testing. The presence of sensory neuropathy was excluded by Pinprick testing (Nather et al., 2008; Blackmore and Siddiqi, 2016). All subjects gave informed written consent in agreement with the Declaration of Helsinki and the study was approved by the local Ethics Committee.

Experimental Setup and Protocol

Gait was initiated from an upright standing on a custom-made force plate (45 × 45 × 6.5 cm; see details in Hirjaková et al., 2017), in-built and located at the beginning of a 5-m walkway. Postural responses were quantified by CoP displacement in the AP direction because changes induced by the vibratory stimulation were also expected in this direction. The CoP data were acquired at 100 Hz sampling frequency and low-pass filtered at 10 Hz cut-off frequency (Mancini et al., 2009; Sinclair et al., 2013). The initial stance position was consistent from trial-to-trial by tracing foot outlines on the force plate.

Before starting each trial, the subjects were required to realign the CoP location to the initial position detected on a monitor.

TABLE 1 | Participant characteristics.

	Young (22–35 years)	Older (65–83 years)	*p*-value
n	22	22	
Gender (M/F)	9/13	9/13	
Age (years)	29.0 (3.4)	73.7 (5.6)	**<0.001**
Height (m)	1.72 (0.07)	1.63 (0.09)	**<0.001**
Weight (kg)	66.5 (13.3)	73.7 (12.2)	0.08
Foot length (cm)	25.8 (1.7)	25.9 (1.6)	0.73

Mean (SD). Significant effects are marked in bold.

The initial CoP position at vibration onset was arbitrarily assigned a value of zero. Proprioceptive stimulation was delivered by custom-made electromechanical vibrators (DC motor with small eccentric rotating mass, weighing 230 g, cylindrical in shape, 9 cm long with a diameter of 4.7 cm) attached with elastic bands. In the case of triceps surae (TS) muscles, vibrators were fixed to the Achilles tendon of both legs, at the level of the ankle joint, and the vibration-induced body tilt was in the same direction as the forthcoming APAs, i.e., backward. In the case of tibialis anterior (TA) muscles, vibrators were fixed on the tendons of the tibialis anterior, 3–5 cm above the ankle joint, and the vibration-induced body tilt was in the opposite direction as the forthcoming APAs, i.e., forwards. The dimensions and positioning of the vibrators did not disrupt locomotion and they were fixed to the tendons during both vibration and control trials (vibrators off). The activation and deactivation of the vibrators were computer-controlled. The stimulation lasted 5 s with an amplitude of 1 mm and a frequency of 80 Hz. Kinematics of the body (reflective markers placed bilaterally on the following landmarks: acromion, greater trochanter, lateral femoral condyle, lateral malleolus, 5th metatarsal, and heel) was recorded by the optoelectronic motion capture system (BTS Bioengineering, Italy) with a sampling frequency of 100 Hz. The vibration-induced body tilt in the sagittal plane was computed from kinematic data as the angle between the shoulder-hip line, i.e., trunk angle (position of the acromion to hip markers) with respect to the vertical (see details in Abrahámová et al., 2009). The final body tilt induced by vibration was quantified during the last second of vibratory stimulation.

Participants stood on a force plate in a natural upright posture with their arms alongside the body, feet approximately pelvis-width apart, and gaze fixating on a visual target set at the eye level and located 5 m away from the starting stance position. After the initial 5 s of quiet stance followed either by 5 s of vibratory stimulation (vibration trials) or another 5 s of quiet stance (control trials), each participant performed a series of GI trials immediately after hearing an acoustic signal (short "beep") delivered by the computer. Participants were instructed to step with their dominant leg at a spontaneous velocity and walk straight ahead to the end of the walkway. The acoustic signal was triggered at the same moment as the vibration offset. Participants performed two practice trials to familiarize with the experimental conditions and then five trials were collected in each of the following conditions (for a total of $N = 15$ trials): (1) GI without previous vibratory stimulation (control trial); (2) GI preceded by tendon vibration of TS muscles; and (3) GI preceded by tendon vibration of TA muscles. The order of conditions was randomized across the subjects.

Data Processing and Analysis

The APAs variables (**Figure 1**) were extracted from backward CoP displacement. The onset of APAs was detected by an automated threshold-based algorithm, with the threshold set as 2.5 SD of CoP signal (Caderby et al., 2014) during the initial, pre-vibration period of each trial. The APAs were considered completed (end of APAs) at the time of swing limb heel-off (Rocchi et al., 2006; Delafontaine et al., 2021). The APAs magnitude (*Peak AP*) was measured by the peak of CoP excursion from the CoP position at the moment of vibration offset which was again arbitrarily assigned a value of zero. Related *Time-to-Peak AP*, from the onset of APAs to the instant of Peak AP was also measured (Mancini et al., 2009). The APAs velocity was calculated as a first derivative of CoP displacement and then the peak of CoP velocity (*Peak Velo AP*) was evaluated. The APAs duration (*APAd*) was measured as the time between the onset and the end of APAs (Mancini et al., 2009; Delafontaine et al., 2021). For comparison between the different body dimensions and subjects, CoP displacement was normalized to the foot length and CoP velocity was normalized to height by detrending normalization (O'Malley, 1996) which aims at removing the dependence of stabilometric parameters on anthropometric features (Chiari et al., 2002).

Algorithms for CoP signal analysis and evaluation of the variables were written in MATLAB R2020b (MathWorks Inc., USA). The mean of five trials was used for statistical analyses. Repeated measures ANOVAs were used to test the effect of vibration (TS, C, TA), the effect of age (young, older), and their interaction on each variable after having checked normal distribution with the Shapiro-Wilk test. Greenhouse-Geisser adjustments were performed in cases where the assumption of sphericity was violated. *Post hoc* pairwise comparisons were conducted to identify further differences between TS and C condition, and TA and C condition within each age group. Follow-up independent samples *t*-tests were used on all dependent APAs variables to evaluate the age-related differences. The relationship between the magnitude of vibration-induced body tilt and the APAs magnitude was investigated by a partial correlation analysis while controlling for age. To reduce Type I error due to the multiple *t*-test comparisons, the Bonferroni correction was applied. All statistical analyses were performed using SPSS 18.0 (SPSS, Inc., IL-IBM, USA). The level of significance was set at $p < 0.05$ and effect size (partial eta squared η^2) was also computed.

RESULTS

Significant main effects of vibration, age, and significant effect of vibration by age interaction were observed on all evaluated APAs variables (**Table 2**), except Peak Velo AP with no age effect. Further *post hoc* comparisons revealed that in young adults, all APAs variables were significantly different in vibration (TS, TA) compared to control (C) condition (**Figure 2A**). Young adults demonstrated a significant increase of *Time-to-Peak AP* and *APAd* in TS, and a significant decrease of *Time-to-Peak AP* and *APAd* in TA compared to the control condition. Oppositely, *Peak AP* and *Peak Velo AP* significantly decreased in TS and increased in TA compared to the control condition. Thus, the positional change of the body verticality induced by lower leg muscles vibration immediately before stepping resulted in significantly different APAs in young adults, which is clearly visible also in **Figure 2B** showing CoP trajectories of one representative young subject during all experimental conditions. Contrary, no significant differences in APAs variables were observed between vibration conditions and control GI in older adults (**Figure 2A**).

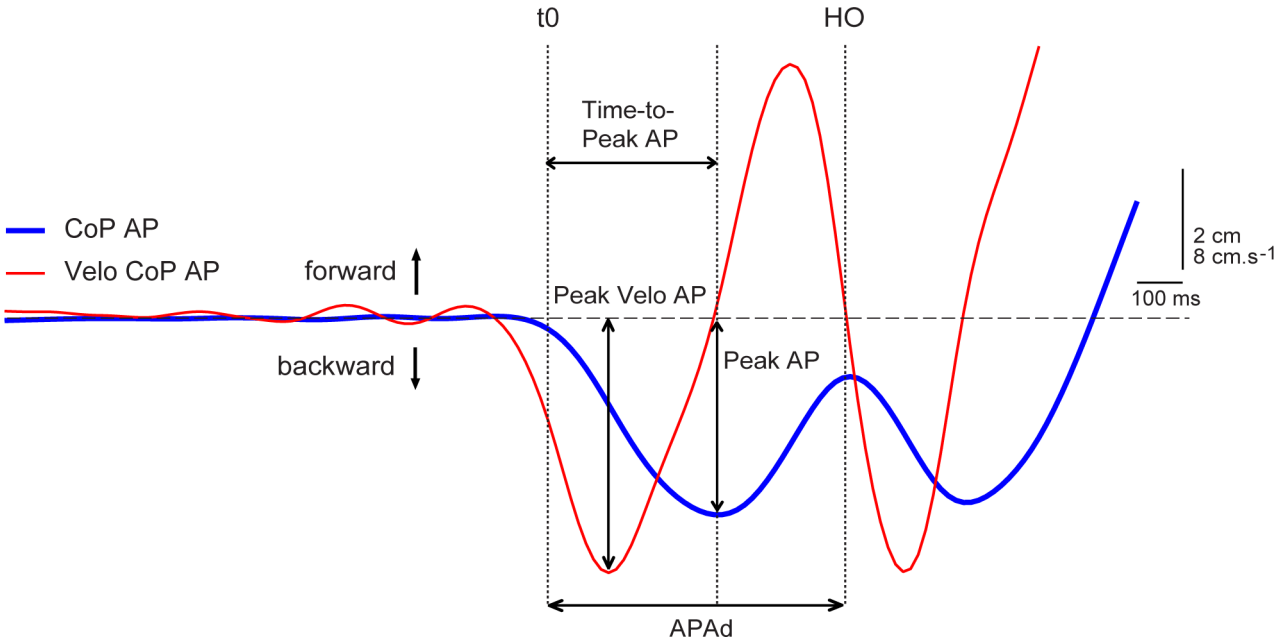

FIGURE 1 | Example of the anticipatory postural adjustments (APAs) variables measured during right-step initiation of the representative young subject during the control trial. Experimental variables evaluated from center of pressure (CoP) displacement (blue line) and velocity of CoP displacement (red line) in anterior-posterior (AP) direction: Peak AP, Time-to-Peak AP, APAd, Peak Velo AP. Vertical dotted lines: t0—onset of APAs; HO—swing limb heel-off.

Unchanged CoP trajectories of one representative older subject across all experimental conditions are displayed in **Figure 2B**.

The partial correlation analysis showed no significant association between the extent of trunk angle induced by vibration of neither TS ($r = 0.074$, $p = 0.636$), nor TA ($r = 0.044$, $p = 0.781$) muscles and the APAs magnitude. Moreover, young and older participants did not significantly differ neither in backward ($0.94 \pm 0.19°$ vs. $0.76 \pm 0.10°$; $p = 0.440$, respectively), nor in forward ($0.98 \pm 0.21°$ vs. $0.70 \pm 0.07°$, $p = 0.218$, respectively) vibration-induced body tilt.

In addition to different anticipatory postural strategies due to the proprioceptive alteration of balance in young and older adults, further analyses revealed significant age-related declines in the APAs variables regardless of the altered proprioception before GI. The older subjects exhibited a significantly shorter *Time-to-Peak AP* in all experimental conditions compared to young adults (**Figure 2A**). Interestingly, *APAd* was significantly reduced in the older group only in TS condition. Moreover, a smaller *Peak AP* and *Peak Velo AP* were observed in older adults during control GI as well as GI preceded by TA vibration.

TABLE 2 | Summary of repeated measures ANOVAs for all evaluated anticipatory postural adjustments (APAs) variables.

Variable	Effect	*F*	*df*	*p*	η_p^2
APAd	Vibration	34.591	(2, 84)	**<0.001**	0.452
	Age	5.954	(1, 42)	**0.019**	0.124
	Vibration × Age	9.401	(2, 84)	**<0.001**	0.183
Time-To-Peak AP	Vibration	33.935	(2, 84)	**<0.001**	0.447
	Age	32.791	(1, 42)	**<0.001**	0.438
	Vibration × Age	7.423	(2, 84)	**0.003**	0.150
Peak AP	Vibration	10.965	(2, 84)	**<0.001**	0.207
	Age	5.855	(1, 42)	**0.020**	0.122
	Vibration × Age	12.628	(2, 84)	**<0.001**	0.231
Peak Velo AP	Vibration	37.403	(2, 84)	**<0.001**	0.471
	Age	0.144	(1, 42)	0.707	0.003
	Vibration × Age	11.238	(2, 84)	**<0.001**	0.211

Significant effects are marked in bold. Note: Greenhouse-Geisser corrected values are reported where appropriate.

DISCUSSION

In this study, we compared the ability of young and older individuals to generate the appropriate APAs in response to the balance perturbation delivered immediately before gait initiation by bilateral vibratory stimulation of lower leg muscles. In line with our first hypothesis, the young participants significantly modified their postural adjustments during the preparatory phase of stepping and changed all APAs variables under both vibration conditions. In detail, the TS vibration before stepping resulted in backward body tilt to which young adults responded by smaller APAs magnitude and velocity and prolonged APAs duration and time-to-peak compared to unperturbed stepping. On the other hand, when they initiated a step from forward body tilt induced by the TA vibration, they increased the APAs magnitude and velocity while shortening both temporal parameters. As we expected, APAs were modulated according to the internal representation of the body verticality shifted by the vibration of lower leg muscles either forward or backward suggesting that the initial posture strongly influences

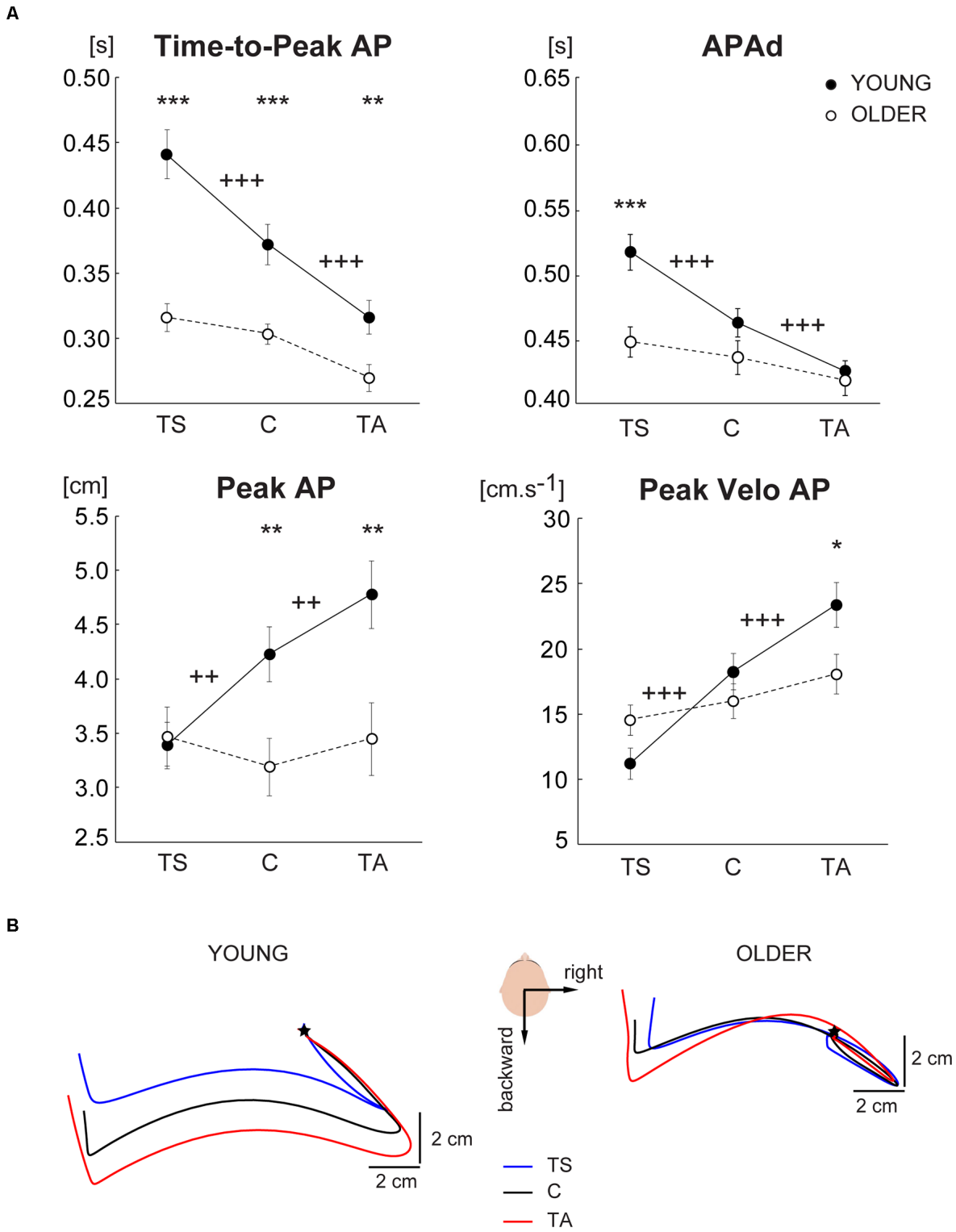

FIGURE 2 | (A) Comparison of APAs variables evaluated from CoP displacement in the anterior-posterior direction across three different experimental conditions (TS—vibration of triceps surae muscles, C—control condition with no vibration, TA—vibration of tibialis anterior muscles) in the group of young and older subjects. The values are presented as group mean ± SEM. *Post hoc* differences between vibration conditions and control condition are marked: $^{++}p < 0.01$, $^{+++}p < 0.001$. Differences between young and older are marked: $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$. **(B)** A bird's-eye view of the mean CoP trajectories during right-step initiation of representative young (left) and older (right) subject during tibialis anterior vibration condition (red), triceps surae vibration condition (blue), and control condition (black). The mean CoP trajectories are realigned according to the APAs onset which is represented by the star.

forthcoming APAs. Our findings agree with previous studies (Rocchi et al., 2006; Dalton et al., 2011), which demonstrated scaling of APAs according to the initial posture. In line with our results, it was concluded that APAs during GI were modulated according to the proprioceptive information originating from the actual position of the body verticality which was altered by translation of support surface (Burleigh and Horak, 1996; Mouchnino and Blouin, 2013), unstable foam support surface (Chastan et al., 2010), the vibration of ankle muscles (Ruget et al., 2010), or applying resistance force at the pelvis (Mille et al., 2014; Laudani et al., 2021). As suggested in these studies, the central nervous system (CNS) utilizes feed-forward prediction for forthcoming voluntary movement, and utilizes immediate afferent information to modify the centrally initiated postural adjustments associated with stepping. Changes of APAs after the delivery of the proprioceptive perturbation suggest that CNS estimated the potentially destabilizing effects of the altered body verticality and acted to modify postural adjustments of GI in order to ensure the stability of the planned movement. The postural adaptations for GI, with respect to changes in proprioceptive information, support a role for multiple, distributed, and interactive systems for postural control (Burleigh and Horak, 1996). However, we found the APAs modulation according to the actual position of the body verticality only in young adults. Thus, the second hypothesis of the study was met as older adults showed a compromised ability to actively respond to the balance perturbation. Although the older subjects showed a similar trend of changing APAs in terms of increasing/decreasing of variables' values with respect to the vibration compared to control condition as young adults, these changes were not significant. The first aspect which can play a role is an age-related decrease in the proprioception sensitivity which alters both the structures and the functioning of the proprioceptive system (Henry and Baudry, 2019). Alteration in the muscle spindles and their afferents, along with the integration of the signal at the supraspinal level, have been shown to influence proprioceptive perception and postural control in older adults (Goble et al., 2012). Based on our findings, it can be hypothesized that when older people experience a proprioceptive disturbance while initiating a step, they may not be able to properly respond by adjusting their anticipatory postural strategies. The second aspect includes the role of motor prediction in posture and locomotion coupling (Mille et al., 2014). Our findings may be supported by previous studies (Claudino et al., 2013; Laudani et al., 2021) indicating no postural prediction and movement coupling in older adults. It is possible that older individuals may have difficulties in utilizing APAs due to a lack of the necessary coupling between APAs and the stepping movement (Laudani et al., 2021) and also may have reduced usability and efficacy of APAs to ensure stability following the perturbation (Claudino et al., 2013). Another aspect concerns the age-related differences in the importance of proprioceptive and visual information for maintaining equilibrium. While the muscle proprioception is more important for balance control than vision in healthy young adults (Eysel-Gosepath et al., 2016), a decreased effect of proprioceptive alteration with aging indicated a lesser reliance on leg proprioception in older adults (Penzer et al., 2015; Deshpande et al., 2016). In line with this, the declines in peripheral sensory perception with aging caused elevated reliance on visual feedback (Franz et al., 2015).

In the current study, we further aimed to investigate the age-related differences in APAs regardless of proprioceptive alteration. During the unperturbed stepping, older adults showed significantly smaller APAs magnitude and shorter Time-to-Peak AP compared to young adults. Congruently, age-related changes in APAs were revealed in previous studies (Henriksson and Hirschfeld, 2005; Jonsson et al., 2007; Khanmohammadi et al., 2015; Laudani et al., 2021), but there are also studies which reported APAs unaffected by age (Plate et al., 2016; Lu et al., 2017). The findings of Plate et al. (2016), however, do not quite reflect the age-related changes in terms of young vs. old, as they considered as young the adults with mean age 43.8 $\pm$ 2.9 years and compared them with middle-aged and older adults (mean age 55.3 $\pm$ 2.8 and 66.4 $\pm$ 4.5 years, respectively). In the same line, Lu et al. (2017) reported an unchanged spatiotemporal profile of the APAs with aging (ages 20–79). Incongruence with our results may come from different instructions for gait initiation, i.e., self-initiated stepping.

Apart from a significantly reduced APAs magnitude and Time-to-Peak AP due to age in control GI, we found similarly reduced APAs variables also in TA vibration condition. However, in the TS vibration condition, older subjects showed a very similar magnitude of APAs as young adults, but the postural adjustments were significantly shorter and slightly faster than in young adults. We speculate that these different anticipatory adjustments in older adults between the two vibration conditions might be associated with a specific response to the vibration offset (i.e., the moment of vibratory stimulation turn off; Bzdúšková et al., 2018). Specifically, we assume that two autonomic motor control programs, i.e., response to vibration offset and forthcoming APAs came into conflict at the moment when the vibration suddenly stopped and simultaneously the acoustic signal indicated to initiate a step. The postural response to the vibration offset in case of soleus muscles vibration is characterized by a backward shift of CoP displacement followed by a forward CoP overshoot in order to establish equilibrium after the perturbation (Bzdúšková et al., 2018). Oppositely, the response to the TA vibration offset is performed as a forward body tilt followed by a backward CoP overshoot. Therefore, as APAs during GI are known as backward CoP shift, overshoot after the TA vibration offset occurs in the direction of forthcoming APAs and contrary, overshoot after the TS vibration offset occurs in the opposite direction as forthcoming APAs. Our results suggest that the latter case might be more challenging for older adults and indicate higher reliance on vision and adopting a stiffening strategy to prevent the loss of balance. In particular, when older adults experienced a significantly larger and faster overshoot after the TS vibration offset (Bzdúšková et al., 2018) and concurrently they had to initiate a step they might have less time for appropriate APAs resulting in faster and thus shorter APAs compared to young adults.

Interestingly, we revealed a significant decrease due to age in parameter APAd only in the TS condition, while Time-to-Peak AP was significantly different between the age groups in all experimental conditions. This indicates that Time-to-Peak would be a more sensitive parameter to detect early APAs impairments as total APAs duration.

A strength of the study was the comparison of the ability to generate APAs in response to the proprioceptive perturbation of balance both forward and backward. For the first time, hence, this study uncovered and reported sensitive scaling of APAs in the sagittal plane according to the externally shifted vertical in young adults, and revealed the inability to modify APAs in older adults. Therefore, these results should be taken into account when designing training and rehabilitation programs for the elderly specifically targeted to improve balance control in different sensory conditions, particularly during the transition from standing to walking in order to enhance a more accurate adjusting of APAs and potentially prevent falling. On the other hand, we acknowledge several limitations of the present study. First, we did not collect electromyographic signals from lower leg muscles during the vibratory stimulation and GI which could provide additional information about APAs and would help to interpret age-related differences. Second, we might benefit from the kinematic analysis of the first step performed immediately after the balance perturbation. Further studies should address these limitations as well as investigate whether it is possible to improve the proprioception from lower leg muscles and thus increase the anticipatory responsiveness to perturbation.

In summary, aging led to significantly reduced APAs during GI performed from the vibratory shifted vertical as well as from the natural body verticality. Moreover, young adults markedly modulated APAs in response to the vibration delivered before GI, which was in contrast with older adults who showed diminished modulation of APAs. Therefore we can conclude that the ability to generate the appropriate APAs in response to vibratory-induced perturbation particularly in the sagittal plane is age-dependent.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the local Ethics Committee of the Center of Experimental Medicine of the Slovak Academy of Sciences. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

JK, ZH, and FH contributed to the conception and design of the study. JK organized the database and wrote the first draft of the manuscript. JK and DB performed the statistical analysis. JK, DB, ZH, and FH reviewed the manuscript. All authors contributed to the article and approved the submitted version.

FUNDING

This work was supported by the Slovak Research and Development Agency (project no. APVV-20-0420) and the Scientific Grant Agency of the Ministry of Education, Science, Research and Sport of the Slovak Republic (project no. VEGA 2/0104/19).

REFERENCES

Abrahámová, D., Mancini, M., Hlavačka, F., and Chiari, L. (2009). The age-related changes of trunk responses to Achilles tendon vibration. *Neurosci. Lett.* 467, 220–224. doi: 10.1016/j.neulet.2009.10.041

Blackmore, D., and Siddiqi, Z. A. (2016). Pinprick testing in small fiber neuropathy: accuracy and pitfalls. *J. Clin. Neuromuscul. Dis.* 17, 181–186. doi: 10.1097/CND.0000000000000116

Burleigh, A., and Horak, F. (1996). Influence of instruction, prediction and afferent sensory information on the postural organization of step initiation. *J. Neurophysiol.* 75, 1619–1628. doi: 10.1152/jn.1996.75.4.1619

Bzdúšková, D., Valkovič, P., Hirjaková, Z., Kimijanová, J., and Hlavačka, F. (2018). Parkinson's disease versus ageing: different postural responses to soleus muscle vibration. *Gait Posture* 65, 169–175. doi: 10.1016/j.gaitpost.2018.07.162

Caderby, T., Yiou, E., Peyrot, N., Begon, M., and Dalleau, G. (2014). Influence of gait speed on the control of mediolateral dynamic stability during gait initiation. *J. Biomech.* 47, 417–423. doi: 10.1016/j.jbiomech.2013.11.011

Chastan, N., Westby, G. W., du Montcel, S. T., Do, M. C., Chong, R. K., Agid, Y., et al. (2010). Influence of sensory inputs and motor demands on the control of the centre of mass velocity during gait initiation in humans. *Neurosci. Lett.* 469, 400–404. doi: 10.1016/j.neulet.2009.12.038

Chiari, L., Rocchi, L., and Cappello, A. (2002). Stabilometric parameters are affected by anthropometry and foot placement. *Clin. Biomech. (Bristol, Avon).* 17, 666–677. doi: 10.1016/s0268-0033(02)00107-9

Claudino, R., dos Santos, E. C., and Santos, M. J. (2013). Compensatory but not anticipatory adjustments are altered in older adults during lateral postural perturbations. *Clin. Neurophysiol.* 124, 1628–1637. doi: 10.1016/j.clinph.2013.02.111

Crenna, P., and Frigo, C. (1991). A motor programme for the initiation of forward-oriented movements in humans. *J. Physiol.* 437, 635–653. doi: 10.1113/jphysiol.1991.sp018616

Dalton, E., Bishop, M., Tillman, M. D., and Hass, C. J. (2011). Simple change in initial standing position enhances the initiation of gait. *Med. Sci. Sports Exerc.* 43, 2352–2358. doi: 10.1249/MSS.0b013e318222bc82

Delafontaine, A., Fourcade, P., Zemouri, A., Diakhaté, D. G., Saiydoun, G., and Yiou, E. (2021). In patients with Parkinson's disease in an OFF-medication state, does bilateral electrostimulation of tibialis anterior improve anticipatory postural adjustments during gait initiation? *Front. Hum. Neurosci.* 15:692651. doi: 10.3389/fnhum.2021.692651

Deshpande, N., Simonsick, E., Metter, E. J., Ko, S., Ferrucci, L., and Studenski, S. (2016). Ankle proprioceptive acuity is associated with objective as well as self-report measures of balance, mobility and physical function. *Age (Dordr.)* 38:53. doi: 10.1007/s11357-016-9918-x

Eysel-Gosepath, K., McCrum, C., Epro, G., Brüggemann, G. P., and Karamanidis, K. (2016). Visual and proprioceptive contributions to postural control of upright stance in unilateral vestibulopathy. *Somatosens. Mot. Res.* 33, 72–78. doi: 10.1080/08990220.2016.1178635

Franz, J. R., Francis, C. A., Allen, M. S., O'Connor, S. M., and Thelen, D. G. (2015). Advanced age brings a greater reliance on visual feedback to maintain balance during walking. *Hum. Mov. Sci.* 40, 381–392. doi: 10.1016/j.humov.2015.01.012

Goble, D. J., Coxon, J. P., Van Impe, A., Geurts, M., Van Hecke, W., Sunaert, S., et al. (2012). The neural basis of central proprioceptive processing in older versus younger adults: an important sensory role for right putamen. *Hum. Brain Mapp.* 33, 895–908. doi: 10.1002/hbm.21257

Halliday, S. E., Winter, D. A., Frank, J. S., Patla, A. E., and Prince, F. (1998). The initiation of gait in young, elderly and Parkinson's disease subjects. *Gait Posture* 8, 8–14. doi: 10.1016/s0966-6362(98)00020-4

Henriksson, M., and Hirschfeld, H. (2005). Physically active older adults display alterations in gait initiation. *Gait Posture* 21, 289–296. doi: 10.1016/j.gaitpost.2004.03.001

Henry, M., and Baudry, S. (2019). Age-related changes in leg proprioception: implications for postural control. *J. Neurophysiol.* 122, 525–538. doi: 10.1152/jn.00067.2019

Hirjaková, Z., Neumannová, K., Kimijanová, J., Šuttová, K., Janura, M., and Hlavačka, F. (2017). Breathing changes accompanying balance improvement during biofeedback. *Neurosci. Lett.* 651, 30–35. doi: 10.1016/j.neulet.2017.04.051

Honeine, J. L., Schieppati, M., Crisafulli, O., and Do, M. C. (2016). The neuro-mechanical processes that underlie goal-directed medio-lateral APA during gait initiation. *Front. Hum. Neurosci.* 10:445. doi: 10.3389/fnhum.2016.00445

Jian, Y., Winter, D. A., Ishac, M. G., and Gilchrist, L. (1993). Trajectory of the body COG and COP during initiation and termination of gait. *Gait Posture* 1, 9–22. doi: 10.1016/0966-6362(93)90038-3

Jonsson, E., Henriksson, M., and Hirschfeld, H. (2007). Age-related differences in postural adjustments in connection with different tasks involving weight transfer while standing. *Gait Posture* 26, 508–515. doi: 10.1016/j.gaitpost.2006.11.206

Khanmohammadi, R., Talebian, S., Hadian, M. R., Olyaei, G., and Bagheri, H. (2015). Preparatory postural adjustments during gait initiation in healthy younger and older adults: neurophysiological and biomechanical aspects. *Brain Res.* 1629, 240–249. doi: 10.1016/j.brainres.2015.09.039

Laudani, L., Rum, L., Valle, M. S., Macaluso, A., Vannozzi, G., and Casabona, A. (2021). Age differences in anticipatory and executory mechanisms of gait initiation following unexpected balance perturbations. *Eur. J. Appl. Physiol.* 121, 465–478. doi: 10.1007/s00421-020-04531-1

Lepers, R., and Brenière, Y. (1995). The role of anticipatory postural adjustments and gravity in gait initiation. *Exp. Brain Res.* 107, 118–124. doi: 10.1007/BF00228023

Lu, C., Amundsen Huffmaster, S. L., Harvey, J. C., and MacKinnon, C. D. (2017). Anticipatory postural adjustment patterns during gait initiation across the adult lifespan. *Gait Posture* 57, 182–187. doi: 10.1016/j.gaitpost.2017.06.010

Mancini, M., Zampieri, C., Carlson-Kuhta, P., Chiari, L., and Horak, F. B. (2009). Anticipatory postural adjustments prior to step initiation are hypometric in untreated Parkinson's disease: an accelerometer-based approach. *Eur. J. Neurol.* 16, 1028–1034. doi: 10.1111/j.1468-1331.2009.02641.x

Martin, T. A., Keating, J. G., Goodkin, H. P., Bastian, A. J., and Thach, W. T. (1996). Throwing while looking through prisms. II. Specificity and storage of multiple gaze-throw calibrations. *Brain* 119, 1199–1211. doi: 10.1093/brain/119.4.1199

McIlroy, W. E., and Maki, B. E. (1999). The control of lateral stability during rapid stepping reactions evoked by antero-posterior perturbation: does anticipatory control play a role? *Gait Posture* 9, 190–198. doi: 10.1016/s0966-6362(99)00013-2

Mickelborough, J., van der Linden, M. L., Tallis, R. C., and Ennos, A. R. (2004). Muscle activity during gait initiation in normal elderly people. *Gait Posture* 19, 50–57. doi: 10.1016/s0966-6362(03)00016-x

Mille, M. L., Simoneau, M., and Rogers, M. W. (2014). Postural dependence of human locomotion during gait initiation. *J. Neurophysiol.* 112, 3095–3103. doi: 10.1152/jn.00436.2014

Mouchnino, L., and Blouin, J. (2013). When standing on a moving support, cutaneous inputs provide sufficient information to plan the anticipatory postural adjustments for gait initiation. *PLoS One* 8:e55081. doi: 10.1371/journal.pone.0055081

Nather, A., Neo, S. H., Chionh, S. B., Liew, S. C., Sim, E. Y., and Chew, J. L. (2008). Assessment of sensory neuropathy in diabetic patients without diabetic foot problems. *J. Diabetes Complications* 22, 126–131. doi: 10.1016/j.jdiacomp.2006.10.007

O'Malley, M. J. (1996). Normalization of temporal-distance parameters in pediatric gait. *J. Biomech.* 29, 619–625. doi: 10.1016/0021-9290(95)00088-7

Patchay, S., Gahéry, Y., and Serratrice, G. (2002). Early postural adjustments associated with gait initiation and age-related walking difficulties. *Mov. Disord.* 17, 317–326. doi: 10.1002/mds.10074

Penzer, F., Duchateau, J., and Baudry, S. (2015). "Contribution of visual and proprioceptive information in postural control differs with age," in *Book of Abstracts of the 20th Annual Congress of the European College of Sport Sciences*, eds A. Radmann, S. Hedenborg, and Tsolakidis (Malmö, Sweden), 24–27.

Plate, A., Klein, K., Pelykh, O., Singh, A., and Bötzel, K. (2016). Anticipatory postural adjustments are unaffected by age and are not absent in patients with the freezing of gait phenomenon. *Exp. Brain Res.* 234, 2609–2618. doi: 10.1007/s00221-016-4665-x

Polcyn, A. F., Lipsitz, L. A., Kerrigan, D. C., and Collins, J. J. (1998). Age-related changes in the initiation of gait: degradation of central mechanisms for momentum generation. *Arch. Phys. Med. Rehabil.* 79, 1582–1589. doi: 10.1016/s0003-9993(98)90425-7

Robinovitch, S. N., Feldman, F., Yang, Y., Schonnop, R., Leung, P. M., Sarraf, T., et al. (2013). Video capture of the circumstances of falls in elderly people residing in long-term care: an observational study. *Lancet* 381, 47–54. doi: 10.1016/S0140-6736(12)61263-X

Rocchi, L., Chiari, L., Mancini, M., Carlson-Kuhta, P., Gross, A., and Horak, F. B. (2006). Step initiation in Parkinson's disease: influence of initial stance conditions. *Neurosci. Lett.* 406, 128–132. doi: 10.1016/j.neulet.2006.07.027

Ruget, H., Blouin, J., Coyle, T., and Mouchnino, L. (2010). Modulation of proprioceptive inflow when initiating a step influences postural adjustments. *Exp. Brain Res.* 201, 297–305. doi: 10.1007/s00221-009-2035-7

Ruget, H., Blouin, J., Teasdale, N., and Mouchnino, L. (2008). Can prepared anticipatory postural adjustments be updated by proprioception? *Neuroscience* 155, 640–648. doi: 10.1016/j.neuroscience.2008.06.021

Shumway-Cook, A., and Woollacott, M. H. (2007). "Chapter 12: Control of normal mobility," in *Motor Control: Translating Research Into Clinical Practice*, 3rd edition (Philadelphia: Lippincott Williams & Wilkins), 300–329.

Sinclair, J., Taylor, P. J., and Hobbs, S. J. (2013). Digital filtering of three-dimensional lower extremity kinematics: an assessment. *J. Hum. Kinet.* 39, 25–36. doi: 10.2478/hukin-2013-0065

Tinetti, M. E., Doucette, J. T., and Claus, E. B. (1995). The contribution of predisposing and situational risk factors to serious fall injuries. *J. Am. Geriatr. Soc.* 43, 1207–1213. doi: 10.1111/j.1532-5415.1995.tb07395.x

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

frontiers in Human Neuroscience

ORIGINAL RESEARCH
published: 16 November 2021
doi: 10.3389/fnhum.2021.761262

Normative Data for the NeuroCom® Sensory Organization Test in Subjects Aged 80–89 Years

Laura Perucca[1,2†], Antonio Robecchi Majnardi[1†], Silvia Frau[2] and Stefano Scarano[1,2]*

[1] Department of Neurorehabilitation Sciences, IRCCS Istituto Auxologico Italiano, Milan, Italy, [2] Department of Biomedical Sciences for Health, University of Milan, Milan, Italy

Aging is known to increase the risk of falling. In older people, whose share in the total population is rising sharply, the Sensory Organization Test (SOT, Equitest NeuroCom) is a useful tool during rehabilitation and in clinical research for assessing postural stability, risk of falling, and balance improvement. Normative data for the SOT in the healthy population older than 79 years have not been previously published. We recruited 53 recreationally active healthy subjects aged 80 years and older from the general population in a cross-sectional study. We presented the normative data for SOT for the 80–84 and 85–89 years groups. Our results showed that the "vestibular" balance control tended to be affected by aging more than the vision and proprioception-based systems. A striking reduction in performance after the age of 85 years was observed. These findings will be useful for clinical and research purposes.

Keywords: normative data, balance, posturography, EquiTest®, Sensory Organization Test, aging

OPEN ACCESS

Edited by:
Martin Descarreaux, Université du Québec à Trois-Rivières, Canada

Reviewed by:
Martin Simoneau, Laval University, Canada
Olivier Hue, Université du Québec à Trois-Rivières, Canada

***Correspondence:**
Laura Perucca
l.perucca@auxologico.it

† These authors have contributed equally to this work and share first authorship

Specialty section:
This article was submitted to Motor Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *19 August 2021*
Accepted: *04 October 2021*
Published: *16 November 2021*

Citation:
Perucca L, Robecchi Majnardi A, Frau S and Scarano S (2021) Normative Data for the NeuroCom® Sensory Organization Test in Subjects Aged 80–89 Years. Front. Hum. Neurosci. 15:761262. doi: 10.3389/fnhum.2021.761262

INTRODUCTION

Humankind is experiencing constant lengthening in life and healthy years. In recent decades, the percentage of the older population has been rising sharply. According to data from the World Population Prospect (2019 Revision), the number of people aged 80 years or older tripled between 1990 and 2019, growing up to 143 million, and this number will triple by 2050, reaching 426 million (United Nations Department of Economic and Social Affairs [UNDESA], 2020). The World Health Organization defines an older person as one with a chronological age of 65 years or older (World Health Organization [WHO], 2013). Various subgroupings have been proposed by gerontologists to distinguish the diversity of older age (Forman et al., 1992; Zizza et al., 2009). The simplest criteria distinguish young old (60–69 years), middle old (70–79 years), and very old (80+ years) (Forman et al., 1992). This subdivision is further articulated by defining the oldest old (OO) as those aged 85+ years (Garfein and Herzog, 1995), thus implicitly limiting the very old (VO) to a 5-year wide group. However, these definitions are frequently updated as life expectancy continues to rise. The old population is the most susceptible to illness and disability (Christensen et al., 2009): the risk of falling increases with aging and is a major risk after 85 years old (Ferrer et al., 2012), becoming one of the main problems associated with aging (Rogers and Mille, 2003).

In physical and rehabilitation medicine, a large variety of clinical and instrumental tests are used to evaluate postural stability, that is, the ability to control the position of the center of mass in relation to a person's base of support, during either static or dynamic tasks. The computed dynamic posturographic EquiTest® System (NeuroCom® International, Inc., Clackamas, OR,

United States) (NeuroCom® International Inc., 2003) provides qualitative and quantitative analysis of balance control performance through the description of the center of gravity (COG) sway during standing (Nashner and Peters, 1990). Within the EquiTest® System, the Sensory Organization Test (SOT) creates sensory-conflict conditions, making the visual and/or the proprioceptive balance control systems unreliable. Scores are assigned to the oscillation of the subject (the higher, the greater the stability). In essence, the reliable system(s), including the vestibular one, are stressed in order to substitute the unreliable ones. Based on the SOT scores in the various conditions, "sensory analysis" (SA) scores are provided. SOT and SA norms are provided for age groups up to 79 years (20–59, 60–69, 70–79) (NeuroCom® International Inc., 2003). Those for subjects aged 80+ years are lacking.

From a quantitative point of view, normative data are crucial in the understanding of balance performance in healthy subjects (Guskiewicz et al., 1997; Ferber-Viart et al., 2007), in patients affected by vestibular (Pedalini et al., 2009; Alahmari et al., 2014) or other neurological disorders (Voorhees, 1990), and in the aging population as such (Anacker and Di Fabio, 1992; Buatois et al., 2007). Since healthy elderly people are known to show greater body sways during balance tasks with respect to younger individuals (Murray et al., 1975; Forth et al., 2007), a tool to assess whether these augmented oscillations have to be considered physiological or not is necessary, for both clinical and research purposes. The SOT has shown a decline in performance with increasing age in healthy adults (Forth et al., 2007). This study aimed to provide normative data for EquiTest SOT and SA for VO (aged 80–84 years) and OO subjects, with the latter group defined for this study in the 85–89 years range.

MATERIALS AND METHODS

Participants

Subjects aged 80+ years were recruited from a general healthy Italian population. To be included, subjects older than 79 years old and younger than 90 years old had to be able to walk without aid for at least 50 m, provide informed consent, and understand the instructions given during clinical and instrumental evaluations. We excluded individuals with diseases affecting the nervous system, both central and/or peripheral (e.g., Parkinson's disease, previous traumatic brain injury, pallesthesia $< 4/8$), previous hip or knee joint replacement or other major surgeries or pathologies affecting the lower limbs or the spine, and acute or chronic pain. Mild visual impairment and mild hearing loss that did not affect activities of daily living were not considered as exclusion criteria. We investigated medication intake to rule out interactions with balance. All participants underwent a standardized neurological examination and structured medical interviews.

The study enrolled 53 subjects fitting the inclusion/exclusion criteria for T0 evaluation. We performed the second evaluation (T1) 2 weeks after T0 to assess the stability and reproducibility of the measurements. Of the 53 subjects, 39 carried out both test sessions. 14 participants dropped out after performing T0 evaluation, for the following reasons: $n = 2$ nausea or dizziness occurred after T0, $n = 1$ gym exercises performed between T0 and T1, $n = 4$ onset of acute pathologies after T0, $n = 3$ reported the testing session as too tiring and refused to participate to the follow-up, and $n = 4$ unsuitable climatic conditions at T1 date (hot summer temperatures).

Motor and cognitive status of the sample was assessed using validated instruments for the main functional domains: Mini Mental State Examination adjusted for age and schooling for cognitive status (Folstein et al., 1975; Magni et al., 1996), Functional Independence Measure for the overall degree of motor and cognitive independence (Linacre et al., 1994), 10-m Walking Test for gait (Brandstater et al., 1983), Equiscale (Tesio et al., 1997), and Dizziness Handicap Inventory short form (Tesio et al., 1999) for balance.

All tests were conducted at the Department of Neurorehabilitation of the Istituto Auxologico Italiano Research Hospital (Milan, Italy). All subjects were informed of the testing procedures and signed a written consent form approved by the hospital's ethics committee, which also approved the study. This trial has been registered at ClinicalTrials.gov (Identifier: NCT04773496).

To assess postural stability, we used an EquiTest System equipped with the Data Acquisition Toolkit (software version 8.6.1). Data on patients' age and height (measured on a precision scale) were provided at the beginning of the test as required by the device software. The EquiTest uses a mobile visual surrounding and a support surface containing a dual-force plate, consisting of two 23 × 46 cm footplates connected by a pin joint that can rotate in the sagittal plane following the patient's anteroposterior sway, thus systematically altering the visual and somatosensory environments. We asked the subjects to stand upright on the instrument support without wearing footwear, with foot placement standardized relative to their height and with arms relaxed at their sides. They had to look straight forward and stand as still as possible during the trials. The SOT measures the sway of the COG under six different conditions (**Table 1**). The visual surround and the force plate, separately or together, may move in a sway-referenced manner, following the patient's own anteroposterior sway, thus delivering inaccurate information to the eyes, feet, and joints. Subjects wore a safety jacket hanging from the top of the instrument frame. Data were recorded during three trials for each condition. Each trial lasted 20 s. The sway gain setting was fixed at 1.00, making the support surface and/or visual surround matching the patient's sway exactly.

In the EquiTest System the amount of sway of the COG is expressed in degrees to allow comparison of scores between individuals of different heights. The angular limits of stability are nearly the same for all normal adults, regardless of height (NeuroCom® International Inc., 2003). The equilibrium score compares the patient's anteroposterior (AP) sway during each trial to a theoretical sway stability limit of 12.5 degrees (NeuroCom® International Inc., 2003). SOT Scores for each condition are given in the range of 0–100, with higher scores representing better performance and participants swaying to the limits of stability receiving low scores (NeuroCom® International Inc., 2003). Score 0 is assigned to a trial marked as "fall" (a

TABLE 1 | The six conditions of the Sensory Organization Test [Adapted from Instructions for Use: EQUITEST® SYSTEM OPERATOR'S MANUAL, Clackamas, OR (United States): NeuroCom® International Inc., 2003].

	Condition 1	Condition 2	Condition 3	Condition 4	Condition 5	Condition 6
Eyes	Open	Closed	Open	Open	Closed	Open
Surroundings	Fixed	n.a.	Sway-referenced	Fixed	n.a.	Sway-referenced
Platform	Fixed	Fixed	Fixed	Sway-referenced	Sway-referenced	Sway-referenced
Sensory System used	Somatosensory	Somatosensory	Somatosensory	Vision	Vestibular	Vestibular

n.a., not applicable.

stepping reaction, hands touching the surround or, in extreme cases, subject being supported by the safety jacket). Score 100 is assigned to full stability (never achievable in practice). A cumulative 0–100 SOT score (composite SOT) is also assigned to the overall test. Normative data are given as age-specific 95th percentile limits.

The SA scores (0–100, the higher the better the condition) were computed as ratio between the mean scores of specific conditions: SOM represents the ratio of the second to the first condition (if reduced it suggests a somatosensory impairment is present); VIS is the ratio of the fourth condition to the first (if reduced i.e., inability to use vision for compensatory purposes); VEST is the ratio of the fifth to the first condition (if reduced i.e., a possible vestibular deficit as in condition 5 balance is entrusted exclusively to the vestibular system). PREF highlights the visual preference (ratio of conditions with unreliable vision compared to those where vision is absent—i.e., conditions $(3 + 6)$ to $(2 + 5)$, when reduced it implies the subject relies on visual information even when those are unreliable (NeuroCom® International Inc., 2003).

The first evaluation (T0) (subject's history, functional scales, and instrumental evaluation) took approximately 90 min for each subject. To assess the reliability of the measurement, we repeated all six conditions of the SOT (T1) 2 weeks later (± 2 days). We asked the participants not to train or practice any kind of exercise between T0 and T1. Data collection was carried out by operators with experience in this assessment or trained for this purpose.

Statistical Analysis

We performed data analysis using STATA statistical software, version 11 (Computing Resource Center, Los Angeles, CA, United States, 2011). Descriptive statistics (mean ± SD, median) for each SOT condition and composite scores were generated. The SOT's score distributions for the entire sample and for the two different populations (VO and OO) were tested for normality (skewness and kurtosis test). Data are represented using bar charts and box plots. To allow comparison with the normative data of the previous 10-year age group, we set the level of significance at $p < 0.05$. We calculated the normative data as stated by NeuroCom, setting the limits of normality at the 5th percentile by applying the following equation: *SOT norms = mean - (SD * 1.67)* (NeuroCom® International Inc., 2003).

To assess the test-retest reliability, we used intraclass correlation coefficients (ICC 3.1, two-way random-effect model, absolute agreement) for the composite SOT and for each condition evaluated at T0 and T1. According to the literature (Koo and Li, 2016), reproducibility is labeled as poor when ICC < 0.5, moderate if between 0.5 and 0.75, good if between 0.75 and 0.9, excellent when > 0.90.

RESULTS

53 subjects participated in the study (25 women, 47%). The mean ± SD age of the entire sample was 83.4 ± 3 years (median: 82 years), with a range of 80–89 years. The mean and median ages did not differ substantially between men (83 ± 3.2 years, median: 81.5 years, range: 80–89 years) and women (83.88 ± 6 years, 84 years, 80–89 years). By applying the stated definition of VO (80–84 years) and OO (for this study 85–89 years), we divided the sample into two populations, as follows: VO, $n = 35$ (66%), and OO, $n = 18$ (34%). For both VO and OO, descriptive statistics for demographics and functional tests are provided in **Table 2**. The subjects were cognitively intact and had no balance, walking, or global functional impairments. T1 assessment was performed by 26 VO and 13 OO participants.

The SOT scores for the entire sample and for the two different groups (VO and OO) were not normally distributed, according to the skewness and kurtosis test. The bimodal distribution of the observed scores seemed to fit the study's originally proposed division between two different populations (VO and OO). The non-parametric Mann–Whitney test confirmed that the scores for each condition (except conditions 3 and 6) and composite SOT were statistically different between the two groups.

Descriptive data (median and interquartile range) for the six conditions and the composite SOT for the two groups are shown as box plots in **Figure 1**, while mean scores for each condition and for the composite SOT are presented in **Figure 2**. **Table 3** summarizes the descriptive statistics (mean ± SD and median), normative data, and variance analysis for SOT. Descriptive statistics (mean ± SD and median) and normative data for SA are presented in **Table 4**. Normative data for each condition and composite SOT are reported in **Figure 3**, while normative data for SA are in **Figure 4**. In **Tables 3**, **4** and **Figures 2**–**4** the data on the 70–79 years age group, as provided by NeuroCom in the User's manual, are reported in order to give the reader a quick comparison among the different age groups. The NeuroCom's sample was composed of 29 participants (14 women and 15 men). No further statistical analysis has been performed on the NeuroCom's sample data.

We tested the test-retest reliability of our sample and the ICC values provided good reproducibility of the Composite SOT

TABLE 2 | Descriptive data on very old (VO) and oldest old (OO) groups.

		VO (80–84 years old) (*n* = 35)	OO (85–89 years old) (*n* = 18)
	Score range (better score)	**Mean ± SD (Median)**	**Mean ± SD (Median)**
Age	n.a.	81.5 ± 1.4 (81)	87.1 ± 1.7 (87)
Male	n.a.	57.1% (*n* = 20)	44.4% (*n* = 8)
Number of medications	n.a.	2.5 ± 2.3 (2)	3.0 ± 2 (3)
MMSE(*)	0–30 (30)	28.6 ± 1.8 (29.1)	29.6 ± 2.4 (30.3)
FIM® —Comprehensive	18–126 (126)	125 ± 1.4 (126)	123.9 ± 2.4 (124)
FIM® —Motor	13–91 (91)	90.1 ± 1.4 (91)	89.6 ± 0.8 (90)
FIM® —Cognitive	5–35 (35)	35 ± 0.16 (35)	34.3 ± 2.4 (35)
Equiscale	0–16 (16)	15.3 ± 1 (16)	14.5 ± 1 (15)
DHI	0–13 (0)	0.6 ± 0.94 (0)	0.8 ± 0.8 (1)
Step length cm	Ability to perform the 10 mWT	64.9 ± 7.6 (65)	57.5 ± 6.9 (58)
Gait speed m/s		1.17 ± 0.2 (1.18)	1.1 ± 0.1 (1.1)

n.a., not applicable; MMSE, Mini Mental State Examination; FIM, Functional Independence Measure; DHI, Dizziness Handicap Inventory short form; 10 mWT, 10-m Walking Test.

(*) MMSE scores have been corrected for age and schooling. The number of medications taken by subjects ranged from 0 to 10 and were mostly in the three main categories of anti-hypertensives, proton-pump inhibitors, and those for benign prostate hypertrophy. Among the subjects, 17% (n = 9) did not take any medication, 17% (n = 9) took only one medication, and 34% (n = 18) took a maximum of two or three drugs per day. Only four subjects used more than six medications per day.

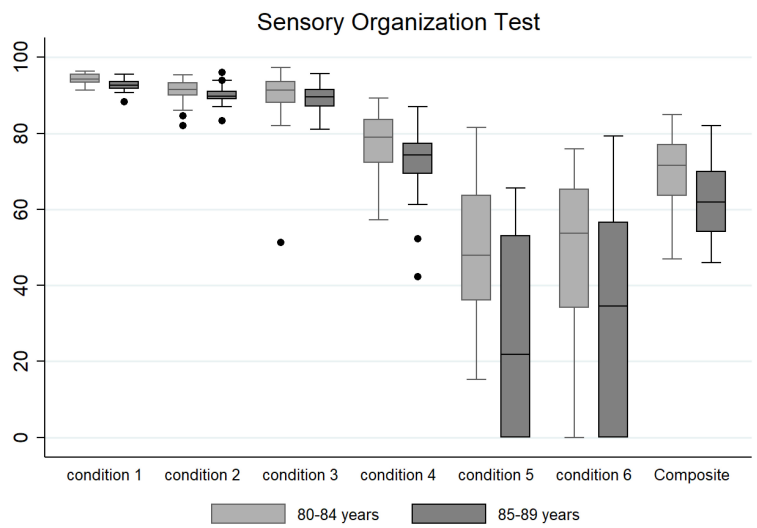

FIGURE 1 | Box plots (median and interquartile range; outliers are represented as dots) for the six testing conditions and for the composite Sensory Organization Test for the very old (80–84 years) and oldest old (85–89 years) groups.

and moderate to good reproducibility for each of the six SOT condition scores. ICC values are reported in **Table 5**.

DISCUSSION

The study of SOT in the healthy population has recently developed (Guskiewicz et al., 1997; Ferber-Viart et al., 2007; Pierchała et al., 2012; Pletcher et al., 2017), but not yet in the population aged 80–89 years. As suggested by the increased incidence of falls in the elderly, one or more of the systems involved in postural control lose efficiency with age (Peterka and Black, 1990). Our results showed that balance control in VO and OO is less effective when vestibular information is the only one available, in particular above 84 years of age. This finding is consistent with previous clinical observations (Ferrer et al., 2012). The older adults of the third millennium are the healthiest, most active, and longest-living in human history and are now a demographic phenomenon in most countries (United Nations Department of Economic and Social Affairs [UNDESA], 2020). The literature deals comprehensively with the concept of healthy aging and the interaction between physiological age-related deficits and actual neurological pathology (Morris and McManus, 1991; Kaye et al., 1994; Nardone et al., 2000; Papegaaij et al., 2014). Aging involves the degeneration of various central nervous system (CNS) and peripheral nervous system (PNS) structures, with a loss in brain volume and weight around 5% per decade after age 40 and possible more above age 70

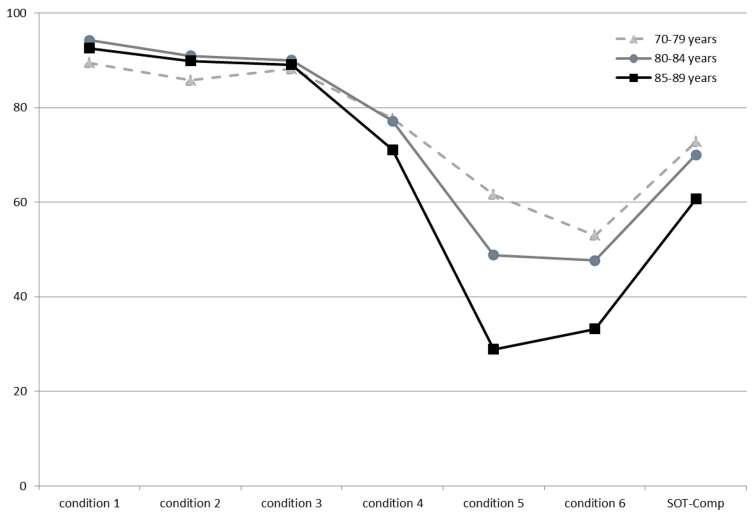

FIGURE 2 | Mean values for the three age groups in the six conditions and for the composite Sensory Organization Test data. The lowest values in condition 5 describe an age-related worsening of vestibular function. Data for the 70–79 age group are provided by NeuroCom® International Inc. (2003).

TABLE 3 | Descriptive, variance analysis, and normative data for each condition and composite SOT for three age groups: 70–79 years (data provided by NeuroCom® International Inc., 2003), very old (VO, 80–84 years), and oldest old (OO, 85–89 years).

Age group	70–79 years	VO 80–84 years	OO 85–89 years	VO vs. OO	70–79 years	VO	OO
	Mean ± SD	Mean ± SD (Median)	Mean ± SD (Median)	Variance analysis	SOT normative data		
Condition 1	89.4 ± 11.4	94.3 ± 1.3 (94.3)	92.6 ± 1.7 (92.6)	$p < 0.000$	70	92	90
Condition 2	85.8 ± 13.5	91.1 ± 3 (91.6)	89.9 ± 2.7 (89.8)	$p < 0.048$	63	86	85
Condition 3	88.2 ± 3.8	90 ± 7.6 (91.3)	89.1 ± 3.4 (89.6)	$p < 0.098$	82	77	83
Condition 4	77.6 ± 5.5	77.2 ± 8.3 (79.0)	71.2 ± 10.4 (74.3)	$p < 0.018$	69	63	54
Condition 5	61.6 ± 10.2	48.8 ± 17.5 (48.0)	28.9 ± 24.6 (21.8)	$p < 0.005$	45	20	0
Condition 6	53.0 ± 15.5	47.7 ± 20.5 (53.6)	33.2 ± 27.3 (34.6)	$p < 0.064$	27	13	0
Composite SOT	72.8 ± 5.4	69.9 ± 8.4 (73.0)	60.7 ± 10.3 (58.5)	$p < 0.003$	64	56	43

SOT, Sensory Organization Test.

(Peters, 2006), and physiological changes in postural control and balance (Kaye et al., 1994; Camicioli et al., 1997; Nardone et al., 2000), related to sensory deficits (Judge et al., 1995), CNS integration abnormalities (Morris and McManus, 1991), and musculoskeletal aging (Judge et al., 1996). From this point of view, a reduction in neurological performance can be defined as a sequela of neuroanatomical and neurofunctional changes (Morris and McManus, 1991; Papegaaij et al., 2014). The risk of falling increases in older adults, and balance impairment is one of the main targets of rehabilitation treatment (Chang et al., 2004).

As expected, mean values decreased in both VO and OO groups from Condition 1 (i.e., all sensory information available) to Condition 5 (i.e., visual information absent and proprioception not reliable). In the variance analysis, we observed that the scores for all conditions and for the composite SOT were statistically different between the VO and OO, with the exception of condition 6 and, broadly, of condition 3. A similar observation for condition 3 has already been provided in a previous study (Pletcher et al., 2017). In that paper statistical differences were seen between military groups with different tactical demands in all SOT conditions with the exception of condition 3; the authors hypothesized that the similar distribution of the SOT scores for condition 3 and somatosensory scores among groups might reflect the disadvantage to the visual system due to the sway-referenced surround. In our sample this result may suggest that aging can affect the use of proprioceptive information less than vestibular information with respect to balance control. However, this aspect requires further investigation.

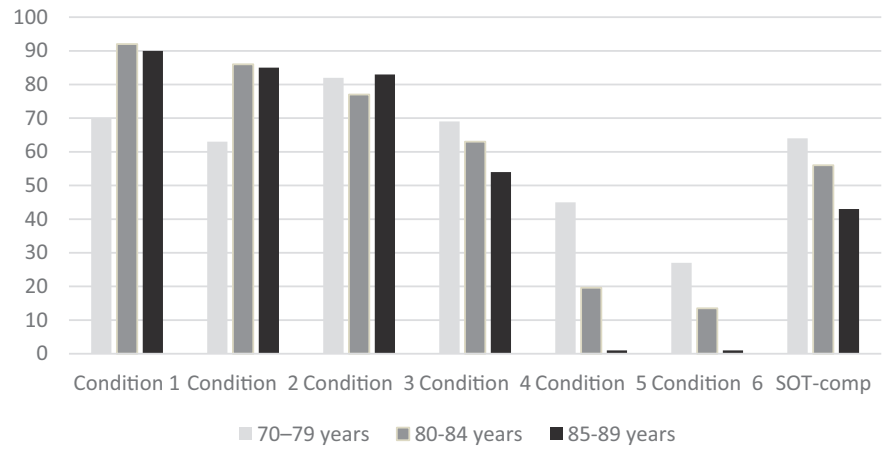

FIGURE 3 | Normative data for the six conditions and for the composite Sensory Organization Test data in the three age groups considered in this study. The striking reduction in norm values in conditions 5 and 6 is due to the wide standard deviation in those conditions. Data for the 70–79 age group are provided by NeuroCom® International Inc. (2003).

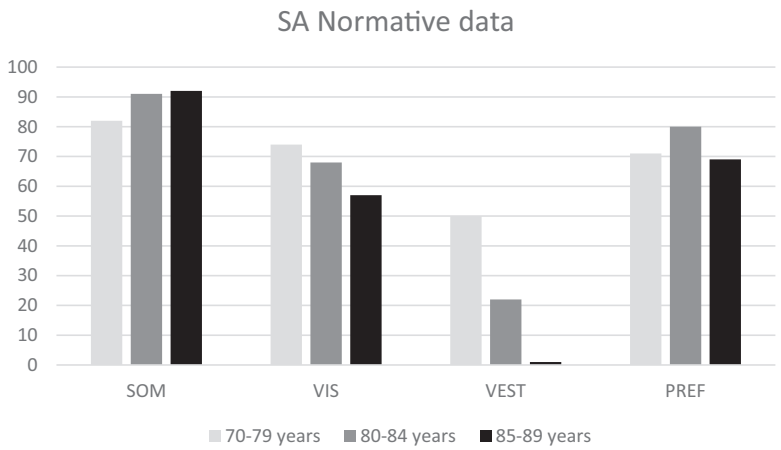

FIGURE 4 | Normative data for sensory analysis (SA) for the three age groups considered in this study. Data for the 70–79 age group are provided by NeuroCom® International Inc. (2003).

The normative data for conditions 1 and 2 are similar between VO and OO. In the OO group the norms for conditions 5 and 6 are equal to zero, and this evidence may imply that vestibular information are not sufficient for OO for maintaining balance control, and that a low vestibular score at the SOT could be considered as "normal" (whereas it would still be considered as pathological in the VO population).

Moreover, the comparison of normative data for the six SOT conditions, composite SOT and SA for VO and OO with those of the previous decade (**Tables 3**, **4**) suggests some thoughts:

- The normative data for conditions 1 and 2 for the two groups in our sample were higher than those stated by NeuroCom for the 70–79 years age group. The reason for this discrepancy could have various origins. First, the sample adopted by NeuroCom for the 70–79 age group was smaller (n = 29, 14 female) than ours. Although declared asymptomatic, their sample was not previously evaluated for functional performance and medication intake. Second, aging for our subjects occurred 20 years later than the NeuroCom original study, so that health care conditions might have improved. Third, subjects who survived for a long time without health concerns could have had a functional advantage during aging. Fourth, the mediterranean environmental context might have fostered a healthier aging.
- The greatest differences with the NeuroCom 70–79 years group can be found for Conditions 5 and 6 norms: both VO and OO display lower values than the 70–79 group. This evidence may suggest that a reduction in the efficiency of

TABLE 4 | Sensory analysis (SA) descriptive (mean ± SD, median) and normative data for three age groups: 70–79 years (data provided by NeuroCom® International Inc., 2003), very old (VO, 80–84 years), and oldest old (OO, 85–89 years).

	70–79 years	VO		OO		SA normative data		
	Mean ± SD	Mean ± SD	Median	Mean ± SD	Median	70–79 years	VO	OO
SOM	95.1 ± 7.9	96.5 ± 3	97	97.1 ± 3.1	97	82	91	92
VIS	85 ± 0.066	81.8 ± 8	82	76.9 ± 11.7	80	74	68	57
VEST	67.3 ± 10.4	51.8 ± 18	52	31.4 ± 27	23	50	22	0
PREF	94.9 ± 14.4	98.5 ± 11	100	105.1 ± 21.8	101	71	80	69

SOM, somatosensory; VIS, visual; VEST, vestibular; PREF, visual preference.

TABLE 5 | Interclass correlation coefficients (ICC) for each condition and for composite SOT in the whole sample between T0 and T1.

	ICC
Condition 1	0.52
Condition 2	0.79
Condition 3	0.55
Condition 4	0.73
Condition 5	0.71
Condition 6	0.67
composite SOT	0.76

SOT, Sensory Organization Test.

the vestibular system can be involved in the increasing rate of falling in the elderly.

The reliability of the measures of SOT scores and of the composite SOT were found to be moderate to good. The reliability of SOT scores for Conditions 1–6 were comparable to those reported in previously published papers for individuals aged 20–80 + (19) and above 65 years of age (Ford-Smith et al., 1995). As already pointed out by Forth et al. (2007), there is a considerable variability in the ICCs of the different SOT conditions, ranging from 0.52 to 0.79 in our sample.

The normative data provided by this work may lead clinicians and researchers in defining the degree of balance impairment in individuals aged 80–89 years old. Moreover, the identification of the impaired sensory systems can guide the development of rehabilitation programs tailored on the patient and the measurement of rehabilitation outcomes. This information, together with other validated tool, will help in assessing the risk of falls in elderly people.

CONCLUSION

This study provided normative data for SOT and SA assessed by the EquiTest® System in healthy older subjects. Poor postural stability is a risk factor for falls and subsequent injury. To our knowledge, this study is the first to present SOT and SA norms for subjects aged 80+ years. Moreover, we investigated subjects in the oldest old category (85–89 years). Data from our research can assist both clinicians and researchers who deal with balance in older subjects.

LIMITS OF THE STUDY

The recorded data for the sample were not normally distributed. The variance analysis revealed how the vestibular performance decreased suddenly over a 5-year horizon (80–84 years vs. 85–89 years) and suggested an opportunity for studies with an older and wider span of older healthy subjects. However, it is not easy to find a large number of healthy subjects aged 85 + years. More studies focused on subjects aged 85 + or 90 + years will be possible and easier in the future, considering the global phenomenon of aging.

DATA AVAILABILITY STATEMENT

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found below: doi: 10.5281/zenodo.5215848.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Comitato Etico—Istituto Auxologico Italiano IRCCS. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

LP designed the study. LP and SF collected the data. LP, AR, and SS analyzed and interpreted the data. AR wrote the manuscript. LP and SS reviewed the manuscript. All authors contributed to the article and approved the submitted version.

FUNDING

This trial has been funded by the Italian Ministry of Health.

ACKNOWLEDGMENTS

We thank Anna Simone for the statistical support. We would like to thank Editage (www.editage.com) for English language editing.

REFERENCES

Alahmari, K. A., Marchetti, G. F., Sparto, P. J., Furman, J. M., and Whitney, S. L. (2014). Estimating postural control with the balance rehabilitation unit: measurement consistency, accuracy, validity, and comparison with dynamic posturography. *Arch. Phys. Med. Rehabil.* 95, 65–73.

Anacker, S. L., and Di Fabio, R. P. (1992). Influence of sensory inputs on standing balance in community-dwelling elders with a recent history of falling. *Phys. Ther.* 72, 574–575. doi: 10.1093/ptj/72.8.575

Brandstater, M. E., de Bruin, H., Gowland, C., and Clark, B. M. (1983). Hemiplegic gait: analysis of temporal variables. *Arch. Phys. Med. Rehabil.* 64, 583–587.

Buatois, S., Gauchard, G. C., Aubry, C., Benetos, A., and Perrin, P. (2007). Current physical activity improves balance control during sensory conflicting conditions in older adults. *Int. J. Sports Med.* 28, 53–58. doi: 10.1055/s-2006-924054

Camicioli, R., Panzer, V. P., and Kaye, J. (1997). Balance in the healthy elderly: posturography and clinical assessment. *Arch. Neurol.* 54, 976–981. doi: 10.1001/archneur.1997.00550200040008

Chang, J. T., Morton, S. C., Rubenstein, L. Z., Mojica, W. A., Maglione, M., and Suttorp, M. J. (2004). Interventions for the prevention of falls in older adults: systematic review and meta-analysis of randomised clinical trials. *BMJ* 328:680. doi: 10.1136/bmj.328.7441.680

Christensen, K., Doblhammer, G., Rau, R., and Vaupel, J. W. (2009). Ageing populations: the challenges ahead. *Lancet* 374, 1196–1208. doi: 10.1016/S0140-6736(09)61460-4

Ferber-Viart, C., Ionescu, E., Morlet, T., Froehlich, P., and Dubreuil, C. (2007). Balance in healthy individuals assessed with Equitest: maturation and normative data for children and young adults. *Int. J. Pediatr. Otorhinolaryngol.* 71, 1041–1046. doi: 10.1016/j.ijporl.2007.03.012

Ferrer, A., Formiga, F., Plana-Ripoll, O., Tobella, M. A., Gil, A., and Pujol, R. (2012). Risk of falls in 85-year-olds is associated with functional and cognitive status: the Octabaix Study. *Arch. Gerontol. Geriatr.* 54, 352–356. doi: 10.1016/j.archger.2011.06.004

Folstein, M. F., Folstein, S. E., and Mchugh, P. R. (1975). "Mini-Mental State". A practical method for grading the cognitive state of patients for the clinician. *J. Psychiat. Res.* 12, 189–198. doi: 10.1016/0022-3956(75)90026-6

Ford-Smith, C. D., Wyman, J. F., Elswick, R. K., Fernandez, T., and Newton, R. A. (1995). Test-retest reliability of the sensory organization test in noninstitutionalized older adults. *Arch. Phys. Med. Rehabil.* 76, 77–81. doi: 10.1016/S0003-9993(95)80047-6

Forman, D. E., Berman, A. D., McCabe, C. H., Baim, D. S., and Wei, J. Y. (1992). PTCA in the elderly: the "young-old" versus the "old-old". *J. Am. Geriatr. Soc.* 40, 19–22. doi: 10.1111/j.1532-5415.1992.tb01823.x

Forth, K. E., Metter, E. J., and Paloski, W. H. (2007). Age associated differences in postural equilibrium control: A comparison between EQscore and minimum time to contact (TTCmin). *Gait Posture* 25, 56–62. doi: 10.1016/j.gaitpost.2005.12.008

Garfein, A. J., and Herzog, A. R. (1995). Robust aging among the young-old, old-old, and oldest-old. *J. Gerontol. B Psychol. Sci. Soc. Sci.* 50, S77–S87. doi: 10.1093/geronb/50b.2.s77

Guskiewicz, K. M., Riemann, B. L., Perrin, D. H., and Nashner, L. M. (1997). Alternative approaches to the assessment of mild head injury in athletes. *Med. Sci. Sports Exerc.* 29, S213–S221. doi: 10.1097/00005768-199707001-00003

Judge, J. O., King, M. B., Whipple, R., Clive, J., and Wolfson, L. I. (1995). Dynamic balance in older persons: effects of reduced visual and proprioceptive input. *J. Gerontol. A Biol. Sci. Med. Sci.* 50, M263–M270. doi: 10.1093/gerona/50a.5.m263

Judge, J., Ounpuu, S., and Davis, R. I. (1996). Effects of age on the biomechanics and physiology of gait.pdf. *Clin. Geratr. Med.* 12, 659–678.

Kaye, J. A., Oken, B. S., Howieson, D. B., Howieson, J., Holm, L. A., and Dennison, K. (1994). Neurologic Evaluation of the Optimally Healthy Oldest Old. *Arch. Neurol.* 51, 1205–1211. doi: 10.1001/archneur.1994.00540240049015

Koo, T. K., and Li, M. Y. A. (2016). Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *J. Chiropr. Med.* 15, 155–163. doi: 10.1016/j.jcm.2016.02.012

Linacre, J. M., Heinemann, A. W., Wright, B. D., Granger, C. V., and Hamilton, B. B. (1994). The structure and stability of the Functional Independence Measure. *Arch. Phys. Med. Rehabil.* 75, 127–132.

Magni, E., Binetti, G., Bianchetti, A., Rozzini, R., and Trabucchi, M. (1996). Mini-Mental State Examination: a normative study in Italian elderly population. *Eur. J. Neurol.* 3, 198–202. doi: 10.1111/j.1468-1331.1996.tb00423.x

Morris, J. C., and McManus, D. Q. (1991). The neurology of aging: normal versus pathologic change. *Geriatrics* 46, 51–54.

Murray, M. P., Seireg, A. A., and Sepic, S. B. (1975). Normal postural stability and steadiness: quantitative assessment. *J. Bone Jt. Surg. Ser. A* 57, 510–516. doi: 10.2106/00004623-197557040-00012

Nardone, A., Galante, M., Corna, S., Grasso, M., Tarantola, J., and Schieppati, M. (2000). "The effects of aging on static and dynamic equilibrium" in *The Ageing Motor System and its Adaptations to Training*. eds P. Capodaglio and M. Narici (Pavia: PI-ME Press). 101–108.

Nashner, L. M., and Peters, J. F. (1990). Dynamic posturography in the diagnosis and management of dizziness and balance disorders. *Neurol. Clin.* 8, 331–349. doi: 10.1016/s0733-8619(18)30359-1

NeuroCom® International Inc. (2003). *Instructions for Use: EQUITEST® SYSTEM OPERATOR'S MANUAL. Version 8*. Clackamas: NeuroCom® International Inc.

Papegaaij, S., Taube, W., Baudry, S., Otten, E., and Hortobágyi, T. (2014). Aging causes a reorganization of cortical and spinal control of posture. *Front. Aging Neurosci.* 6:28. doi: 10.3389/fnagi.2014.00028

Pedalini, M. E. B., Cruz, O. L. M., Bittar, R. S. M., Lorenzi, M. C., and Grasel, S. S. (2009). Sensory organization test in elderly patients with and without vestibular dysfunction. *Acta Otolaryngol.* 129, 962–965. doi: 10.1080/00016480802468930

Peterka, R. J., and Black, F. O. (1990). Age-related changes in human posture control: Sensory organization tests. *J. Vestib. Res.* 1, 73–85. doi: 10.3233/ves-1990-1108

Peters, R. (2006). Ageing and the brain. *Postgrad. Med. J.* 82, 84–88. doi: 10.1136/pgmj.2005.036665

Pierchała, K., Lachowska, M., Morawski, K., and Niemczyk, K. (2012). [Sensory Organization Test outcomes in young, older and elderly healthy individuals–preliminary results]. *Otolaryngol. Pol.* 66, 274–9.

Pletcher, E. R., Williams, V. J., Abt, J. P., Morgan, P. M., Parr, J. J., Wohleber, M. F., et al. (2017). Normative Data for the NeuroCom Sensory Organization Test in US Military Special Operations Forces. *J. Athl. Train.* 52, 129–136. doi: 10.4085/1062-6050-52.1.05

Rogers, M. W., and Mille, M.-L. (2003). Lateral stability and falls in older people. *Exerc. Sport Sci. Rev.* 31, 182–187. doi: 10.1097/00003677-200310000-00005

Tesio, L., Alpini, D., Cesarani, A., and Perucca, L. (1999). Short form of the Dizziness Handicap Inventory: construction and validation through Rasch analysis. *Am. J. Phys. Med. Rehabil.* 78, 233–241.

Tesio, L., Perucca, L., Franchignoni, F. P., and Battaglia, M. A. (1997). A short measure of balance in multiple sclerosis: validation through Rasch analysis. *Funct. Neurol.* 12, 255–265.

United Nations Department of Economic and Social Affairs [UNDESA] (2020). *World Population Ageing 2019 (ST/ESA/SER.A/444)*. United States: United Nations Department of Economic and Social Affairs.

Voorhees, R. L. (1990). Dynamic posturography findings in central nervous system disorders. *Otolaryngol. Head Neck Surg.* 103, 96–101. doi: 10.1177/019459989010300114

World Health Organization [WHO] (2013). *Definition of an Older or Elderly Person. Proposed Working Definition of an Older Person in Africa for the MDS Project*. Switzerland: World Health Organization.

Zizza, C. A., Ellison, K. J., and Wernette, C. M. (2009). Total water intakes of community-living middle-old and oldest-old adults. *J. Gerontol. A Biol. Sci. Med. Sci.* 64, 481–486. doi: 10.1093/gerona/gln045

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Neurology

ORIGINAL RESEARCH
published: 22 November 2021
doi: 10.3389/fneur.2021.756984

Specific Posture-Stabilising Effects of Vision and Touch Are Revealed by Distinct Changes of Body Oscillation Frequencies

Stefania Sozzi[1], *Antonio Nardone*[2] *and Marco Schieppati*[3]*

[1] Centro Studi Attività Motorie (CSAM), Istituti Clinici Scientifici Maugeri SB (Istituto di Ricovero e Cura a Carattere Scientifico, IRCCS), Pavia, Italy, [2] Neurorehabilitation and Spinal Unit, Department of Clinical-Surgical, Diagnostic and Pediatric Sciences, Istituti Clinici Scientifici Maugeri SB (Istituto di Ricovero e Cura a Carattere Scientifico, IRCCS), University of Pavia, Pavia, Italy, [3] Istituti Clinici Scientifici Maugeri SB, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS), Pavia, Italy

We addressed postural instability during stance with eyes closed (EC) on a compliant surface in healthy young people. Spectral analysis of the centre of foot pressure oscillations was used to identify the effects of haptic information (light-touch, EC-LT), or vision (eyes open, EO), or both (EO-LT). Spectral median frequency was strongly reduced by EO and EO-LT, while spectral amplitude was reduced by all "stabilising" sensory conditions. Reduction in spectrum level by EO mainly appeared in the high-frequency range. Reduction by LT was much larger than that induced by the vision in the low-frequency range, less so in the high-frequency range. Touch and vision together produced a fall in spectral amplitude across all windows, more so in anteroposterior (AP) direction. Lowermost frequencies contributed poorly to geometric measures (sway path and area) for all sensory conditions. The same subjects participated in control experiments on a solid base of support. Median frequency and amplitude of the spectrum and geometric measures were largely smaller when standing on solid than on foam base but poorly affected by the sensory conditions. Frequency analysis but not geometric measures allowed to disclose unique tuning of the postural control mode by haptic and visual information. During standing on foam, the vision did not reduce low-frequency oscillations, while touch diminished the entire spectrum, except for the medium-high frequencies, as if sway reduction by touch would rely on rapid balance corrections. The combination of frequency analysis with sensory conditions is a promising approach to explore altered postural mechanisms and prospective interventions in subjects with central or peripheral nervous system disorders.

Keywords: stance, critical conditions, body oscillation, spectral analysis, centre of foot pressure, length and area of sway path, vision, haptic

OPEN ACCESS

Edited by:
Eric Yiou,
Université Paris-Saclay, France

Reviewed by:
Alain Hamaoui,
Université Paris-Sud, France
Jana Kimijanová,
Slovak Academy of Sciences (SAS), Slovakia

***Correspondence:**
Marco Schieppati
marco.schieppati@icsmaugeri.it

Specialty section:
This article was submitted to Neurorehabilitation, a section of the journal Frontiers in Neurology

Received: *11 August 2021*
Accepted: *25 October 2021*
Published: *22 November 2021*

Citation:
Sozzi S, Nardone A and Schieppati M (2021) Specific Posture-Stabilising Effects of Vision and Touch Are Revealed by Distinct Changes of Body Oscillation Frequencies. Front. Neurol. 12:756984. doi: 10.3389/fneur.2021.756984

INTRODUCTION

The sensory control of bipedal human stance has been a matter of investigation for many years (1–3). A plethora of studies has been published on this topic, including some from our group (4, 5). Body sway when standing upright on a solid base of support is normally almost negligible in healthy subjects, witnessing accurate and precise neural control (6, 7) based on the internal

model of gravitational and inertial forces (8) and on multiple inputs from the receptors detecting the body state. The excursions of the centre of foot pressure (CoP) of subjects standing quietly on the firm ground are approximately contained within the size of a dime, even if there is a large variability in sway across different healthy subjects (9). In several conditions, though, sway area can significantly increase, such as standing on sloped surfaces or when leaning forward or backward (4, 10), or decrease when subjects stand on elevated platforms (11). Standing on viscoelastic, compliant support like a foam pad produces larger sway and obvious body unsteadiness (12–14). This can in some cases lead to falls (15, 16), especially when vision is not available (17) or when sensory deficits are present (18–20).

Vision is important for body stabilisation during standing (21, 22). Sway may increase without vision compared to eyes open during quiet stance on a firm platform (23) with the effects depending on the distance between the feet (22, 24–26). Vision is also able to gate the effects of vibration (activating the primary receptors of the muscle spindles) of the neck muscles, consisting of a large forward sway when the eyes are closed (27). Vision also moderates the postural effects of the Achilles tendon vibration (28) and plays a more important role in postural stability under challenging conditions compared to quiet stances, such as on a mobile platform or on a foam surface (13, 29–31). When vision is available, subjects reduce reliance on proprioception and increase reliance on visual information (25).

Proprioception is crucial in the control of body stability and orientation in space (32–35), and various manoeuvres have been put in place to clarify its role, including muscle vibration as a tool for activating the spindles (36) or leg ischemia by compression to attenuate the transmission of their firing (37, 38). However, the contribution of the spindles to standing posture may not have been completely elucidated, not to speak of the role of the information from the foot sole and from the intrinsic foot muscles (39–41). These inputs under a quiet stance on the firm ground would play a limited function because the information originating in the primary spindle terminations, which are mainly sensitive to the velocity of muscle stretch (42), may not be crucial in the absence of rapid changes in muscle length. Under a quiet stance, the small-diameter fibres originating in the secondary spindle terminations may play a predominant role (43). Further, reweighting of the proprioceptive information normally occurs, as attested by the reduction in the amplitude of the soleus muscle H-reflex during unperturbed stance (44). Moreover, the reflex excitability of the motor neurons of the leg muscles is decreased when the stance is stabilised by holding onto a solid frame (45, 46) or by lightly touching fixed support (47). The role of proprioception can be more important when the balance is challenged (48) without vision. Under perturbed conditions or with a major reduction of the support surface (49, 50), when the postural muscle activity plays a major stabilising role, the role of proprioception is amplified and that of vision becomes of minor importance (51, 52). Moreover, velocity information would be crucial to stabilise posture during standing on foam support, where the task difficulty is increased and balance is controlled by many muscles acting at several joints (49, 53–57).

Haptic information is effective in reducing postural sway. The effect of a light fingertip touch is comparable to that obtained by opening the eyes (58–63). It can selectively originate from touch receptors (64) and occurs with contact forces below those necessary to mechanically stabilise the body (65–67). Touch-induced stabilisation occurs both when standing on firm ground and when standing on foam (68, 69) or after a balance perturbation (70, 71). With eyes closed, a light touch of an object next to the body, or a touch of the ground by the cane (66, 72), modifies the control of posture, because finger or cane can be appropriately moved to get the information they are searching for (73). The integration of visual and haptic cues in the control of stance has received much less attention than for the identification of object features (74, 75), but the same operating principles might underpin the effects of either or both inflows. For that matter, reaching and grasping (76) are in fact coordinated with postural adjustments (46, 77).

It is easy to measure sway. The force platform upon which subjects stand captures the path of the wandering centre of foot pressure in a given time period, and its length can be measured along with the surface covered by its journey. The geometric and statistical measures of sway (length of sway path and ellipses containing 95% of the acquired points) show a reasonable reproducibility (78) but bear large inter subject variability (79). Further, although sway path and sway area often co-vary, the correspondence between the former and the latter measure may not be consistent across subjects or patients (27, 80), because the same length of the oscillation skein may not occupy the same surface all the time (81). These measures can also overlap between eyes-open and eyes-closed conditions or between young and elderly (82, 83). In turn, the stabilising effect of vision is indistinguishable from that of touch (62). A different analytical approach might more consistently disclose unique attributes of the visual and haptic stabilising effects (21, 84).

When vision and touch are available, sway can further decrease compared to either information alone (63, 74). On the other hand, removal of peripheral sensation, as by anaesthesia or cooling of the skin of the foot sole, increases body oscillations (40). It might be supposed that integration of multiple inputs, as from the eye, the skin, the proprioceptors, or the graviceptors, can afford excellent body stabilisation (reduction of CoP sway) in accordance with the assumption that "more is better." This view would implicitly assume the existence of one posture-controlling centre able to integrate the sensory inputs and produce the adequate motor commands, which are evidently optimally designed when the centre receives the best possible amount of information. Body oscillations during quiet stance should then diminish monotonically as a function of the number and competence of the sensory inputs.

The assumption of the present study is that potential differences in the effect of vision or touch on stance control cannot be clearly evinced from the geometric analysis of the standard sway variables such as sway path length or area. Sway metrics more closely connected to the muscle synergies and to the presumably responsible supra-spinal and spinal control modes, expressed by the rambling and trembling behaviour (85, 86), would be more telling. Other methods, like indexing postural

dynamics, have been exploited with attention to the multiple time scales of control that subserve standing postures (87, 88), such as the stabilogram-diffusion analysis (89, 90), the wavelet-based spectral analysis (91–93), and the sample entropy (94, 95), which provides measures advising automaticity of postural behaviour.

The purpose of this study has been to increase our knowledge on the role of the sensory control of stance by leveraging the tool of spectral frequency analysis (96–99) rather than through the sole use of geometric sway measures, such as the amplitude of sway area and length of sway path (23). Since oscillations frequencies have a strong relationship to leg and foot muscle activity (100), we hypothesised that the frequencies prevalent under certain conditions may offer a straightforward way of identifying whether the control of stance selects distinct balancing modes under a given sensory condition.

Different laboratories have identified a few frequency windows within the frequency spectrum and have connected these windows to the contribution of vestibular or visual or somatosensory information (99, 101–105). Occasionally, criteria for choosing the width of the frequency windows (106) have been provided. Further, the opinion that proprioception would be disrupted when standing on foam is at variance with the plain consideration that proprioception may be modest and downweighed in a quiet stance (see above), while a massive proprioceptive input must reach the central nervous system during the complex adjustments (often unconsciously produced) carried out when standing on foam (107).

Hence, we addressed the sensory modulation (visual, haptic) of postural behaviour in healthy young people through the use of spectral analysis of the CoP displacement. We have hypothesised that vision and touch stabilise body sway through at least partially different modes of action detectable by the spectral analysis. We first critically examined the use of this tool since there is a wide divergence in the way frequency spectra and frequency windows are defined by different laboratories. We then considered the distribution of the frequency spectrum oscillations when stabilisation was achieved through the use of haptic information (light touch, EC-LT) or vision (EO) or both (EO-LT). In addition, we compared the data obtained by the frequency analysis to those based on geometric sway measures. Finally, we compared the results obtained on the foam to those obtained on a solid base of support (BoS). Consistent modulations of the median frequency of the spectrum and of specific frequency windows thereof emerged, suggesting different neural mechanisms of sway-minimisation strategy for vision and haptic sense.

MATERIALS AND METHODS

Participants

Nineteen healthy young adults (9 men and 10 women) participated in the study. Their average age was 29 ± 4.2 years (mean ± SD), height 172.6 ± 7.2 cm, and weight 68.9 ± 13.5 kg. All subjects were free of neurological and musculoskeletal disorders and either had no sight problems or if so, had their visual acuity corrected during the procedure. All gave written informed consent to participate in the experiments that were performed in accordance with the Declaration of Helsinki and approved by the institutional Ethics Committee (Istituti Clinici Scientifici Maugeri, approval number #2564CE).

Procedures

Subjects stood barefoot for at least 100 s on a force platform (Kistler 9286BA, Switzerland). The outer profiles of the parallel feet were set at hip width. The head was facing forward. Balance was measured under two Base of Support (BoS) conditions, solid and foam, two visual conditions, eyes open (EO) and eyes closed (EC), and two touch conditions, no-touch and light-touch (LT), resulting in eight experimental conditions. The foot position was marked on a paper sheet placed on top of the platform or of the foam pad (Airex-Balance Pad 50 cm L × 41 cm W × 6 cm H) for consistency across trials.

Subjects were asked to stand at ease (108), not to stare at a fixed point (109) but to look at the visual scene of the laboratory wall at 6 m distance, featuring the horizontal and vertical profiles of a bookcase. They were asked to avoid the head pitch, roll, and yaw movements, and if possible, ample gaze deviations. In the EC condition, subjects were asked to close their eyes before the start of the acquisition epoch and to keep their eyes closed throughout the trial. In the LT condition, the index finger of the dominant hand was kept on the surface of a haptic device made by a flat horizontal wooden square (10 × 10 cm) fixed on top of a strain gauge (**Figure 1**). The instruction was to maintain a constant "light touch" on this smooth plane. The output of the strain gauge was recorded by a device that beeped when the vertical force passed the threshold of 1 N. The haptic device was located in front of the subject at about the height of the belly button and distant about 15 cm from it in the sagittal plane. There was no instruction to keep the finger immobile on the force pad and hence, small fluctuations in the hand and finger position were allowed. The finger never slipped off the force pad. The device seldom beeped, mostly in the time period before the acquisition.

The data presented here originate from an investigation that required each volunteer to come to the laboratory eight times on separate days. Each day, the subject completed eight equal-duration (100 s) consecutive standing trials in one of the conditions of interest (EC, EO, EC-LT, and EO-LT). In the following analysis, only the first of the eight trials for each sensory condition has been considered and analysed because an adaptation process proved to take place in the successive trials (manuscript in preparation).

Data Acquisition and Processing

The last 90s epoch of each 100s stance trial was acquired in order to avoid the accustoming phase occurring immediately after mounting on the platform (with/without foam). This duration of the trials had been selected in order to be the longest possible to avoid exhaustion while at the same time allowing a good resolution of the oscillation frequencies. Critical parameters to obtain a reliable power spectrum were the duration of the acquired epoch (that defines the lowest detectable frequency) and the sampling rate (that defines the highest detectable frequency) (110–112).

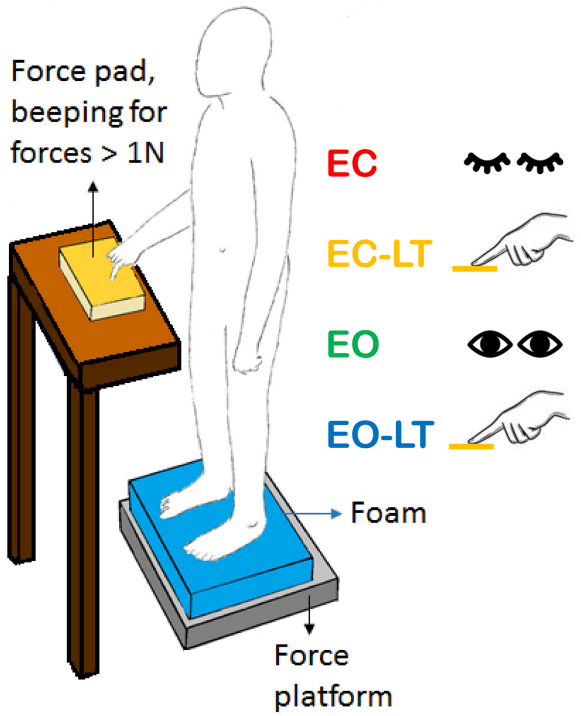

FIGURE 1 | Sketch of the test situation showing a standing subject in front of the force pad (yellow) during the light-touch (LT) trials. The force pad device beeped when the force exceeded 1 N. Subjects rarely reached this force level during the trials. In the sketch, the foam is shown (blue). In the absence of touch, both arms were along the trunk. The same position(s) were assumed with the eyes closed (EC) or open (EO).

All platform data and the data from the haptic device were captured at the sampling frequency of 140 Hz by a PC on which the dedicated software was running (Smart-D, BTS, Italy). All data were moved to another PC for *post-hoc* analysis, and calculations were done using the Excel software and customised LabVIEW programs (National Instrument, USA). The force platform signals of the CoP displacements along both the anteroposterior (AP) and mediolateral (ML) directions were high-pass filtered at 0.01 Hz with a 4th order Butterworth philtre after removing the respective mean values. The length of the sway path was the total length of the wandering CoP during the 90 s epoch, calculated using a software compiled on LabVIEW, and sway area was the surface of the 95% ellipse fitted to the dispersion of the time-series of the AP data plotted against those of the ML recorded in the same epoch (113).

The frequency analysis was performed by applying the fast Fourier transform to the ML and AP CoP time-series data of each trial, subject, sensory, and BoS conditions. This was done by means of the Auto power spectrum VI algorithms of the LabVIEW functions. The frequency resolution, i.e., the sampling frequency (140 Hz) divided by the number of samples acquired by the platform (12,600 samples), was 0.011 Hz. The power spectrum signal was expressed as cm^2_{rms} since the root mean square (rms) of a signal is defined by $u_{rms} = \sqrt{\frac{1}{T}\int_0^T u(t)^2 * t}$. For example, in the case of a sinusoidal waveform like u (t) = A sin ($2\pi/T^*t$), where A is the peak amplitude, T = 1/f, and f is the waveform frequency, the rms of this waveform is $u_{rms} = A/\sqrt{2} = 0.707^*A$. In the case of a sinusoidal peak to peak displacement of 10 cm amplitude, the amplitude of the power spectrum signal would be about 18 cm^2_{rms}.

An example of this analysis is shown in **Figure 2**. The analysis has been applied to the data of a pilot test made under dynamic EO foam condition consisting of continuous deliberate mediolateral oscillations around 0.5 Hz (left panels) performed by one experimenter following the rhythm of a metronome for a 90 s period. The amplitude of the rhythmic ML displacement was set by the distance between the feet. The computed oscillation frequency in the ML direction (**Figure 2A**, red) has a peak around 0.5 Hz, and the amplitude of this peak is about 21 $cm^2_{rms.}$ In the AP direction (green), the oscillations are smaller and less regular than in the ML direction with a peak frequency of about 1 Hz (**Figure 2G**). In the right panels of the Figure, the results of the same analysis are reported and applied to a performance during which the same subject was asked to deliberately shake like a raving lunatic on the foam for 90 s (**Figures 2C,D**). In this case, the spectral analysis shows oscillations at frequencies >2 Hz, and the amplitude of the spectrum is negligible above 5 Hz (**Figures 2F,H**).

In the analysis of our experimental trials performed under quiet stance, the frequency range of interest was not predefined. However, we decided to limit the analysis to the part of the frequency spectrum below 2 Hz owing to the negligible amplitude of the power spectrum from 2 Hz onwards. In the EC foam condition, the area under the profile (calculated as the sum of the amplitude of the values of every sample) of the spectrum from 0.01 to 2 Hz corresponded to the 98.8 and 99.0% of the area of the entire spectrum from 0.01 to 70 Hz, for ML and AP, respectively (114).

The amplitude of the body sway (area of the 95% confidence ellipse fitted to the CoP path in the horizontal plane) was hardly affected by oscillation frequencies beyond 2 Hz. **Figure 3** shows that the ellipse fitted onto the CoP of the ML and AP traces plotted after high-pass filtering at 2 Hz (**Figure 3B**) contains a very small percentage (0.7%) of the original unfiltered signal (**Figure 3A**). The CoP path length diminishes to a much smaller extent (52%).

Median frequency and mean level of the spectrum were calculated for each sensory and BoS condition between 0.01 and 2 Hz for the AP and the ML CoP displacements. Median frequency (at which the power spectrum is divided into two parts of equal area) was calculated by means of Matlab software. Then, specific frequency windows (Ws) were identified for further analysis of the effects of the manipulation of conditions on the power spectrum. The Ws identification was made based on the "default" condition (the EC foam trial), which featured the maximum overall amplitude of the entire power spectrum profile compared to all other conditions tested. Then, the boundaries of the Ws were selected based on the profile of the mean power spectrum obtained by averaging the profiles of the EC foam trial of all the subjects (**Figure 4**). In detail, the Ws have been operationally identified by the superimposition of the mean EC

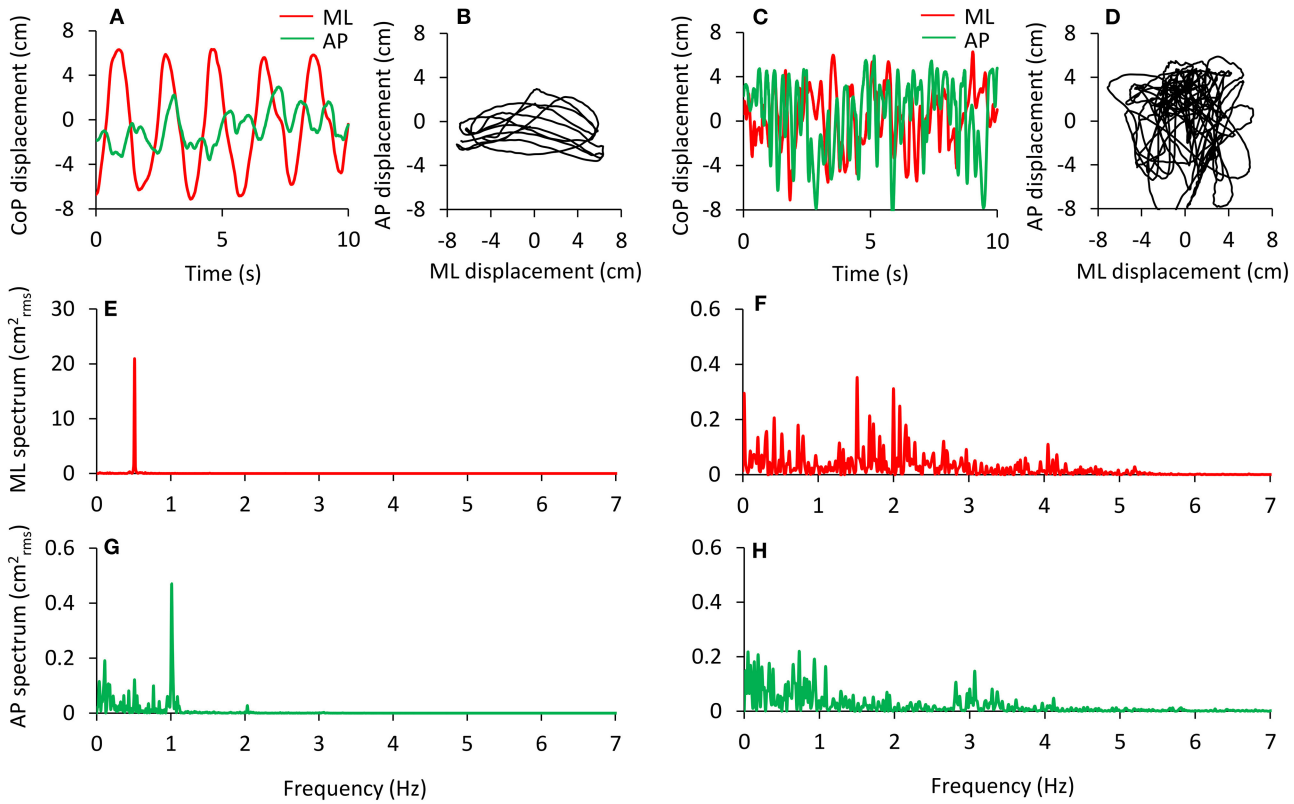

FIGURE 2 | Examples of deliberate sway of the body are performed in order to test the recording and analysis procedures. Voluntary, wide, and rhythmic predominantly mediolateral oscillations were performed in response to 0.5 Hz beeps of a metronome **(A,B)**. The relevant power spectrum profiles in the frontal (ML, with a large peak at 0.5 Hz) and sagittal (AP) planes are reported in **(E,G)**. Note the difference in the ordinates of **(E,G)**. The same subject deliberately performed large body movements at the highest frequency possible **(C,D)**. The relevant power spectrum profiles are shown in **(F,H)**. Now the oscillation frequencies have a wider range and smaller peak amplitudes. Under both circumstances, the deliberate oscillations were performed with the eyes open and lasted 90 s. In **(A–D)**, only 10 s are depicted for easily identifying the CoP oscillations. The traces are dispersed around zero because their mean value has been removed. The power spectra are computed over the 90 s trial.

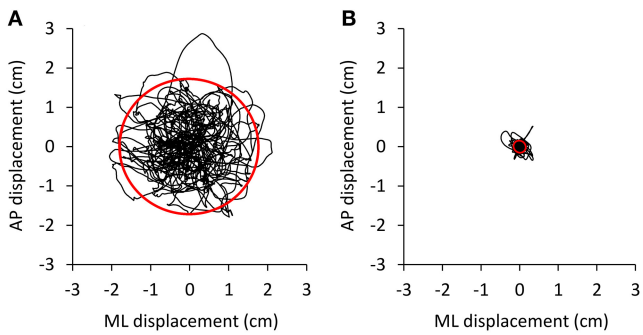

FIGURE 3 | Effect of high-pass filtering. Body oscillations during a 90 s trial were performed with EC on the foam base of support by a representative subject. The oscillations normally ranged about 3–4 cm in both mediolateral (ML) and anteroposterior (AP) directions **(A)**. **(B)** The shrink of the oscillation pattern of the same trial as in A when the AP and ML time series were computed on the 2 Hz high-pass filtered signals.

power spectra separately for the frontal (ML) and the sagittal (AP) planes. The local *minima* were identified in successive epochs of 0.05 Hz of the traces. The same procedure was repeated for the local *minima* of the profile of the SD trace of the mean power spectrum as a companion criterion. It turned out that the local *minima* in the successive epochs of the mean power spectrum trace and of its SD trace almost coincided in most cases. These points would correspond to oscillation frequencies poorly represented in our population. They were arbitrarily considered critical discriminating points for the identification of the boundaries of the Ws. Further, in order to simplify the interpretation, some of the *minima* were disregarded and a few adjacent Ws merged. Hence, the analysis was restricted to six windows only.

Moreover, based on the visual comparison of the profiles of the mean power spectra obtained for the ML and AP directions of CoP oscillations and of their SD, which were similar and almost superimposable across the entire frequency range, we decided to utilise the same Ws identified for the ML direction for the AP direction. This procedure allowed to identify the following frequency Ws, which were equal for both the ML and the AP directions: W1 (the lowest frequency), from 0.01 to 0.055 Hz; W2, 0.055 to 0.2 Hz; W3, 0.2 to 0.44 Hz; W4, 0.44 to 0.8 Hz; W5, 0.8 to

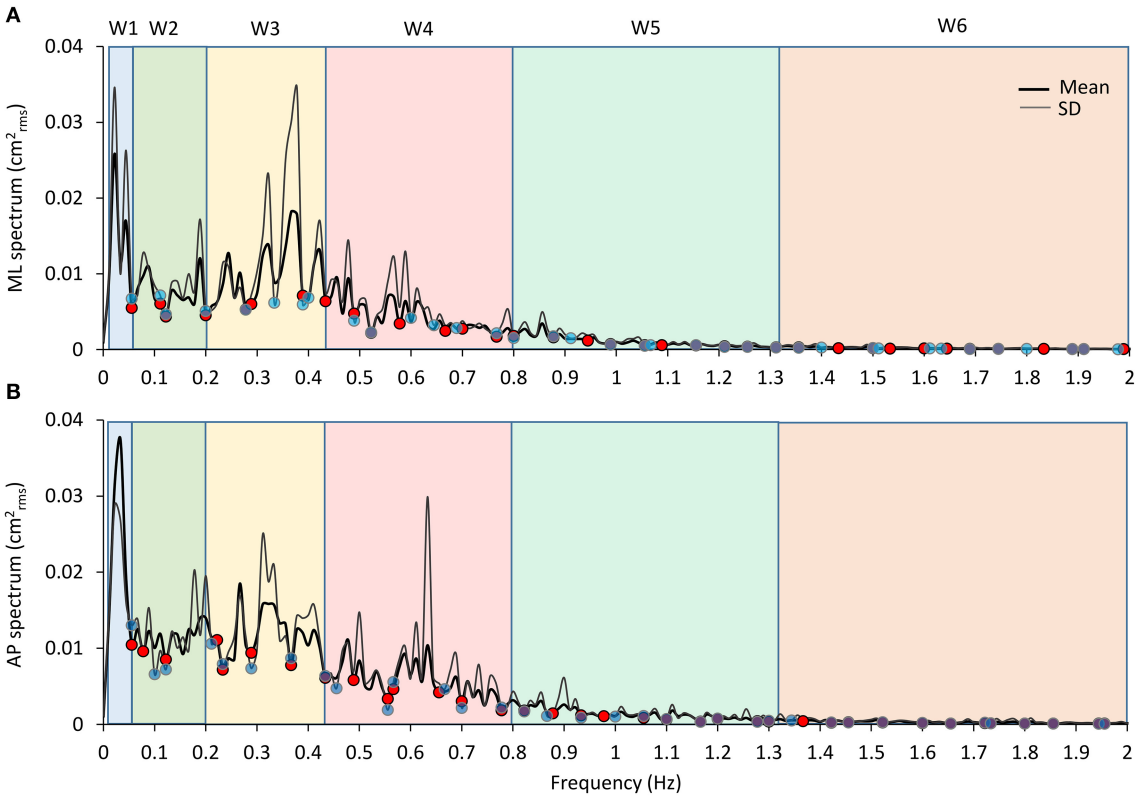

FIGURE 4 | Frequency windows identification. The graphs show the mean profile of the power spectrum (average of the profiles obtained in all the subjects, the thick black line) in the ML and AP directions [**(A,B)**, respectively]. The thin dark grey lines are the corresponding profiles of the SD of the means. A similar pattern for the ML and AP spectra is obvious. The superimposed SD traces largely reproduce the up and downs of the mean spectra and show minimum values close to the relative minimum values of the mean spectra. The blue and red dots correspond to the local minima of the mean and SD traces, respectively, computed in the consecutive 0.05 Hz windows. The pale-coloured rectangles indicate the frequency windows used in the analysis.

1.31 Hz; and W6, 1.31 to 2 Hz. For each W, the mean level of the spectrum was calculated and compared across the sensory and BoS conditions.

Data Treatment and Statistics

The mean power spectra profiles (mean + SD) obtained for the CoP oscillations were point-by-point compared by Student's *t*-test according to a procedure used in this laboratory (115). The oscillation frequencies at which the Student's *t*-test value bypassed the probability of 0.05 (two-tailed pairwise test) were taken as the frequencies at which ML and AP oscillations became different. This procedure was used to compare the ML and AP power spectra in the EC condition and the spectra under both EC-LT and EO conditions on foam in order to investigate the differences in the contribution to the stabilisation process of touch and vision.

The data pertaining to the mean profile of the AP power spectrum were plotted against those of the mean profile of the ML power spectrum for the EC foam condition. This relationship was studied by a linear regression model and the coefficient of determination (R^2) was calculated. Also, the relationships between the mean level of the ML and AP spectrum in each frequency window and the CoP path length and sway area were studied by a linear regression model and the R^2 was calculated.

Assumptions for parametric statistics were met for all variables of interest as assessed by the Kolmogorov-Smirnov and Levene's test. The following analyses were performed separately for the two BoS conditions (solid and foam). A 2 (ML and AP directions) × 4 (vision and touch conditions) repeated measure (rm) ANOVA was used to compare the median frequency and the mean level of the spectrum between 0.01 and 2 Hz. A 2 (ML and AP directions) × 4 (vision and touch conditions) × 6 (frequency windows) rm ANOVA was used to compare the mean level of the spectrum calculated in each frequency window. In order to highlight the difference between sensory conditions in each window, a 2 (ML and AP directions) × 4 (vision and touch conditions) rm ANOVA was applied to the mean level, separately for each window. The effects of the different sensory conditions on path length and sway area of the CoP were compared by a 1-way rm ANOVA. A two-tailed paired *t*-test was used to compare the force exerted by the subjects on the touch pad between EC-LT and EO-LT conditions.

The main effects of BoS (foam and solid) on the median frequency and on the mean level of the spectrum between 0.01 Hz

and 2 Hz were compared by a 2 (BoS) × 2 (ML and AP directions) ×4 (vision and touch conditions) rm ANOVA. A 2 (BoS) × 4 (vision and touch conditions) rm ANOVA was used to test the effect of the two BoS on CoP path length and sway area. A 2 (BoS) × 2 (EC-LT and EO-LT conditions) rm ANOVA was used to compare the effect of the base of support on the force exerted by the subjects on the touch pad. The *post-hoc* was the Fisher's LSD test. The significance level was set at 0.05. The value of η_p^2 was reported as well. Where the differences were significant, the Cohen's d effect sizes highlighted the strength of the difference. Statistical tests were performed using Statistica (Statsoft, USA).

RESULTS

The findings are itemised for the sake of clarity. The CoP data collected in the foam condition are presented first, followed by those recorded in the solid BoS condition. Within each branch of the investigation, the power spectrum data in the different experimental conditions are presented first, followed by the geometric data of path length and sway area and by the comparisons of frequency and geometric data. In both cases, the data regarding the ML precede those of the AP oscillations. The comparisons between foam and solid BoS conditions are reported at the end of the section.

Foam Base of Support

Power Spectrum

ML and AP Oscillations (EC) Have Similar Profiles

The analysed range of the power spectrum reached from 0.01 to 2 Hz. The area under the curve of this range corresponded to more than 98% of that of the entire spectrum (along both the ML and the AP directions). In particular, no frequency peak however small was obvious in the profile of the power spectrum beyond 2 Hz.

Figure 5 shows the mean power spectra superimposed for the ML and AP oscillations (**Figure 5A**) in the EC condition and the result of applying the *t*-test to each of the frequency values (**Figure 5C**). The profiles were similar. However, differences between the two spectra were detected by the Student's *t*-test between 0.1 and 0.3 Hz and in scattered positions for higher frequencies. In inset **Figure 5B**, the data pertaining to the mean profile of the AP power spectrum were plotted against those of the mean ML power spectrum for the EC condition. Each sampled frequency point is considered ($n = 180$ data points corresponding to the frequency units). Clearly, there is a good regression line, indicating that when the value of the power spectrum profile at a certain sampled frequency was low in ML, the corresponding AP value was also low and vice versa.

Sensory Conditions

The mean profiles of the power spectra in the four tested conditions (EC, EC-LT, EO, EO-LT) when standing on foam are shown in **Figures 6A,B**. For each condition and each subject, the median frequency and the mean level of the spectrum was calculated (**Figures 6C–F**). All conditions included, the median frequency was not different between ML and AP [$F_{(1, 18)} = 0.86$, $p = 0.36$]. However, there was a significant difference in the median frequency between sensory conditions [$F_{(3, 54)} = 64.5$, $p < 0.001$, $d = 3.76$, $\eta_p^2 = 0.78$] and a significant interaction between ML and AP directions and sensory conditions [$F_{(3, 54)} = 3.16$, $p = 0.03$, $d = 0.84$, $\eta_p^2 = 0.15$]. For both ML and AP, the median frequency was higher with EC (EC and EC-LT) than with EO (EO and EO-LT) (*post-hoc*, $p < 0.05$ for all comparisons). In the ML direction, there was no difference in the median frequency between EC and EC-LT ($p = 0.76$) and between EO and EO-LT ($p = 0.73$). In the AP direction, instead, the median frequency was higher with EC-LT than with EC ($p < 0.001$), but there was no significant difference between EO and EO-LT ($p = 0.14$). All conditions included, there was a significant difference in the mean level of the spectrum between ML and AP directions [$F_{(1, 18)} = 5.53$, $p = 0.03$, $d = 1.1$, $\eta_p^2 = 0.23$], a significant difference between sensory conditions [$F_{(3, 54)} = 88.35$, $p < 0.001$, $d = 4.43$, $\eta_p^2 = 0.83$] and a significant interaction between ML and AP directions and sensory conditions [$F_{(3, 54)} = 27.11$, $p < 0.001$, $d = 2.45$, $\eta_p^2 = 0.6$]. In the ML direction, the mean level of the spectrum under EC condition was the highest (*post-hoc*, $p < 0.001$ for all comparisons) and became the smallest

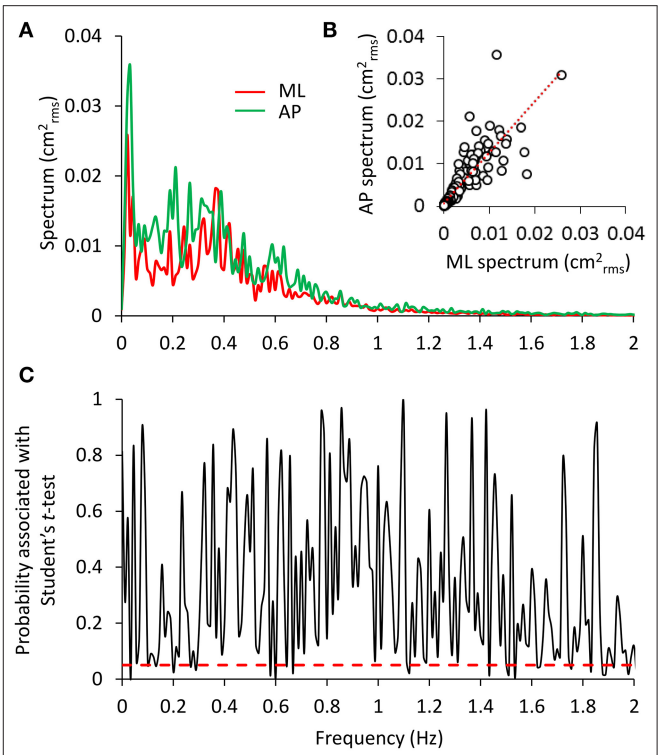

FIGURE 5 | Comparison between the ML and AP spectra. In **(A)**, the superimposed power spectra in the ML and AP directions (EC) appear similar, except for a slightly higher amplitude of the AP (green) compared to the ML spectrum (red). The regression line fitted to the data points of AP vs. ML **(B)** has a slope slightly higher than 1 and the intercept close to origin of the axes ($y = 1.15 \times + 0.0008$, $R^2 = 0.72$, $p < 0.001$). The plot in **(C)** shows the probability values associated with the *t*-test of the point-to-point differences between the two spectra. The red dashed line indicates the significance of the differences at $p < 0.05$. Consistent but limited differences between the two spectra were observed at low frequencies.

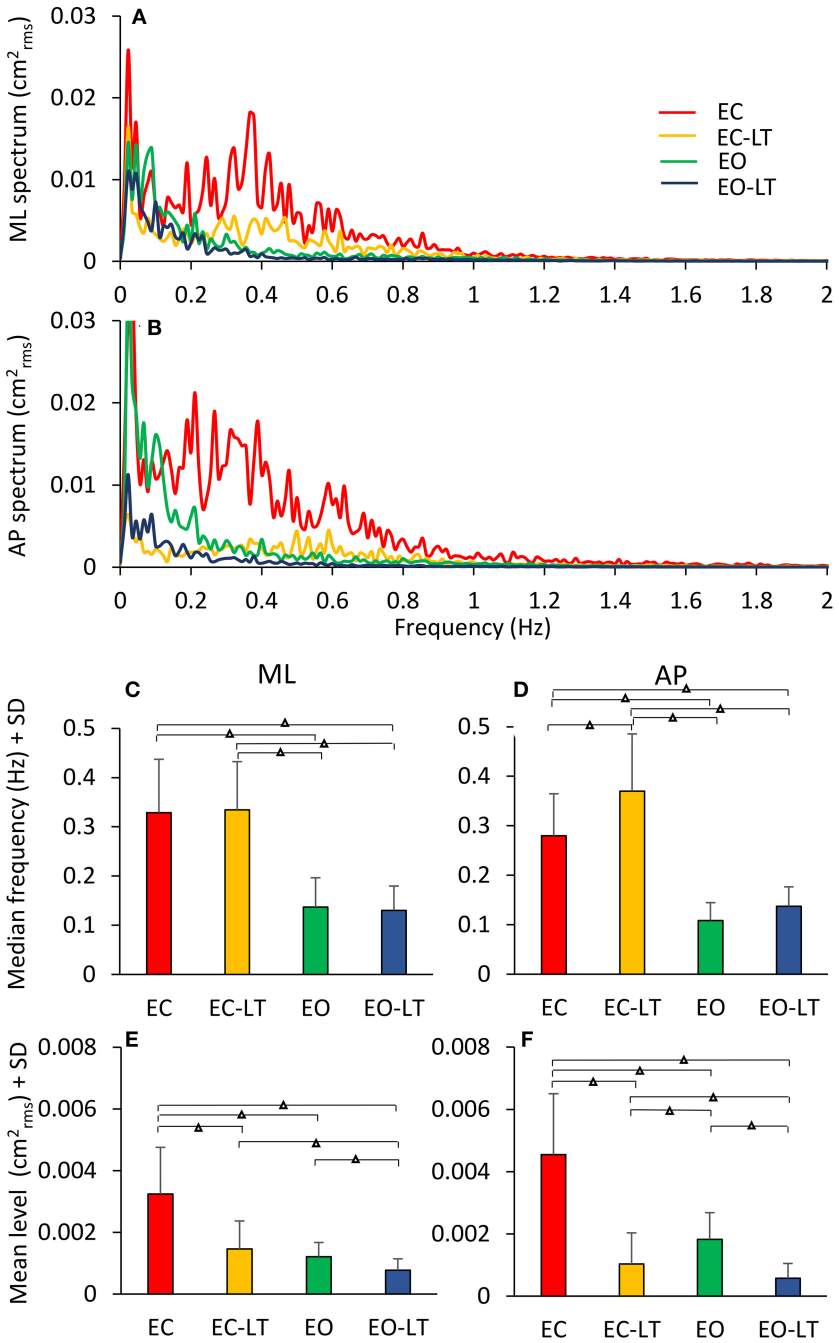

FIGURE 6 | Power spectra under different sensory conditions. This contrasts the spectra during the trials performed on foam without vision (EC, red), with vision (EO, green), and with the addition of touch (EC-LT, yellow; EO-LT, blue). Obviously, the level of the spectrum for all the "stabilised" conditions is smaller than with EC **(A,B)**. The median frequency of the spectrum **(C,D)** is definitely smaller with vision (EO and EO-LT) than without vision (EC and EC-LT), both in the frontal and sagittal plane. Conversely, the mean level **(E,F)** is small in the three "stabilised" conditions. In this case, the reduction in the mean level also applies to EC-LT. Triangles indicate significant differences ($^{\Delta}p < 0.001$).

in the EO-LT condition ($p < 0.01$ for all comparisons). In the EC-LT condition, the mean level was not different to the mean level under EO ($p = 0.1$). Also, in the AP direction, the mean level of the spectrum under EC condition was the highest (*post-hoc*, $p < 0.001$ for all comparisons) and became the smallest in the EO-LT condition ($p < 0.01$ for all comparisons). Moreover, in the EC-LT condition, the mean level of the AP spectrum was smaller than in the EO condition ($p < 0.001$).

In **Figure 7**, the median frequency of the spectrum is plotted against its mean level for ML and AP directions in the four sensory conditions for each subject. A large variability across subjects is obvious in the plots. However, it is clear that the red and yellow circles (no vision, EC and EC-LT, respectively), have high median-frequency values, while the green and blue circles (vision, EO and EO-LT, respectively) mostly include low frequencies values. Conversely, touch (EC-LT and EO-LT, the clusters of the yellow and blue symbols, respectively), produced the largest reduction in the mean level, regardless of the visual condition. This consideration applies to both ML and AP directions. In the plots, the large circles correspond to the mean values of the clusters. As expected, the conditions EO and EO-LT feature small values for both variables. The median frequencies with touch were just larger (even not significantly so for the ML direction) than under the corresponding EC and EO conditions (without touch) for both the ML and the AP directions.

Distinct Effects Are Elicited by the Sensory Conditions in the Different Frequency Windows

Figure 8 shows the mean level of the spectrum calculated for the ML (**Figure 8A**) and AP directions (**Figure 8B**) across all the subjects in each of the identified frequency windows. In the bottom panels (**Figures 8C,D**), the percent changes with respect to the EC condition are reported for the 'stabilised' conditions. There was a difference between the mean level of the spectra of the ML and AP directions, all conditions included [$F_{(1, 18)} = 13.1$, $p < 0.01$, $d = 1.7$, $\eta_p^2 = 0.42$], a difference between sensory conditions [$F_{(3, 54)} = 96.6$, $p < 0.001$, $d = 4.62$, $\eta_p^2 = 0.84$] and between frequency windows [$F_{(5, 90)} = 115.6$, $p < 0.001$, $d = 5.06$, $\eta_p^2 = 0.86$]. There was a significant interaction between ML and AP directions and sensory conditions [$F_{(3, 54)} = 22.2$, $p < 0.001$, $d = 2.23$, $\eta_p^2 = 0.55$], ML and AP directions and frequency windows [$F_{(5, 90)} = 3.4$, $p < 0.01$, $d = 0.87$, $\eta_p^2 = 0.16$], between sensory conditions and frequency windows [$F_{(15, 270)} = 15.4$, $p < 0.001$, $d = 1.83$, $\eta_p^2 = 0.45$], and between ML and AP directions, sensory conditions and frequency windows [$F_{(15, 270)} = 5.26$, $p < 0.001$, $d = 1.08$, $\eta_p^2 = 0.23$].

Figures 8C,D give an easy view of the similarities and differences in the mean levels of the distinct frequency windows in the three "stabilised" conditions. In W1 and W2, vision (EO, green) had a small effect in ML and AP compared to EC. For all remaining frequency windows, vision reduced the mean level to a large extent in AP and ML. Touch without vision (EC-LT, yellow) moderately reduced the mean level in all frequency windows in ML, more so in AP. Touch and vision (EO-LT, blue) reduced the mean level of the entire spectrum in ML, particularly for the W3–W6, more so in AP.

ML Direction. In detail, in W1, the mean levels in the EC and EO conditions were not much different (*post-hoc*, $p = 0.09$). The mean level with EC was >2 conditions with touch (EC-LT and EO-LT, $p < 0.05$ for both comparisons). When touch was added (EC-LT condition), the mean level of the spectrum was not different from the mean level of the EO and of the EO-LT conditions ($p > 0.4$ for both comparisons). When touch was added to vision (EO-LT), there was no difference compared to the EO condition ($p = 0.67$). In W2, touch diminished the mean level of the spectrum with respect to the corresponding visual condition without touch (*post-hoc*, EC-LT vs. EC: $p < 0.001$; EO-LT vs. EO: $p < 0.05$). Touch under the EC condition diminished the mean level with respect to EO ($p < 0.01$). EC and EO were not different ($p = 0.6$). In W3, EC had the largest spectrum than the other sensory conditions ($p < 0.001$ for all comparisons). When touch was added (EC-LT), the spectrum diminished to less than half of EC ($p < 0.001$) but remained greater than EO ($p < 0.05$) and EO-LT ($p < 0.01$). When touch was added to vision, there was no difference in the amplitude of the spectrum compared to EO ($p = 0.33$). In W4, the EC had the largest spectrum compared to the other sensory conditions ($p < 0.001$ for all comparisons). With EC-LT, the mean level was greater than with EO and EO-LT ($p < 0.05$ for both comparisons). There was no difference between EO and EO-LT ($p = 0.51$). In W5, EC was greater than EO ($p < 0.05$). When touch was added (EC-LT), the mean level was smaller with respect to EC ($p < 0.001$). There was no difference between EO and EO-LT ($p = 0.14$). In W6, the mean level in the EC condition was the greatest ($p < 0.05$ for all comparisons).

AP Direction. In W1, touch with respect to no-touch diminished the mean level of the spectrum both with EC and EO (*post-hoc*, $p < 0.001$ for all comparisons). There was no difference between EC and EO either with (EC-LT vs. EO-LT, $p = 0.62$) or without touch (EC vs. EO, $p = 0.39$). The mean level in W2 behaved similarly to W1. Again, touch diminished the mean level of the spectrum with respect to the corresponding visual condition without touch (EC-LT vs. EC, $p < 0.001$; EO-LT vs. EO: $p < 0.01$). The mean level without vision (EC) was reduced by a touch more than by vision ($p < 0.001$). There was a significant difference in this window between EC and EO ($p < 0.01$), but there was no difference between EC-LT and EO-LT ($p = 0.18$). The pattern of the spectrum in the four sensory conditions was broadly reproduced in W3, W4, W5, and W6. EC had the largest mean level than the other sensory conditions ($p < 0.001$ for all comparisons within each window). When touch was added (EC-LT), the spectrum became similar to EO ($p > 0.08$ in each window). There was a difference between EO and EO-LT in W3 and W5 ($p < 0.05$ for both windows) but not in W4 and W6 ($p > 0.14$ for both windows).

Touch and Vision

The potentially different processes subserving the "stabilising" effects of touch without vision (EC-LT) and of vision without touch (EO) have been the object of additional analysis. In **Figure 9**, the spectrum of the EC-LT condition is superimposed to that of the EO condition for the ML (**Figure 9A**) and AP (**Figure 9B**) directions, and the result of applying the point-by-point *t*-test analysis (**Figures 9C,D**) is shown. For the ML direction, touch (EC-LT) significantly decreased the amplitude of the spectrum between 0.07 and 0.15 Hz (approximately corresponding to the frequency window W2) with respect to the EO (no-touch), while the amplitude of the spectrum was greater for EC-LT with respect to EO between 0.3 and 0.8 Hz

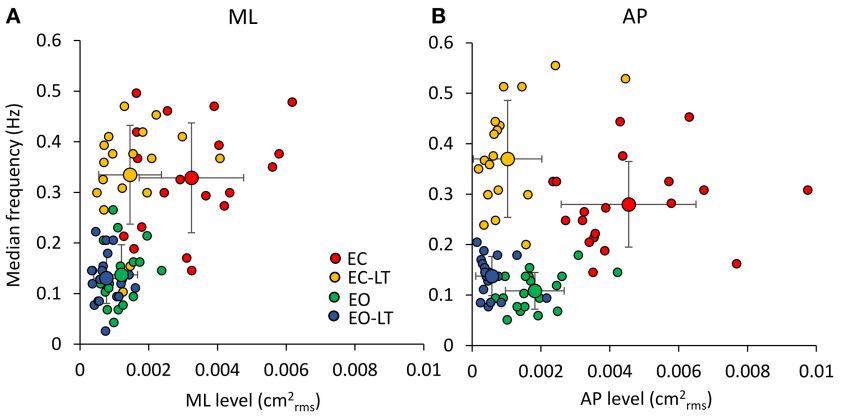

FIGURE 7 | Relationship between median frequency and mean level of the spectrum. There is a weak relationship between the value of the median frequency and the mean value of the entire spectra in each subject ($n = 19$), in both the frontal **(A)** and the sagittal planes **(B)**. The relatively large variability across subjects is underscored by the plots. However, when the mean values of each of the coloured clusters are considered (the large circles with their SDs), it appears that vision (EO, green) and vision and touch (EO-LT, blue) feature small oscillation frequencies with small oscillation amplitudes. Without vision, however, touch clearly reduces the mean level (EC-LT, yellow) compared to no-vision (EC, red), while the oscillation frequencies are hardly changed, particularly along the ML direction.

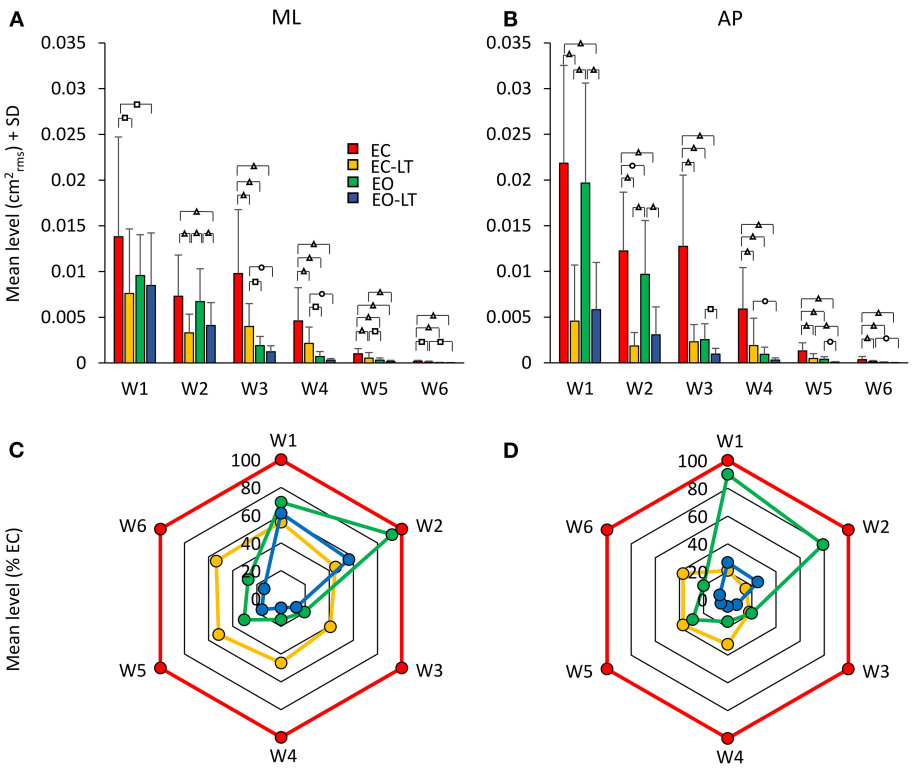

FIGURE 8 | Mean levels of the spectrum in the frequency windows (Ws) standing on foam. The mean level of the spectrum is irregularly distributed across the distinct Ws **(A,B)**. The EC condition (red bars) features a large mean level compared to the other sensory conditions in all the Ws, regardless of the ML or AP direction and of the progressive decrease in amplitude at the higher frequencies. The "stabilised" conditions show a non-uniform pattern depending on Ws and sensory conditions. EC-LT reduces the mean level in all the Ws in ML and more so in AP. Whereas, in ML and AP, EO (green) shows large mean levels at the low frequencies. Overall, the mean level at the highest frequencies is broadly reduced in all "stabilised" conditions. Distinct symbols indicate significant differences ($^{\square}p < 0.05$; $^{\circ}p < 0.01$; $^{\Delta}p < 0.001$). A compact compendium of the percent reduction compared to EC (red outermost trace) in the mean level of the distinct frequency Ws under the EC-LT, EO, EO-LT conditions is given by the radar plots in **(C)** (ML) and **(D)** (AP).

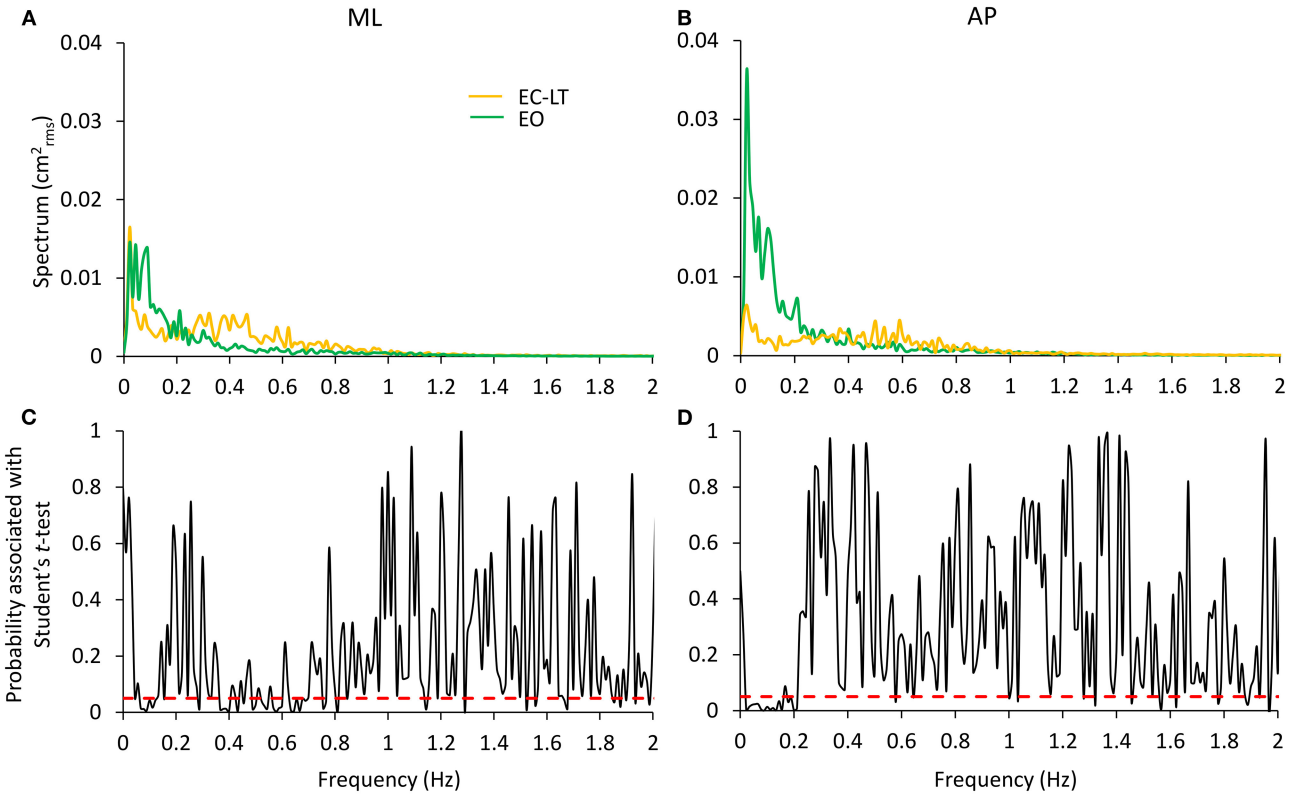

FIGURE 9 | Comparison of the effects of the "stabilising" touch and vision conditions. EC-LT (yellow) and EO (green) are compared in **(A,B)** for the ML and AP directions, respectively. Touch compared to vision remarkably decreases the spectrum in the very low frequency range (~0.01–0.2 Hz) but increases its level in the range 0.3–0.8 Hz. Graphs **(C,D)** (reporting the *p*-values of the point-to-point differences between the mean values of the entire spectra) show that the mean levels are significantly different in these ranges. The differences are less strong in the higher frequency range for the AP direction. The red dashed lines indicate the level at which the differences are significant at $p < 0.05$.

(approximately corresponding to W4). For the AP direction, the amplitude of the spectrum was smaller with EC-LT than EO only at low frequency, while there was an increased amplitude for frequencies in W4 (EC-LT > EO). This analysis confirms the emergence of a relatively large high-frequency component of the spectrum, for both ML and AP, selective for touch. However, this component did not raise the spectrum up to its EC values and disappeared when vision was available (EO-LT, see **Figures 5**, **7**).

Geometric Sway Measures

The statokinesigrams of a representative subject under the four different conditions while standing on the foam BoS are shown in **Figures 10A–D**. Sway area diminished with touch and with vision with respect to EC. The bottom panels show the mean CoP path length (**Figure 10E**) and the mean sway area (**Figure 10F**) calculated across all subjects. The CoP path length was different between conditions [$F_{(3, 54)} = 18.4$, $p < 0.001$, $d = 4.76$, $\eta_p^2 = 0.85$] and there was a difference between each condition (EC > EC-LT > EO > EO-LT, *post-hoc*, $p < 0.01$, for all paired comparisons). When vision and touch were combined (EO-LT), the CoP path length became the smallest ($p < 0.001$ for all paired comparisons). Of note, the force applied by the fingertip to the force pad (**Figure 10G**) was virtually the same regardless of the vision condition (EC-LT and EO-LT, paired *t*-test, $p = 0.63$).

Similar but not identical results were obtained considering the sway area. There was a significant difference between conditions [$F_{(3, 54)} = 83.4$, $p < 0.001$, $d = 4.3$, $\eta_p^2 = 0.82$]. With EC, the sway area was the largest with respect to the other sensory conditions (*post-hoc*, $p < 0.0001$ for all comparisons) and became the smallest with EO-LT ($p < 0.0001$ for all comparisons). When touch was added to EC, the sway area become not different from EO (EC-LT vs. EO, $p = 0.23$) but remained greater than with EO-LT ($p < 0.001$).

The relationship between the mean level of the spectrum in the ML (**Figures 11A–F**) and AP directions (**Figures 11G–L**) vs. the CoP path length and sway area in the different frequency windows are shown in **Figure 11**. W1 and W2 are shown in the first two columns. In the panels of the right column, the frequency windows from W3 to W6 (containing the highest frequencies) and their levels are merged. There was no relationship between the mean level of the ML or AP spectrum and the CoP path length or sway area in the first frequency window (W1). The relationship improved from the W2 to the higher frequency windows, especially for the CoP sway area ($p <$ 0.001 for all regression lines) for both ML and AP directions. The

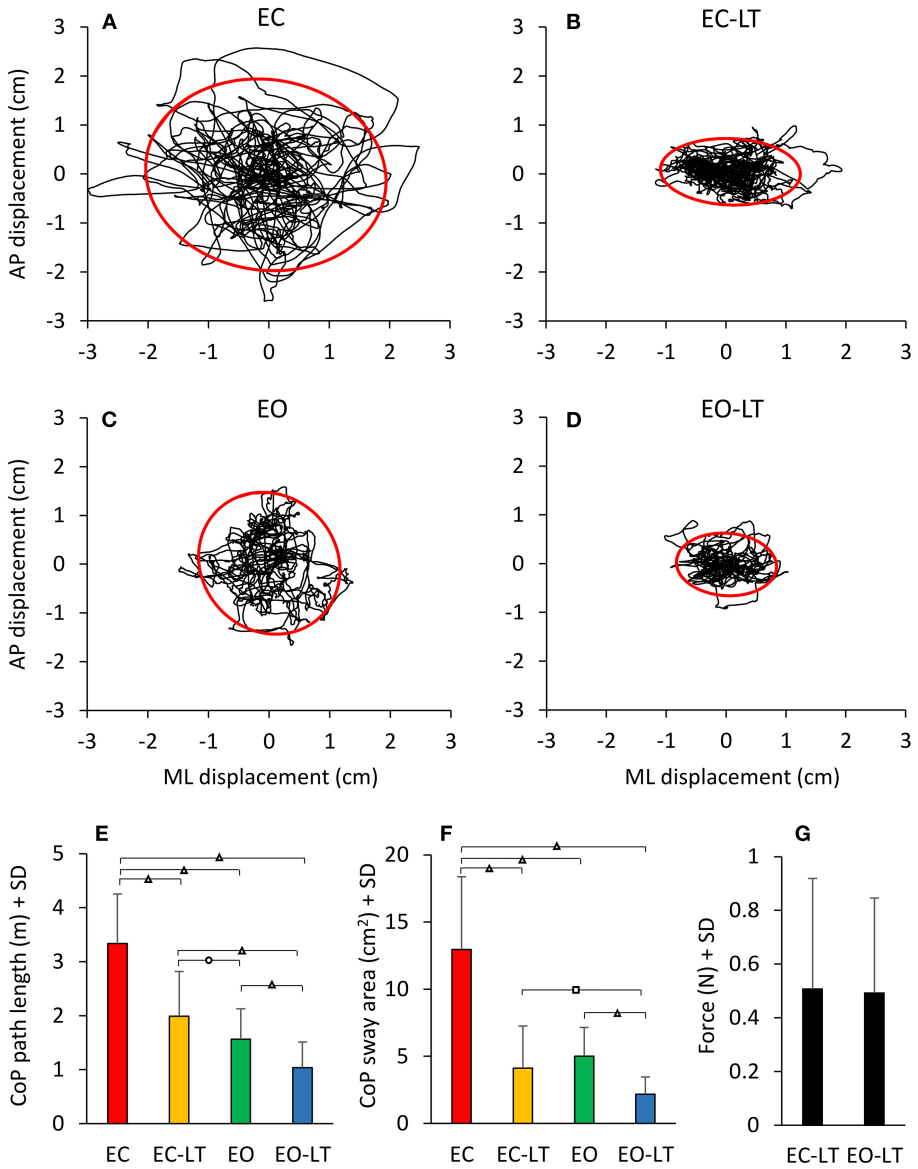

FIGURE 10 | Geometric sway measures. The four top panels show representative diagrams of the CoP sway trajectory (black line) together with the 95% ellipse profile (red) in one subject in the four sensory conditions tested on foam **(A–D)**. The diagrams broadly match the mean values of path length **(E)** and sway area **(F)** of the entire cohort of subjects. There is a discordance in the two metrics (length and area), whereby the path length diminishes with EC-LT and EO-LT, but the sway area decreases proportionally more. **(G)** The fingertip forces applied to the force pad during the touch conditions (both EC-LT and EO-LT) were similar. Distinct symbols indicate significant differences ($^{\square}p < 0.05$; $^{\circ}p < 0.01$; $^{\vartriangle}p < 0.001$).

equation of the regression lines fitted to the data is reported in **Table 1** for the ML and AP directions.

Solid Base of Support

Power Spectrum

The mean power spectra profiles computed for the four tested conditions (EC, EC-LT, EO, EO-LT) when standing on the solid BoS are shown in **Figures 12A,B**. For each condition and for each subject, the median frequency and the mean level of the spectrum were calculated between 0.01 and 2 Hz (**Figures 12C–F**).

Sensory Conditions

All conditions included, the median frequency was not different between ML and AP [$F_{(1, 18)} = 0.2$, $p = 0.65$]. There was a difference between conditions [$F_{(3, 54)} = 4.1$, $p < 0.05$, $d = 4.25$, $\eta_p^2 = 0.18$] and an interaction between median frequency of ML and AP directions and sensory conditions [$F_{(3, 54)} = 4.01$, $p < 0.05$, $d = 4.14$, $\eta_p^2 = 0.18$]. For the ML direction, the median frequency was much higher with EC than with all other sensory conditions (*post-hoc*, $p < 0.05$ for all comparisons). There was no difference between EC-LT and the two conditions with eyes open (EO and EO-LT) ($p > 0.4$ for both comparisons) and between EO

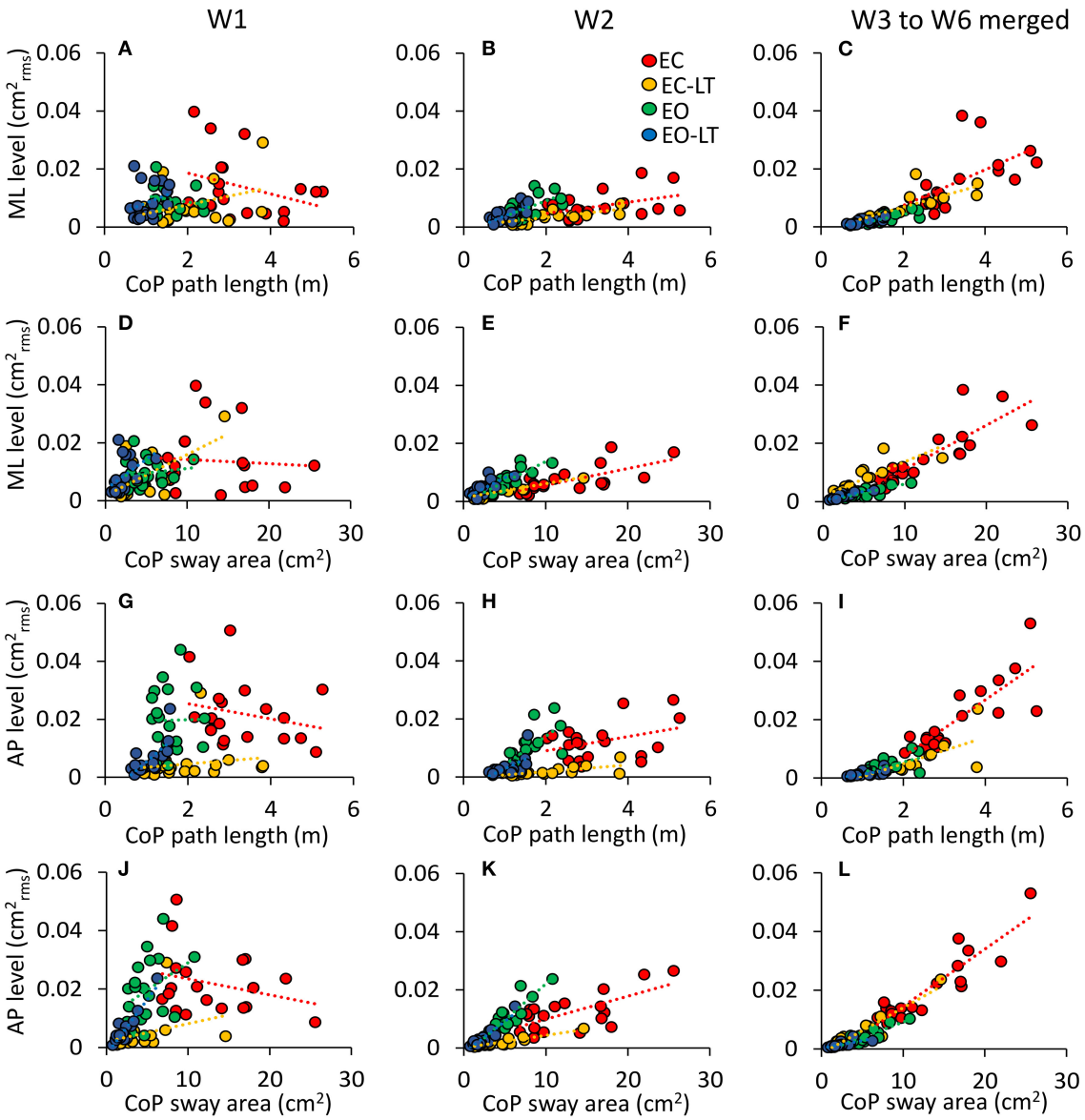

FIGURE 11 | Not all the frequency windows match the geometric sway measures. The contribution of the ML **(A–F)** and AP **(G–L)** sway frequencies to the geometric sway measures is limited to high frequency windows (EC, red; EC-LT, yellow; EO, green; EO-LT, blue). The columns refer to W1 **(A,D,G,J)**, W2 **(B,E,H,K)**, and from W3–W6 **(C,F,I,L)**. Each symbol refers to one subject. **(A–C,G–I)** The spectrum amplitudes vs. the CoP path length, and **(D–F,J–L)** the spectrum amplitudes vs. the sway area. For both sway area and path length, the slope of the regression lines increases with frequency under all sensory conditions but only for W2 onwards.

and EO-LT ($p = 0.22$). For the AP direction, EC was not different from the other sensory conditions ($p > 0.1$ for all comparisons). EC-LT was larger with respect to EO ($p < 0.05$) and EO-LT ($p < 0.05$). There was no difference between EO and EO-LT conditions ($p = 0.44$).

The mean level of the spectrum between 0.01 and 2 Hz was different between ML and AP [$F_{(1, 18)} = 16.45$, $p < 0.001$, $d = 1.91$, $\eta_p^2 = 0.48$]. There was a difference between conditions [$F_{(3, 54)} = 11.4$, $p < 0.001$, $d = 1.59$, $\eta_p^2 = 0.39$] and an interaction between ML and AP directions and sensory conditions [$F_{(3, 54)} = 12.6$, $p < 0.001$, $d = 1.67$, $\eta_p^2 = 0.41$]. For ML, the mean level was not different between sensory conditions (*post-hoc*, $p > 0.2$ for all comparisons). For AP, the mean level with EC was higher than with EC-LT and EO-LT ($p < 0.001$), but was not different from EO ($p = 0.35$). The mean level with EC-LT was smaller than EO ($p < 0.001$) and similar to EO-LT ($p = 0.57$). Compared to the foam condition, the median frequency was lower for the solid BoS [$F_{(1, 18)} = 60.7$, $p < 0.001$, $d = 3.66$, $\eta_p^2 = 0.77$] when all sensory conditions were included. The mean level of the spectrum between 0.01 and 2 Hz was also different between foam and solid BoS [foam > solid, $F_{(1, 18)} = 108.19$, $p < 0.001$, $d = 4.89$, $\eta_p^2 = 0.86$].

TABLE 1 | Relationship between level of mediolateral (ML, left part) and anteroposterior (AP, right part) spectrum and CoP path length and sway area.

FW	Condition	ML spectrum vs. CoP path length			ML spectrum vs. sway area			AP spectrum vs. CoP path length			AP spectrum vs. sway area		
Entire spectrum (from 0.01 to 2 Hz)		Equation	R^2	*p*-value	Equation	R^2	*p*-value	Equation	R^2	*p*-value	Equation	R^2	*p*-value
	EC	$y = -0.001x - 0.00006$	0.41	<0.01	$y = 0.0003x - 0.0001$	0.85	<0.001	$y = 0.0016x - 0.0009$	0.7	<0.001	$y = 0.0003x + 0.0003$	0.8	<0.001
	EC LT	$y = 0.0009x - 0.0003$	0.68	<0.001	$y = 0.0003x + 0.0003$	0.89	<0.001	$y = 0.0009x - 0.0007$	0.58	<0.001	$y = 0.0003x - 0.0002$	0.94	<0.001
	EO	$y = 0.0009x - 0.0002$	0.54	<0.001	$y = 0.0002x + 0.0001$	0.94	<0.001	$y = 0.0013x - 0.0003$	0.4	<0.01	$y = 0.0004x - 0.0002$	0.96	<0.001
	EO LT	$y = 0.0009x - 0.0002$	0.56	<0.01	$y = 0.0003x + 0.0002$	0.74	<0.001	$y = 0.0012x - 0.0007$	0.57	<0.001	$y = 0.0004x - 0.0002$	0.9	<0.001
FW 1	EC	$y = -0.0036x + 0.026$	0.1	0.2	$y = -0.0001x + 0.016$	0.005	0.77	$y = -0.0026x + 0.03$	0.06	0.32	$y = -0.0005x + 0.03$	0.08	0.25
	EC LT	$y = 0.003x + 0.0016$	0.13	0.13	$y = 0.0014x + 0.002$	0.4	<0.01	$y = 0.0012x + 0.002$	0.03	0.5	$y = 0.0006x + 0.002$	0.1	0.19
	EO	$y = -0.002x + 0.013$	0.035	0.44	$y = 0.0003x + 0.008$	0.02	0.54	$y = 0.0005x + 0.02$	0.0003	0.95	$y = 0.002x + 0.01$	0.13	0.12
	EO LT	$y = -0.0055x + 0.003$	0.08	0.18	$y = 0.0021x + 0.004$	0.2	0.05	$y = 0.012x - 0.007$	0.5	<0.001	$y = 0.004x - 0.002$	0.85	<0.001
FW 2	EC	$y = 0.002x + 0.0008$	0.18	0.07	$y = 0.0006x - 0.0002$	0.5	<0.001	$y = 0.0025x + 0.004$	0.14	0.11	$y = 0.0006x - 0.0002$	0.5	<0.001
	EC LT	$y = 0.0015x + 0.0002$	0.41	<0.01	$y = 0.0005x + 0.001$	0.55	<0.001	$y = 0.0011x - 0.0004$	0.43	<0.01	$y = 0.0005x + 0.001$	0.55	<0.001
	EO	$y = 0.0054x - 0.0017$	0.35	<0.01	$y = 0.0014x - 0.0003$	0.7	<0.001	$y = 0.0099x - 0.006$	0.43	<0.01	$y = 0.0014x - 0.0003$	0.7	<0.001
	EO LT	$y = 0.006x - 0.0021$	0.5	0.07	$y = 0.0014x + 0.001$	0.54	<0.001	$y = 0.0067x - 0.004$	0.42	<0.01	$y = 0.0014x + 0.001$	0.54	<0.001
FW 3	EC	$y = 0.0036x - 0.0024$	0.26	<0.05	$y = 0.001x - 0.003$	0.57	<0.001	$y = 0.0053x - 0.005$	0.45	<0.01	$y = 0.001x - 0.003$	0.57	<0.001
	EC LT	$y = 0.0016x + 0.0008$	0.3	<0.05	$y = 0.0005x + 0.002$	0.38	<0.01	$y = 0.0015x - 0.0006$	0.44	<0.01	$y = 0.0005x + 0.002$	0.38	<0.01
	EO	$y = 0.0015x - 0.0005$	0.35	<0.01	$y = 0.0003x + 0.0003$	0.46	<0.01	$y = 0.0017x - 0.0001$	0.15	0.1	$y = 0.0003x + 0.0003$	0.46	<0.01
	EO LT	$y = 0.0016x - 0.0004$	0.5	<0.05	$y = 0.0004x + 0.0003$	0.63	<0.001	$y = 0.0014x - 0.0005$	0.41	<0.01	$y = 0.0004x + 0.0003$	0.63	<0.001
FW 4	EC	$y = 0.002x - 0.002$	0.3	<0.05	$y = 0.0005x - 0.001$	0.46	<0.01	$y = 0.0036x - 0.006$	0.6	<0.001	$y = 0.0005x - 0.001$	0.46	<0.01
	EC LT	$y = 0.0018x - 0.0014$	0.72	<0.001	$y = 0.0005x + 0.001$	0.74	<0.001	$y = 0.0025x - 0.003$	0.5	<0.001	$y = 0.0005x + 0.001$	0.74	<0.001
	EO	$y = 0.0009x - 0.0006$	0.38	<0.01	$y = 0.0002x - 0.0003$	0.65	<0.001	$y = 0.0012x - 0.001$	0.4	<0.01	$y = 0.0002x - 0.0003$	0.65	<0.001
	EO LT	$y = 0.0005x - 0.0002$	0.85	<0.05	$y = 0.0001x + 5*10^{-5}$	0.78	<0.001	$y = 0.0006x - 0.0004$	0.6	<0.001	$y = 0.0001x + 5*10^{-5}$	0.78	<0.001
FW 5	EC	$y = 0.0004x - 4*10^{-4}$	0.5	<0.001	$y = 0.00006x + 0.0002$	0.37	<0.01	$y = 0.0006x - 0.0006$	0.43	<0.01	$y = 0.00006x + 0.0002$	0.37	<0.01
	EC LT	$y = 0.0005x - 0.0006$	0.58	<0.001	$y = 0.0002x - 0.0002$	0.76	<0.001	$y = 0.0005x - 0.0004$	0.6	<0.001	$y = 0.0002x - 0.0002$	0.76	<0.001
	EO	$y = 0.0006x - 0.0006$	0.92	<0.001	$y = 0.000007x - 4*10^{-5}$	0.4	<0.01	$y = 0.0005x - 0.0004$	0.45	<0.01	$y = 0.000007x - 4*10^{-5}$	0.4	<0.01
	EO LT	$y = 0.0004x - 2*10^{-4}$	0.75	<0.001	$y = 0.00009x - 4*10^{-5}$	0.77	<0.001	$y = 0.0001x - 7*10^{-5}$	0.63	<0.001	$y = 0.00009x - 4*10^{-5}$	0.77	<0.001
FW 6	EC	$y = 0.00009x - 0.0001$	0.64	<0.001	$y = 0.00001x + 2*10^{-5}$	0.43	<0.01	$y = 0.0003x - 0.0005$	0.56	<0.001	$y = 0.00001x + 2*10^{-5}$	0.43	<0.01
	EC LT	$y = 0.0001x - 9*10^{-5}$	0.7	<0.001	$y = 0.00003x - 1*10^{-5}$	0.75	<0.001	$y = 0.0001x - 0.0001$	0.76	<0.001	$y = 0.00003x - 1*10^{-5}$	0.75	<0.001
	EO	$y = 0.00005x - 3*10^{-5}$	0.7	<0.001	$y = 0.000007x + 1*10^{-5}$	0.78	<0.001	$y = -0.00009x - 7*10^{-5}$	0.62	<0.001	$y = 0.000007x + 1*10^{-5}$	0.78	<0.001
	EO LT	$y = 0.00005x - 3*10^{-5}$	0.74	<0.001	$y = 0.00001x + 4*10^{-6}$	0.54	<0.001	$y = 0.00005x - 3*10^{-5}$	0.4	<0.01	$y = 0.00001x + 4*10^{-6}$	0.54	<0.001

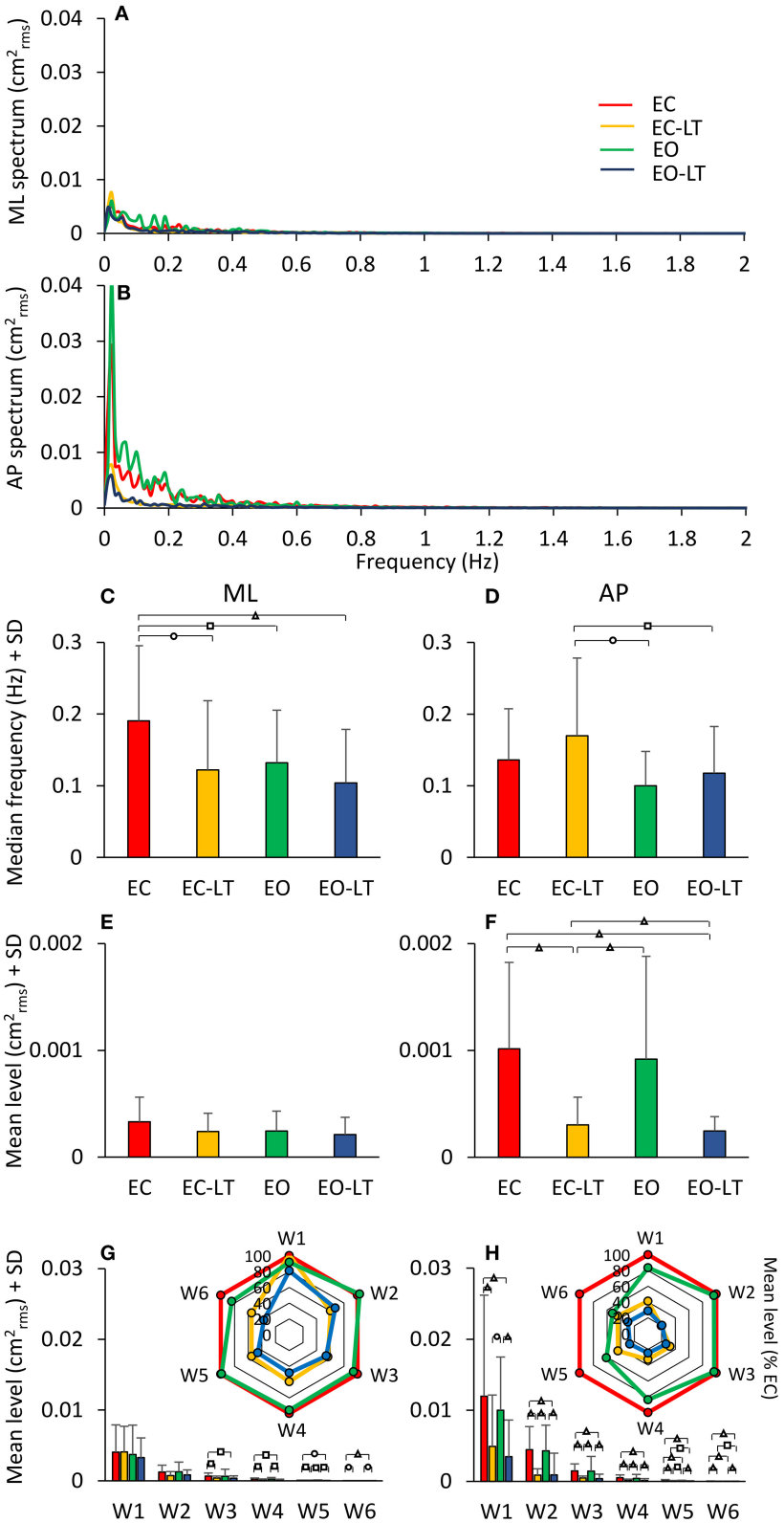

FIGURE 12 | Power spectrum on solid BoS. **(A,B)** compare the power spectra during quiet stance EC (red), EO (green), EC-LT (yellow), and EO-LT (blue). For the low-frequency range, the mean level with EO was not smaller than with EC (for both ML and AP directions). Touch (EC-LT) and vision (EO) produced the smallest

(Continued)

FIGURE 12 | amplitudes of the spectrum. The median frequency of the entire spectrum was not much different across conditions **(C,D)**. However, the mean level was larger in AP than ML (both EC and EO), and much larger without touch **(E,F)**. Overall, median frequencies were about half, and the mean level was about half to a quarter of those with foam (compare to **Figure 5**). The changes with respect to EC of the distinct frequency windows are shown in the radar plots **(G,H)** for both ML and AP directions. Compared to the foam conditions (see **Figure 8**), the mean levels are less than half. Distinct symbols indicate significant differences ($^{\square}p < 0.05$; $^{\circ}p < 0.01$; $^{\blacktriangle}p < 0.001$).

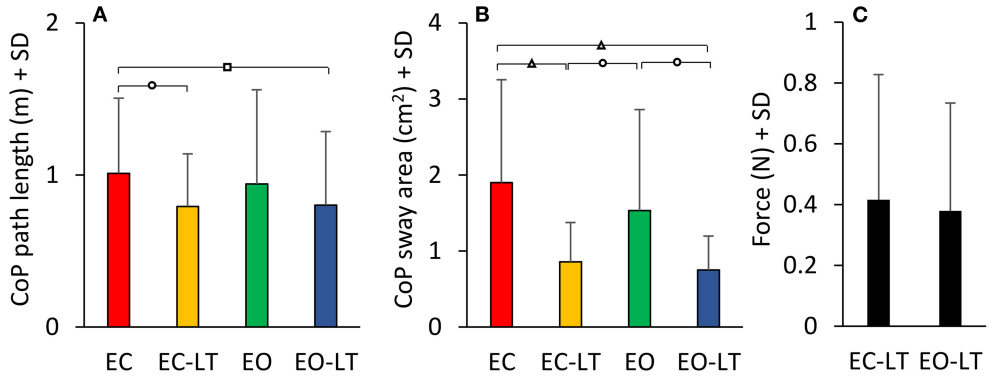

FIGURE 13 | CoP path length and sway area on solid BoS. The path length and 95% ellipse area with the solid BoS are much smaller than in the foam condition. While the path length is not very different across sensory conditions **(A)**, sway area shows larger differences across conditions, the minimal excursions of the CoP being present when touch is available **(B)**. In the solid BoS condition, the touch forces **(C)** are similar, with and without vision. Distinct symbols indicate significant differences ($^{\square}p < 0.05$; $^{\circ}p < 0.01$; $^{\blacktriangle}p < 0.001$).

Frequency Windows

In **Figures 12G,H**, the mean level of the spectrum in the different frequency windows and their percent reduction with respect to EC condition is reported for each sensory condition.

There was a difference in the spectrum mean level between the ML and AP directions when all conditions included [$F_{(1, 18)} = 17.4$, $p < 0.001$, $d = 1.97$, $\eta_p^2 = 0.49$]. There was also a difference between conditions [$F_{(3, 54)} = 9.08$, $p < 0.001$, $d = 1.42$, $\eta_p^2 = 0.33$] and between frequency windows [$F_{(5, 90)} = 38.1$, $p < 0.001$, $d = 2.91$, $\eta_p^2 = 0.68$]. There was an interaction between ML and AP directions and sensory conditions [$F_{(3, 54)} = 10.3$, $p < 0.001$, $d = 1.51$, $\eta_p^2 = 0.36$], ML and AP directions and frequency windows [$F_{(5, 90)} = 8.6$, $p < 0.001$, $d = 1.38$, $\eta_p^2 = 0.32$], between sensory conditions and frequency windows [$F_{(15, 270)} = 4.8$, $p < 0.001$, $d = 1.03$, $\eta_p^2 = 0.21$], and between ML and AP directions, sensory conditions and frequency windows [$F_{(15, 270)} = 4.5$, $p < 0.001$, $d = 0.99$, $\eta_p^2 = 0.20$]. For the ML direction, there was no significant difference between sensory conditions for W1 and W2 (*post-hoc*, $p > 0.2$ for all comparisons). In W3 to W6 there was no difference in the mean levels between EC-LT and EO-LT ($p > 0.6$ for all comparisons) and between EC and EO ($p > 0.3$). Touch reduced the level under both EC-LT and EO-LT conditions ($p < 0.05$). The level of the EC-LT condition was not much different to EO ($p > 0.07$), and that of EO-LT was smaller than EO ($p < 0.05$). For the AP direction, touch reduced the mean levels in all the frequency windows (EC-LT vs. EC and EO-LT vs. EO, $p < 0.001$). There was no difference between EC and EO ($p > 0.07$). Similarly, EC-LT and EO-LT were not different across the windows ($p > 0.3$).

Geometric Sway Measures

The mean CoP path length and the mean sway area calculated across subjects standing on solid BoS are shown in **Figures 13A,B**. ANOVA on the CoP path length showed a difference between sensory conditions [$F_{(3, 54)} = 3.46$, $p = 0.02$, $d = 0.88$, $\eta_p^2 = 0.16$]. With EC, the path length was greater than EC-LT and EO-LT (*post-hoc*, $p < 0.05$ for both comparisons), but not different from EO ($p = 0.4$). There was no difference between the two conditions with touch (EC-LT vs. EO-LT, $p = 0.92$). ANOVA, on the sway area, showed a significant difference between sensory conditions [$F_{(3, 54)} = 11$, $p < 0.001$, $d = 1.56$, $\eta_p^2 = 0.38$]. Sway area with EC and EO was greater than EC-LT (*post-hoc*, $p < 0.01$ for both comparisons) and EO-LT ($p < 0.01$ for both comparisons). There was no difference in sway area between EC and EO ($p = 0.17$) and between EC-LT and EO-LT ($p = 0.68$). Path length [$F_{(1, 18)} = 90.5$, $p < 0.001$, $d = 4.48$, $\eta_p^2 = 0.83$] and sway area [$F_{(1, 18)} = 93.97$, $p < 0.001$, $d = 4.56$, $\eta_p^2 = 0.84$] were greater with foam than solid BoS when all sensory conditions are included. Much as with foam, during the trials performed on the solid BoS vision did not affect the force applied by the subjects onto the force pad (**Figure 13C**) (paired *t*-test, $p = 0.29$). In turn, the touch forces exerted on solid BoS were not different from those recorded when standing on foam [$F_{(1, 18)} = 2.6$, $p = 0.12$].

DISCUSSION

Our hypothesis was that vision and light touch stabilise body sway through at least partially different actions (31). To this objective, we have computed and analysed both the usual

stabilometric indices (sway path and sway area) and the power spectra of the oscillation frequency along with both the frontal and the sagittal planes in healthy young subjects standing on a compliant and on a solid surface.

Spectral analysis of body oscillations during stance has been repeatedly exploited in order to understand the processes underpinning the control of equilibrium in the absence of external perturbations (35–39, 116–120). Singh et al. (98) had a contiguous research question and emphasised open issues in attributing specific frequencies to the effect of different sensory modalities on standing posture. Inconsistencies in the methodological approach across the literature might have detracted researchers and clinicians from the use of standardised approaches. The span of considered frequencies varies across laboratories, and one wonders whether frequencies as high or higher than, say, 2 Hz can have a practical counterpart for the interpretation of the sway of healthy, non-trembling subjects (121, 122). Moreover, the value of the ordinate in the power spectrum is sometimes of difficult interpretation, also because of dissimilar modes in the signal processing (e.g., filtered/non-filtered) and the metrics used in different studies, so that attention seems to have been devoted more to the frequencies themselves than to the effective amplitude of their power spectrum. We have leveraged this approach in order to test the possibility that the effects of different sensory conditions and support bases on the body sway can be easily detected by the frequency analysis compared to the commonly used metrics and can yield details not granted by the simple analysis of the CoP path length or sway area.

We have tried to identify ranges and amplitudes of oscillation frequencies presumably having an actual physical counterpart in the wandering of the CoP of the standing body, and to detect spectrum windows which could be questioned for elucidating the effects of adding haptic and visual sensory information on the CoP oscillations identified in the most unstable condition (eyes closed, EC). As a consequence, we have limited our analysis to the region of the power spectrum (below 2 Hz) encompassing about 99% of the total available spectrum (i.e., containing the frequencies up to 70 Hz, which depend on the frequency of sampling of the CoP signal). We have also checked that the oscillations beyond 2 Hz represent a tiny proportion of the geometric metrics, the sway area, and the path length. The oscillations beyond 2 Hz do indeed represent a minor part of the sway area (<1%) (see **Figure 3B**). They contribute to the path length by about 50%, though. The incongruous length of the sway path compared to its area is due to the long period of acquisition, when the filtered signal does negligibly oscillate but may show minimal displacements, the sum of which gives rise to sizeable total lengths over the 90 s epoch. Perhaps, for this reason, frequencies from 2 to 20 Hz have been considered in some studies on dizzy patients (123, 124).

With EC foam, the frequency spectra and their amplitudes were broadly similar in both ML and AP directions, but larger in AP for frequencies in the W1 and W2. This was not unexpected because the spontaneously oscillating body during quiet stance does not really care about the space directions along which to move, and the balancing strategies of a double-inverted pendulum are not really functionally separated (56, 125) unless imposed by the feet distance (24, 126, 127). In our subjects, this distance (the outer profile of the feet was about the hip distance) was appropriate for promoting omni-directional sway, as obvious in the shape of the wandering of the CoP on the horizontal plane (see **Figures 3A**, **10A,C**).

The median frequencies are higher without vision (EC). The median frequencies remain high (or get relatively higher in the AP direction) when touch is added to EC. Hence, the median frequency is not a good predictor of the effect of the haptic information. Conversely, vision is associated with low median frequency values. This is true both with and without touch. In general, vision diminishes the median frequency, while touch diminishes the amplitude of the spectrum. It seems that vision prescribes the frequency of oscillation, upon which touch quantitatively modulates the amplitude. As expected, there is a broad correspondence between the amplitude of the spectra and the geometric sway measures (compare **Figures 6E,F** with **Figures 10E,F**). Across the sensory conditions, the length of the sway path is broadly reflected in the amplitude of the mean level of the spectrum along the ML direction, and the sway area is rather reflected in the mean level along the AP direction.

Vision and Touch Stabilise the Standing Body on the Foam

Vision

The power spectrum of the oscillation frequencies with EC foam has been considered here the default condition, against which to compare the stabilising effects of vision and touch and both together. Compared to EC, vision (EO) reduced the area of the ellipse by about 61% and the CoP path length by about 53% (see **Figure 10**). In the spectral analysis, the addition of vision remarkably lowered the median frequency of the entire spectrum. This diminution affected the entire spectrum both in the ML (63%) and in the AP (60%) directions (see **Figure 5**). This was consistent with a decrease in the amplitude of the medium-high frequencies with sparing of the low frequencies. While the amplitude of each of the oscillation frequency windows was smaller with EO than with EC, the vision had no effect on the spectral mean level of the low-frequency windows in the ML and AP directions. This is in keeping with the findings by Yamagata et al. (86), who showed that slow oscillations, or drifts, appear to be poorly sensitive to vision. Conversely, the reduction was conspicuous for the subsequent windows (between 0.2 and 0.8 Hz), i.e., for oscillation cycles lasting from 5 to nearly 1 s. The highest-frequency windows (beyond 0.8 Hz) were scarcely influenced by vision, much as had been previously shown (56, 117). Under unstable conditions (as standing on an inclined surface or on a balance trainer ball), the slow components of the postural sway appear to depend on vision compared to more stable conditions (128–130). No significant vision effects on the oscillation frequency were noted by Šarabon et al. (82), probably because they measured the average frequency. In our hands, the reduction was clear in the median frequency,

just because of the preserved low-frequency and reduced high-frequency oscillations. The frequency window W3 (from 0.2 to 0.44 Hz) should contain frequencies related to ventilation (131), i.e., broadly between 0.2 and 0.3 Hz for ventilation cycles from 12 to 18 per minute, which are probably blunted in the mean spectrum by inter-subject variability. In our hands, the amplitude of the postulated ventilation component diminishes with the general decay of the mean level of the spectrum in the stabilised conditions, making it difficult to draw strong deductions. Interestingly, stabilisation by vision (EO vs. EC) reduced both length and area of the CoP wandering without decreasing the level of the lowest part of the spectrum (the frequency Ws 1 and 2, spanning 0.01–0.2 Hz). The absence of influence of this part of the spectrum on the geometric sway measures is "compensated" by the strong relationships between the level of the higher-frequency windows with CoP path length and sway area (see **Figure 11**).

Touch

A light touch is a potent stabilising stimulus, able to replace vision in subjects with impaired vestibular system (132–134). In the present study, like in several others [(7), see Lackner (47) for a recent review], the haptic information arose from the index fingertip lightly touching the force pad and from the muscles active in this task. In many studies, the vertical force of the fingertip on the force pad representing the earth-fixed reference was generally well-below 1 N and was considered to be inadequate for mechanical stabilisation (60, 135, 136). Importantly, during our experimental trials, the force did not change across the different sensory or BoS conditions.

Compared to EC, the light touch without vision (EC-LT) reduced the sway area (by about 68%) and the path length (40%). In the frequency domain, EC-LT had minimal effects on the median frequencies of the ML and AP spectra (see **Figures 6–9**). However, EC-LT reduced the level of the spectrum, along with the ML (by 55%) and more so along with the AP (77%) direction (137–139). It is not unlikely that the haptic reference helped diminish the "slow" sway oscillations more in the sagittal than in the frontal plane (140, 141). This would depend on the haptic task, whereby the reference (the fingertip onto the force pad) was located just in front of the subjects, almost coinciding with the sagittal plane, and broadly congruent with the direction of the gaze (142, 143). However, we would not exclude that, when standing on foam, a minor but non-negligible additional advantage might have been furnished by the contact of the finger with the force pad. We have no information on the amplitude or direction of the friction forces on the force pad, though. Although minimal, these cannot be disregarded (144). Since the body oscillations reduction along the ML direction was similar for touch and vision, we suppose that the added reduction in the AP direction was due to the anterior position of the force pad. Qualitative changes occur, however, even when the haptic stimulus is applied to diverse body sites and has no definite direction of action (145). As to the location of the haptic device, we would remind that similar stabilising effects are obtained by using a cane touching the ground (146). The use of a tool is as helpful as the fingertip input and does not produce a different stabilisation.

Touch and Vision Stabilise Balance Through Distinct Actions

The stabilising effects of touch (EC-LT) and vision (EO) have been directly compared. While both conditions resulted in a similar reduction of path length and sway area (147), their modulation of the spectrum frequencies was definitely divergent. This was clear in the superimposition of the frequency spectra obtained in the two conditions on foam. While the addition of vision (EO) had no effect on the very low frequencies of the spectrum, the same frequencies abated with touch (EC-LT). Conversely, while the higher frequencies were reduced with vision, a broad peak intruded with touch between 0.3 and 0.8 Hz (148), as if the former frequency window drop and the increase of the latter were a necessary quality of the touch effect. It has been known for decades that touching or even aiming to a stable structure diminishes the amplitude of the leg muscle long-latency reflex responses to stretch (46, 149, 150), whereas the short-latency responses are hardly affected. Touch would not be powerful enough for cancelling the medium-high frequencies, likely sustained by continuous operation of short-chain reflexes that represent a major share of the oscillations EC. Further, a new inter-foot coordination pattern (26) would emerge when a midline reference (the LT in front of the subject) is available and attenuate slow omnidirectional oscillations in favour of fast, short displacements. The sway area reflects this effect, as shown by the major shrinkage of the ellipses fitted to the EC-LT (but not EO) data, with a minor reduction in path length. One might speculate that touch *without* vision sustains the elevated level of excitability of the proprioceptive circuits operating with EC as if this would serve prompt postural corrections when an obstacle challenges the equilibrium in the frontal plane. We would add that, while the spectrum profiles of EC-LT and EO (i.e., during stabilisation by vision or touch) clearly intersected on foam (**Figure 8**), this pattern disappeared when standing on solid BoS. On the other hand, even the differences between EC and EO disappear with solid BoS, where the sensory information is less crucial for stabilisation.

The Combination of Touch and Vision Produces the Maximal Stabilisation

The integration of touch and vision has been often studied in the context of studies on space perception (151). The interaction of both inputs would take place in cortical areas that are related, among other things, with the control of equilibrium (152–155). In our hands, the condition touch and vision together (EO-LT) clearly proved to be able to further reduce the sway area and the path length (more so the area than the path length) compared to EC (area and path length were reduced by 83 and 69%, respectively). Sway area and path length were also reduced compared to touch (EC-LT) (by 47 and 48%) (see **Figure 10**) and to EO when separately considered (by 57 and 34%), confirming the findings of Honeine et al. (63). Regarding the frequency spectrum, EO-LT was superior in attenuating the oscillations on foam compared to vision alone (EO). However, EO-LT was not

superior to touch without vision (EC-LT) in the low-frequency windows (W1 and W2). In this vein, we would mention that, while the integration of haptic and visual inputs in cortical regions likely plays a role, other probably concurrent processes cannot be overlooked. Effectiveness in visuo-haptic integration is enhanced by object-selective brain regions with increased salience of the stimulus (156). Salience can be attributed to our light touch here because attention was devoted to keeping the force within the required range, even if subjects did not look at the force pad with EO. The level of attention would be most likely different in the foam than in the solid BoS condition. In the former case, a precision task would be implicit (141), even if not expressly required. In the latter case, the task can be more easily carried out and provide a simple haptic reference in the absence of accidental displacement (73).

Foam and Solid BoS

The solid BoS, compared to foam, diminished the median frequency of the spectra almost selectively for the EC condition (both EC and EC-LT), whereas the median frequencies with vision (both EO and EO-LT) were similar in the two BoS conditions. However, the oscillations in the 0.3–0.8 Hz and higher frequency windows (W3–W6) under EC-LT conditions appear only when standing on foam, as if this frequency range were a distinctive feature of standing on a compliant surface. Instead, the mean level of the spectrum was much reduced for all sensory conditions on solid BoS in both ML and AP directions. The effect of touch on the mean level seems to be proportionally stronger on foam in keeping with the observation that unstable balance enhances the haptic sensitivity (157). Generally speaking, it seems that the distinct qualitative contributions to the stabilisation process by vision, touch, or both are hard-wired. These contributions are modulated in amplitude. When the body is in a stable condition (solid BoS), it would continue to operate but are adaptively scaled (or "downweighed") to the new state.

The balancing behaviour standing on a compliant surface must adapt to the spring-like properties of the foam that influence sway by its own mechanical compliance. This would favour higher activity in the muscles controlling mediolateral oscillations (49, 98). For example, the mean levels of the AP and ML spectra were less different on foam than on solid BoS, suggesting proportionally larger mediolateral adjustments on foam. The inverted pendulum model does not apply to this condition, and movements at several joints contribute to the equilibrium control (13, 158). Analogously, it seems simplistic to posit that the proprioceptive system is disturbed, or its contribution attenuated or invalidated when standing on foam (43, 159, 160). Sway while on foam compared to solid BoS may be less useful for "exploration" of the support base (161) and for "resetting" of the input from the adapting receptors of the foot sole (40). Whereas, pelvis and trunk movements may be more important in getting information about body segments' orientation in space when task difficulty increases (134, 162). The continuous corrections of the body segment displacements on the foam are likely dependent on proprioceptive volleys, which send a continuous (meaningful) input to various regions of the brain and produce appropriate short- and long-latency reflexes (163). Conversely, the vibration of the leg muscles, producing a non-meaningful proprioceptive input, has a smaller effect on body sway while standing on foam (164) or on an unstable support (165, 166). If anything, these findings support the notion that proprioception continues to operate (and likely much more) on a compliant (foam) than solid BoS. The vibration of trunk muscles has, instead, a larger effect compared to the vibration of the leg muscles (164), a finding that we interpret as a shift in excitability of different circuits rather than mere disruption of proprioceptive information by vibration. Of note, touch increases the postural tone in trunk muscles (167). It is not clear, though, whether the new trunk postural activity can be responsible for the relative increase in medium-high frequencies seen while standing on foam in EC-LT condition (168, 169).

With EC, our subjects were actually unstable on foam (but never made a step during these trials) and became stable with touch (EC-LT). Touch devoid of mechanical action (always $<$ 1 N) could have had such effect just because proprioception was properly working. In a sense, the ampler the joint movements on foam, the more substantial the proprioceptive input from multiple muscles, not excluding those of the forearm muscles enabling and contributing to a significant haptic input (64, 170). Mastering a complex proprioceptive input can be difficult and lead to instability. However, there must be a large safety margin compensating for unpredictable alteration in proprioceptive input. Young subjects, healthy except for the Marfan syndrome, a disorder targeting the connective tissue, show impaired balance control under critical conditions (unstable BoS, eyes closed) (171). However, just a few of them had to be supported during the trials despite presumably altered reflex patterns due to their unique joint hypermobility.

Frontal and Sagittal Planes

Control of balance in the mediolateral direction is critical (52, 172) and is often impaired in older adults and when the asymmetry of stance is present, like for instance in stroke patients (173, 174). There were considerable differences in the mean level of the spectrum of all the frequency windows between ML and AP directions, and the overall pattern of the effects of touch and vision were distinct along the frontal and sagittal planes and both on foam and solid BoS (compare **Figures 8**, **12**). On the other hand, the median frequency was not different between the frontal and the sagittal planes for both foam and solid BoS. Touch compared to no-touch, regardless of vision availability, exerted a larger stabilising effect in the AP than in the ML direction. Such a stabilised condition (EC-LT and EO-LT) may have reduced the "rambling" component of the control while favouring the "trembling" omponent (86, 175), thanks to the haptic reference in the AP direction. With vision, a difference also emerged between ML and AP directions in the mean level of the spectrum because spectrum amplitude relatively prevailed in the AP direction on solid BoS.

Limitations

The sample size was not determined prior to the study. However, the effect size of the significant differences indicates always

large effects. Given our sample size of 19 participants, the study proved to have a sufficient power (>80%) to detect an effect in median frequency larger than 0.12 Hz between the EC-LT and EO conditions. The data have been collected here and analysed on the basis of one single trial per subject per condition (i.e., the first trial of a series of eight trials), administered in order to investigate the effect of the sensory conditions in the adaptation to repeated stance performances. Given the inter-individual variability in the stance performance (9, 176), particularly when standing on foam, this procedure is certainly a limitation however hardly avoidable because repetition of stance trials produces significant adaptation in the balancing pattern (8, 127, 177–180). Alsubaie et al. (181) have recently shown that different measures of postural sway are reliable when recorded at two visits 1 week apart, including measures with unstable BoS and sensory conditions. We do not know whether the frequencies might change as a function of the viewing scene (the characteristics of the patterned environment or the visual target being close or far) or of the position, texture, and orientation with respect to the body of the force pad, or of the force exerted by the finger. Further, the effect of the inner mechanical spring-like properties of the foam on the recorded signal has not been addressed, thereby preventing quantitative considerations on the role of proprioception standing on foam (or on solid BoS as well) and its potential interaction with vision and touch. Moreover, the feet position has not been manipulated, contrary to Šarabon et al. (82), who however found no major difference in the oscillation frequencies across different positions.

No estimation of the role of the vestibular information is provided here (182, 183), and no measure of the displacement in space of body segments such as the head and the pelvis. The information from the plantar foot sole, certainly different between foam and solid BoS, must have played a role. It has been proposed that our perception of verticality on a compliant surface, dependent in part on the plantar foot mechanoreceptor input, decreases when vision is not available (39, 184). We made no attempt to assess the contribution of these receptors. Electrical activity of the muscles involved in the control of equilibrium under the tested conditions has not been recorded, either. This information would help define the coordination properties underpinning the changes in oscillation frequency prescribed by the sensory conditions and the factors leading to the specific power spectrum features of postural sway. Moreover, this preliminary investigation is limited to young adult healthy subjects, and no information on the behaviour of aged healthy persons (185–187) or of patients with equilibrium disorders has been collected and analysed in these conditions according to this methodology (188).

CONCLUSION

The data suggest that the oscillation frequency analysis, in spite of its relative complexity, gives information on the control mode of critical stance exerted by different sensory inputs, not supplied by common and simpler geometric sway measures. The use of foam highlighted a significant increase in medium-high frequencies with touch in the absence of vision compared to vision alone. In perspective, the approach based on the analysis of distinct windows in the frequency spectrum of the body oscillations would help postulate the existence, and define the respective mechanisms, of the specific process through which different sensory information contributes to body stabilisation under critical conditions (31). Differences in balance control between young and older subjects would also be easily defined and exploited as a measure of balance alterations in patients due to impairments of various origins (189–192).

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article. Further inquiries can be directed to the authors upon reasonable request.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Comitato Tecnico Scientifico Ethics Board at the ICS Maugeri SB (Institute of Care and Research, IRRCS). All subjects provided written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

MS conceived the idea for the manuscript. SS performed the recruitment of participants and the collection of data. SS and MS performed the data analysis and drafted the article. AN revised it critically for important intellectual content. All authors approved the submitted version.

FUNDING

The funding for this study was provided by the Ricerca Corrente of the Italian Ministry of Health.

ACKNOWLEDGMENTS

The authors would like to thank the ICS Maugeri SB, Pavia, Italy, that helped make this work possible.

REFERENCES

1. Honeine JL, Schieppati M. Time-interval for integration of stabilizing haptic and visual information in subjects balancing under static and dynamic conditions. *Front Syst Neurosci.* (2014) 8:190. doi: 10.3389/fnsys.2014.00190
2. Forbes PA, Chen A, Blouin JS. Sensorimotor control of standing balance. *Handb Clin Neurol.* (2018) 159:61–83. doi: 10.1016/B978-0-444-63916-5.00004-5
3. Peterka RJ. Sensory integration for human balance control. *Handb Clin Neurol.* (2018) 159:27–42. doi: 10.1016/B978-0-444-63916-5.00002-1

4. Schieppati M, Hugon M, Grasso M, Nardone A, Galante M. The limits of equilibrium in young and elderly normal subjects and in parkinsonians. *Electroencephalogr Clin Neurophysiol.* (1994) 93:286–98. doi: 10.1016/0168-5597(94)90031-0
5. Nardone A, Tarantola J, Giordano A, Schieppati M. Fatigue effects on body balance. *Electroencephalogr Clin Neurophysiol.* (1997) 105:309–20. doi: 10.1016/S0924-980X(97)00040-4
6. Masani K, Popovic MR, Nakazawa K, Kouzaki M, Nozaki D. Importance of body sway velocity information in controlling ankle extensor activities during quiet stance. *J Neurophysiol.* (2003) 90:3774–82. doi: 10.1152/jn.00730.2002
7. Morasso P. Centre of pressure versus centre of mass stabilization strategies: the tightrope balancing case. *R Soc Open Sci.* (2020) 7:200111. doi: 10.1098/rsos.200111
8. Lhomond O, Juan B, Fornerone T, Cossin M, Paleressompoulle D, Prince F, et al. Learned overweight internal model can be activated to maintain equilibrium when tactile cues are uncertain: evidence from cortical and behavioral approaches. *Front Hum Neurosci.* (2021) 15:635611. doi: 10.3389/fnhum.2021.635611
9. Sakanaka TE, Lakie M, Reynolds RF. idiosyncratic characteristics of postural sway in normal and perturbed standing. *Front Hum Neurosci.* (2021) 15:660470. doi: 10.3389/fnhum.2021.660470
10. Svensson I, Gao C, Halder A, Gard G, Magnusson M. Standing balance on inclined surfaces with different friction. *Ind Health.* (2018) 56:292–99. doi: 10.2486/indhealth.2018-0005
11. Cleworth TW, Carpenter MG. Postural threat influences conscious perception of postural sway. *Neurosci Lett.* (2016) 620:127–31. doi: 10.1016/j.neulet.2016.03.032
12. Teasdale N, Stelmach GE, Breunig A. Postural sway characteristics of the elderly under normal and altered visual and support surface conditions. *J Gerontol.* (1991) 46:B238–44. doi: 10.1093/geronj/46.6.B238
13. Patel M, Fransson PA, Johansson R, Magnusson M. Foam posturography: standing on foam is not equivalent to standing with decreased rapidly adapting mechanoreceptive sensation. *Exp Brain Res.* (2011) 208:519–27. doi: 10.1007/s00221-010-2498-6
14. Hsiao D, Belur P, Myers PS, Earhart GM, Rawson KS. The impact of age, surface characteristics, and dual-tasking on postural sway. *Arch Gerontol Geriatr.* (2020) 87:103973. doi: 10.1016/j.archger.2019.103973
15. Johansson J, Nordström A, Gustafson Y, Westling G, Nordström P. Increased postural sway during quiet stance as a risk factor for prospective falls in community-dwelling elderly individuals. *Age Ageing.* (2017) 46:964–70. doi: 10.1093/ageing/afx083
16. Anson E, Bigelow RT, Studenski S, Deshpande N, Agrawal Y. Failure on the foam eyes closed test of standing balance associated with reduced semicircular canal function in healthy older adults. *Ear Hear.* (2019) 40:340–44. doi: 10.1097/AUD.0000000000000619
17. Kapoula Z, Lê TT. Effects of distance and gaze position on postural stability in young and old subjects. *Exp Brain Res.* (2006) 173:438–45. doi: 10.1007/s00221-006-0382-1
18. Horlings CG, Küng UM, Bloem BR, Honegger F, Van Alfen N, Van Engelen BG, et al. Identifying deficits in balance control following vestibular or proprioceptive loss using posturographic analysis of stance tasks. *Clin Neurophysiol.* (2008) 119:2338–46. doi: 10.1016/j.clinph.2008.07.221
19. Morrison S, Rynders CA, Sosnoff JJ. Deficits in medio-lateral balance control and the implications for falls in individuals with multiple sclerosis. *Gait Posture.* (2016) 49:148–54. doi: 10.1016/j.gaitpost.2016.06.036
20. Allum JH, Carpenter MG. A speedy solution for balance and gait analysis: angular velocity measured at the centre of body mass. *Curr Opin Neurol.* (2005) 18:15–21. doi: 10.1097/00019052-200502000-00005
21. Amblard B, Crémieux J, Marchand AR, Carblanc A. Lateral orientation and stabilization of human stance: static versus dynamic visual cues. *Exp Brain Res.* (1985) 61:21–37. doi: 10.1007/BF00235617
22. Day BL, Steiger MJ, Thompson PD, Marsden CD. Effect of vision and stance width on human body motion when standing: implications for afferent control of lateral sway. *J Physiol.* (1993) 469:479–99. doi: 10.1113/jphysiol.1993.sp019824
23. Nardone A, Schieppati M. The role of instrumental assessment of balance in clinical decision making. *Eur J Phys Rehabil Med.* (2010) 46:221–37.
24. Šarabon N, Rosker J, Loefler S, Kern H. Sensitivity of body sway parameters during quiet standing to manipulation of support surface size. *J Sports Sci Med.* (2010) 9:431–8.
25. Goodworth AD, Mellodge P, Peterka RJ. Stance width changes how sensory feedback is used for multisegmental balance control. *J Neurophysiol.* (2014) 112:525–42. doi: 10.1152/jn.00490.2013
26. Wang Z, Newell KM. Inter-foot coordination dynamics of quiet standing postures. *Neurosci Biobehav Rev.* (2014) 47:194–202. doi: 10.1016/j.neubiorev.2014.08.007
27. Bove M, Bonzano L, Trompetto C, Abbruzzese G, Schieppati M. The postural disorientation induced by neck muscle vibration subsides on lightly touching a stationary surface or aiming at it. *Neuroscience.* (2006) 143:1095–103. doi: 10.1016/j.neuroscience.2006.08.038
28. Kabbaligere R, Lee BC, Layne CS. Balancing sensory inputs: sensory reweighting of ankle proprioception and vision during a bipedal posture task. *Gait Posture.* (2017) 52:244–50. doi: 10.1016/j.gaitpost.2016.12.009
29. Lord SR, Menz HB. Visual contributions to postural stability in older adults. *Gerontology.* (2000) 46:306–10. doi: 10.1159/000022182
30. De Nunzio AM, Schieppati M. Time to reconfigure balancing behaviour in man: changing visual condition while riding a continuously moving platform. *Exp Brain Res.* (2007) 178:18–36. doi: 10.1007/s00221-006-0708-z
31. Lee IC, Pacheco MM, Newell KM. Constraints specific influences of vision, touch and surface compliance in postural dynamics. *Gait Posture.* (2018) 59:117–21. doi: 10.1016/j.gaitpost.2017.09.014
32. Fitzpatrick R, Rogers DK, McCloskey DI. Stable human standing with lower-limb muscle afferents providing the only sensory input. *J Physiol.* (1994) 480:395–403. doi: 10.1113/jphysiol.1994.sp020369
33. Fitzpatrick RC, Gorman RB, Burke D, Gandevia SC. Postural proprioceptive reflexes in standing human subjects: bandwidth of response and transmission characteristics. *J Physiol.* (1992) 458:69–83. doi: 10.1113/jphysiol.1992.sp019406
34. Gatev P, Thomas S, Kepple T, Hallett M. Feedforward ankle strategy of balance during quiet stance in adults. *J Physiol.* (1999) 514:915–28. doi: 10.1111/j.1469-7793.1999.915ad.x
35. Courtine G, De Nunzio AM, Schmid M, Beretta MV, Schieppati M. Stance- and locomotion-dependent processing of vibration-induced proprioceptive inflow from multiple muscles in humans. *J Neurophysiol.* (2007) 97:772–9. doi: 10.1152/jn.00764.2006
36. Gritti I, Schieppati M. Short-latency inhibition of soleus motoneurones by impulses in Ia afferents from the gastrocnemius muscle in humans. *J Physiol.* (1989) 416:469–84. doi: 10.1113/jphysiol.1989.sp017772
37. Bussel B, Morin C, Pierrot-Deseilligny E. Mechanism of monosynaptic reflex reinforcement during jendrassik manoeuvre in man. *J Neurol Neurosurg Psychiatry.* (1978) 41:40–4. doi: 10.1136/jnnp.41.1.40
38. Leukel C, Lundbye-Jensen J, Gruber M, Zuur AT, Gollhofer A, Taube W. Short-term pressure induced suppression of the short-latency response: a new methodology for investigating stretch reflexes. *J Appl Physiol.* (2009) 107:1051–8. doi: 10.1152/japplphysiol.00301.2009
39. Nedelkou A, Hatzitaki V, Chatzinikolaou K, Grouios G. Does somatosensory feedback from the plantar foot sole contribute to verticality perception? *Somatosens Mot Res.* (2021) 13:1–9. doi: 10.1080/08990220.2021.1949977
40. Felicetti G, Thoumie P, Do MC, Schieppati M. Cutaneous and muscular afferents from the foot and sensory fusion processing: physiology and pathology in neuropathies. *J Peripher Nerv Syst.* (2021) 26:17–34. doi: 10.1111/jns.12429
41. Schieppati M, Nardone A, Siliotto R, Grasso M. Early and late stretch responses of human foot muscles induced by perturbation of stance. *Exp Brain Res.* (1995) 105:411–22. doi: 10.1007/BF00233041
42. Roll JP, Vedel JP, Ribot E. Alteration of proprioceptive messages induced by tendon vibration in man: a microneurographic study. *Exp Brain Res.* (1989) 76:213–22. doi: 10.1007/BF00253639
43. Nardone A, Schieppati M. Group II spindle fibres and afferent control of stance. Clues from diabetic neuropathy. *Clin Neurophysiol.* (2004) 115:779–89. doi: 10.1016/j.clinph.2003.11.007
44. Bove M, Trompetto C, Abbruzzese G, Schieppati M. The posture-related interaction between Ia-afferent and descending input on the spinal reflex excitability in humans. *Neurosci Lett.* (2006) 397:301–6. doi: 10.1016/j.neulet.2005.12.049

45. Nardone A, Giordano A, Corrà T, Schieppati M. Responses of leg muscles in humans displaced while standing. Effects of types of perturbation and of postural set. *Brain.* (1990) 113 (Pt. 1):65–84. doi: 10.1093/brain/113.1.65
46. Schieppati M, Nardone A. Free and supported stance in Parkinson's disease. The effect of posture and 'postural set' on leg muscle responses to perturbation, and its relation to the severity of the disease. *Brain.* (1991) 114 (Pt. 3):1227–44. doi: 10.1093/brain/114.3.1227
47. Lackner JR. The importance of being in touch. *Front Neurol.* (2021) 12:646640. doi: 10.3389/fneur.2021.646640
48. De Nunzio AM, Nardone A, Schieppati M. Head stabilization on a continuously oscillating platform: the effect of a proprioceptive disturbance on the balancing strategy. *Exp Brain Res.* (2005) 165:261–72. doi: 10.1007/s00221-005-2297-7
49. Fransson PA, Gomez S, Patel M, Johansson L. Changes in multi-segmented body movements and EMG activity while standing on firm and foam support surfaces. *Eur J Appl Physiol.* (2007) 101:81–9. doi: 10.1007/s00421-007-0476-x
50. Mademli L, Mavridi D, Bohm S, Patikas DA, Santuz A, Arampatzis A. Standing on unstable surface challenges postural control of tracking tasks and modulates neuromuscular adjustments specific to task complexity. *Sci Rep.* (2021) 11:6122. doi: 10.1038/s41598-021-84899-y
51. Allum JH, Pfaltz CR. Visual and vestibular contributions to pitch sway stabilization in the ankle muscles of normals and patients with bilateral peripheral vestibular deficits. *Exp Brain Res.* (1985) 58:82–94. doi: 10.1007/BF00238956
52. Sozzi S, Honeine JL, Do MC, Schieppati M. Leg muscle activity during tandem stance and the control of body balance in the frontal plane. *Clin Neurophysiol.* (2013) 124:1175–86. doi: 10.1016/j.clinph.2012.12.001
53. Jeka J, Kiemel T, Creath R, Horak F, Peterka R. Controlling human upright posture: velocity information is more accurate than position or acceleration. *J Neurophysiol.* (2004) 92:2368–79. doi: 10.1152/jn.00983.2003
54. Horlings CG, Küng UM, Honegger F, Van Engelen BG, Van Alfen N, Bloem BR, et al. Vestibular and proprioceptive influences on trunk movements during quiet standing. *Neuroscience.* (2009) 161:904–14. doi: 10.1016/j.neuroscience.2009.04.005
55. Hsu WL, Scholz JP, Schöner G, Jeka JJ, Kiemel T. Control and estimation of posture during quiet stance depends on multijoint coordination. *J Neurophysiol.* (2007) 97:3024–35. doi: 10.1152/jn.01142.2006
56. Zhang Y, Kiemel T, Jeka J. The influence of sensory information on two-component coordination during quiet stance. *Gait Posture.* (2007) 26:263–71. doi: 10.1016/j.gaitpost.2006.09.007
57. Kelly LA, Kuitunen S, Racinais S, Cresswell AG. Recruitment of the plantar intrinsic foot muscles with increasing postural demand. *Clin Biomech.* (2012) 27:46–51. doi: 10.1016/j.clinbiomech.2011.07.013
58. Holden M, Ventura J, Lackner JR. Stabilization of posture by precision contact of the index finger. *J Vestib Res.* (1994) 4:285–301.
59. Jeka JJ, Lackner JR. Fingertip contact influences human postural control. *Exp Brain Res.* (1994) 100:495–502. doi: 10.1007/BF02738408
60. Jeka JJ, Lackner JR. The role of haptic cues from rough and slippery surfaces in human postural control. *Exp Brain Res.* (1995) 103:267–76. doi: 10.1007/BF00231713
61. Wing AM, Johannsen L, Endo S. Light touch for balance: influence of a time-varying external driving signal. *Philos Trans R Soc Lond B Biol Sci.* (2011) 366:3133–41. doi: 10.1098/rstb.2011.0169
62. Sozzi S, Do MC, Monti A, Schieppati M. Sensorimotor integration during stance: processing time of active or passive addition or withdrawal of visual or haptic information. *Neuroscience.* (2012) 212:59–76. doi: 10.1016/j.neuroscience.2012.03.044
63. Honeine JL, Crisafulli O, Sozzi S, Schieppati M. Processing time of addition or withdrawal of single or combined balance-stabilizing haptic and visual information. *J Neurophysiol.* (2015) 114:3097–110. doi: 10.1152/jn.00618.2015
64. Rocha-Silva C, Magalhães FH, Kohn AF. Fingertip-Coupled spindle signaling does not contribute to reduce postural sway under light touch. *Front Physiol.* (2019) 10:1072. doi: 10.3389/fphys.2019.01072
65. Kouzaki M, Masani K. Reduced postural sway during quiet standing by light touch is due to finger tactile feedback but not mechanical support. *Exp Brain Res.* (2008) 188:153–8. doi: 10.1007/s00221-008-1426-5
66. Sozzi S, Crisafulli O, Schieppati M. Haptic cues for balance: use of a cane provides immediate body stabilization. *Front Neurosci.* (2017) 11:705. doi: 10.3389/fnins.2017.00705
67. Prado-Rico JM, Alouche SR, Sodré AC, Garbus RBSC, Freitas SMSF. Effect of force magnitude of touch on the components of postural sway. *Gait Posture.* (2018) 65:15–19. doi: 10.1016/j.gaitpost.2018.06.164
68. Dickstein R. Stance stability with unilateral and bilateral light touch of an external stationary object. *Somatosens Mot Res.* (2005) 22:319–25. doi: 10.1080/08990220500420640
69. Afzal MR, Byun HY, Oh MK, Yoon J. Effects of kinesthetic haptic feedback on standing stability of young healthy subjects and stroke patients. *J Neuroeng Rehabil.* (2015) 12:27. doi: 10.1186/s12984-015-0020-x
70. Kaulmann D, Saveriano M, Lee D, Hermsdörfer J, Johannsen L. Stabilization of body balance with light touch following a mechanical perturbation: adaption of sway and disruption of right posterior parietal cortex by cTBS. *PLoS ONE.* (2020) 15:e0233988. doi: 10.1371/journal.pone.0233988
71. Shiva T, Misiaszek JE. Activation of ankle muscles following rapid displacement of a light touch contact during treadmill walking. *Exp Brain Res.* (2018) 236:563–576. doi: 10.1007/s00221-017-5151-9
72. Albertsen IM, Temprado JJ, Berton E. Effect of haptic supplementation provided by a fixed or mobile stick on postural stabilization in elderly people. *Gerontology.* (2012) 58:419–29. doi: 10.1159/000337495
73. Bolton DA, McIlroy WE, Staines WR. The impact of light fingertip touch on haptic cortical processing during a standing balance task. *Exp Brain Res.* (2011) 212:279–91. doi: 10.1007/s00221-011-2728-6
74. Ernst MO, Banks MS. Humans integrate visual and haptic information in a statistically optimal fashion. *Nature.* (2002) 415:429–33. doi: 10.1038/415429a
75. Lacey S, Sathian K. Crossmodal and multisensory interactions between vision and touch. *Scholarpedia.* (2015) 10:7957. doi: 10.4249/scholarpedia.7957
76. Camponogara I, Volcic R. Integration of haptics and vision in human multisensory grasping. *Cortex.* (2021) 135:173–85. doi: 10.1016/j.cortex.2020.11.012
77. Jeannerod M. Intersegmental coordination during reaching at natural visual objects. In: Long J, Baddeley A, editors. *Attention Performance IX*. Hillsdale, MI: Erlbaum (1981). p. 153–68.
78. Ruhe A, Fejer R, Walker B. The test-retest reliability of centre of pressure measures in bipedal static task conditions - a systematic review of the literature. *Gait Posture.* (2010) 32:436–45. doi: 10.1016/j.gaitpost.2010.09.012
79. Yamamoto T, Smith CE, Suzuki Y, Kiyono K, Tanahashi T, Sakoda S, et al. Universal and individual characteristics of postural sway during quiet standing in healthy young adults. *Physiol Rep.* (2015) 3:e12329. doi: 10.14814/phy2.12329
80. Marchese R, Bove M, Abbruzzese G. Effect of cognitive and motor tasks on postural stability in Parkinson's disease: a posturographic study. *Mov Disord.* (2003) 18:652–8. doi: 10.1002/mds.10418
81. Fitzgerald JE, Murray A, Elliott C, Birchall JP. Comparison of body sway analysis techniques. Assessment with subjects standing on a stable surface. *Acta Otolaryngol.* (1994) 114:115–9. doi: 10.3109/00016489409126028
82. Šarabon N, Rosker J, Loefler S, Kern H. The effect of vision elimination during quiet stance tasks with different feet positions. *Gait Posture.* (2013) 38:708–11. doi: 10.1016/j.gaitpost.2013.03.005
83. Bergamin M, Gobbo S, Zanotto T, Sieverdes JC, Alberton CL, Zaccaria M, et al. Influence of age on postural sway during different dual-task conditions. *Front Aging Neurosci.* (2014) 6:271. doi: 10.3389/fnagi.2014.00271
84. Schmid M, Nardone A, De Nunzio AM, Schmid M, Schieppati M. Equilibrium during static and dynamic tasks in blind subjects: no evidence of cross-modal plasticity. *Brain.* (2007) 130 (Pt. 8):2097–107. doi: 10.1093/brain/awm157
85. Zatsiorsky VM, Duarte M. Rambling and trembling in quiet standing. *Motor Control.* (2000) 4:185–200. doi: 10.1123/mcj.4.2.185
86. Yamagata M, Popow M, Latash ML. Beyond rambling and trembling: effects of visual feedback on slow postural drift. *Exp Brain Res.* (2019) 237:865–71. doi: 10.1007/s00221-019-05470-w
87. Bottaro A, Casadio M, Morasso PG, Sanguineti V. Body sway during quiet standing: is it the residual chattering of an intermittent stabilization process? *Hum Mov Sci.* (2005) 24:588–615. doi: 10.1016/j.humov.2005.07.006

88. Duarte M, Freitas MSF, Zatsiorsky V. Control of equilibrium in humans. Sway over sway. In: Danion F, Latash M, editors. *Motor Control: Theories, Experiments, and Applications*. Oxford: Oxford University Press (2011). p. 219–42. doi: 10.1093/acprof:oso/9780195395273.003.0010
89. Collins JJ, De Luca CJ. Open-loop and closed-loop control of posture: a random-walk analysis of center-of-pressure trajectories. *Exp Brain Res.* (1993) 95:308–18. doi: 10.1007/BF00229788
90. Rougier PR. What insights can be gained when analysing the resultant centre of pressure trajectory? *Neurophysiol Clin.* (2008) 38:363–73. doi: 10.1016/j.neucli.2008.09.006
91. Lacour M, Bernard-Demanze L, Dumitrescu M. Posture control, aging, and attention resources: models and posture-analysis methods. *Neurophysiol Clin.* (2008) 38:411–21. doi: 10.1016/j.neucli.2008.09.005
92. Potvin-Desrochers A, Richer N, Lajoie Y. Cognitive tasks promote automatization of postural control in young and older adults. *Gait Posture.* (2017) 57:40–5. doi: 10.1016/j.gaitpost.2017.05.019
93. St-Amant G, Rahman T, Polskaia N, Fraser S, Lajoie Y. Unveilling the cerebral and sensory contributions to automatic postural control during dual-task standing. *Hum Mov Sci.* (2020) 70:102587. doi: 10.1016/j.humov.2020.102587
94. Roerdink M, De Haart M, Daffertshofer A, Donker SF, Geurts AC, Beek PJ. Dynamical structure of center-of-pressure trajectories in patients recovering from stroke. *Exp Brain Res.* (2006) 174:256–69. doi: 10.1007/s00221-006-0441-7
95. King AC, Patton J, Dutt-Mazumder A, Newell KM. Center-of-pressure dynamics of upright standing as a function of sloped surfaces and vision. *Neurosci Lett.* (2020) 737:135334. doi: 10.1016/j.neulet.2020.135334
96. Schumann T, Redfern MS, Furman JM, El-Jaroudi A, Chaparro LF. Time-frequency analysis of postural sway. *J Biomech.* (1995) 28:603–7. doi: 10.1016/0021-9290(94)00113-I
97. Hufschmidt A, Dichgans J, Mauritz KH, Hufschmidt M. Some methods and parameters of body sway quantification and their neurological applications. *Arch Psychiatr Nervenkr.* (1980) 228:135–50. doi: 10.1007/BF00365601
98. Singh NB, Taylor WR, Madigan ML, Nussbaum MA. The spectral content of postural sway during quiet stance: influences of age, vision and somatosensory inputs. *J Electromyogr Kinesiol.* (2012) 22:131–6. doi: 10.1016/j.jelekin.2011.10.007
99. Kanekar N, Lee YJ, Aruin AS. Frequency analysis approach to study balance control in individuals with multiple sclerosis. *J Neurosci Methods.* (2014) 222:91–6. doi: 10.1016/j.jneumeth.2013.10.020
100. Tanabe H, Fujii K, Kouzaki M. Large postural fluctuations but unchanged postural sway dynamics during tiptoe standing compared to quiet standing. *J Electromyogr Kinesiol.* (2012) 22:975–82. doi: 10.1016/j.jelekin.2012.05.006
101. Golomer E, Dupui P, Bessou P. Spectral frequency analysis of dynamic balance in healthy and injured athletes. *Arch Int Physiol Biochim Biophys.* (1994) 102:225–9. doi: 10.3109/13813459409007543
102. Paillard T, Noé F, Rivière T, Marion V, Montoya R, Dupui P. Postural performance and strategy in the unipedal stance of soccer players at different levels of competition. *J Athl Train.* (2006) 41:172–6.
103. Tanaka S, Ando K, Kobayashi K, Nakashima H, Seki T, Ishizuka S, et al. Locomotive syndrome and the power spectral characteristics of body sway. *Geriatr Gerontol Int.* (2020) 20:691–6. doi: 10.1111/ggi.13937
104. Nagy E, Toth K, Janositz G, Kovacs G, Feher-Kiss A, Angyan L, et al. Postural control in athletes participating in an ironman triathlon. *Eur J Appl Physiol.* (2004) 92:407–13. doi: 10.1007/s00421-004-1157-7
105. Diaz-Artiles A, Karmali F. Vestibular precision at the level of perception, eye movements, posture, and neurons. *Neuroscience.* (2021) 468:282–320. doi: 10.1016/j.neuroscience.2021.05.028
106. Mezzarane RA, Kohn AF. Postural control during kneeling. *Exp Brain Res.* (2008) 187:395–405. doi: 10.1007/s00221-008-1308-x
107. Hlavačka F, Njiokiktjien C. Sinusoidal galvanic stimulation of the labyrinths and postural responses. *Physiol Bohemoslov.* (1986) 35:63–70.
108. Bonnet CT. Advantages and disadvantages of stiffness instructions when studying postural control. *Gait Posture.* (2016) 46:208–10. doi: 10.1016/j.gaitpost.2015.12.026
109. Stoffregen TA, Smart LJ, Bardy BG, Pagulayan RJ. Postural stabilization of looking. *J. Exp. Psychol. Hum. Percept. Performa.* (1999) 25:1641–58. doi: 10.1037/0096-1523.25.6.1641
110. Michalak K, Jaśkowski P. Dimensional complexity of posturographic signals: I. Optimization of frequency sampling and recording time. *Curr Topics Biophys.* (2002) 26:235–44.
111. Vieira TM, Oliveira LF, Nadal J. Estimation procedures affect the center of pressure frequency analysis. *Braz J Med Biol Res.* (2009) 42:665–73. doi: 10.1590/S0100-879X2009000700012
112. Scoppa F, Capra R, Gallamini M, Shiffer R. Clinical stabilometry standardization: basic definitions–acquisition interval–sampling frequency. *Gait Posture.* (2013) 37:290–2. doi: 10.1016/j.gaitpost.2012.07.009
113. Schubert P, Kirchner M. Ellipse area calculations and their applicability in posturography. *Gait Posture.* (2014) 39:518–22. doi: 10.1016/j.gaitpost.2013.09.001
114. Jurkojć J. Balance disturbances coefficient as a new value to assess ability to maintain balance on the basis of FFT curves. *Acta Bioeng Biomech.* (2018) 20:143–51.
115. Sozzi S, Monti A, De Nunzio AM, Do MC, Schieppati M. Sensori-motor integration during stance: time adaptation of control mechanisms on adding or removing vision. *Hum Mov Sci.* (2011) 30:172–89. doi: 10.1016/j.humov.2010.06.002
116. Taguchi K. Spectral analysis of body sway. *ORL J Otorhinolaryngol Relat Spec.* (1977) 39:330–7. doi: 10.1159/000275375
117. Krizková M, Hlavačka F, Gatev P. Visual control of human stance on a narrow and soft support surface. *Physiol Res.* (1993) 42:267–72.
118. Nakagawa H, Ohashi N, Watanabe Y, Mizukoshi K. The contribution of proprioception to posture control in normal subjects. *Acta Otolaryngol. Suppl.* (1993) 504:112–6. doi: 10.3109/00016489309128134
119. Demura S, Kitabayashi T. Comparison of power spectrum characteristics of body sway during a static upright standing posture in healthy elderly people and young adults. *Percept Mot Skills.* (2006) 102:467–76. doi: 10.2466/pms.102.2.467-476
120. Demura S, Kitabayashi T, Noda M. Power spectrum characteristics of sway position and velocity of the center of pressure during static upright posture for healthy people. *Percept Mot Skills.* (2008) 106:307–16. doi: 10.2466/pms.106.1.307-316
121. Morrison S, Kerr G, Newell KM, Silburn PA. Differential time- and frequency-dependent structure of postural sway and finger tremor in Parkinson's disease. *Neurosci Lett.* (2008) 443:123–8. doi: 10.1016/j.neulet.2008.07.071
122. Schinkel-Ivy A, Singer JC, Inness EL, Mansfield A. Do quiet standing centre of pressure measures within specific frequencies differ based on ability to recover balance in individuals with stroke? *Clin Neurophysiol.* (2016) 127:2463–71. doi: 10.1016/j.clinph.2016.02.021
123. Krafczyk S, Schlamp V, Dieterich M, Haberhauer P, Brandt T. Increased body sway at 3.5-8 Hz in patients with phobic postural vertigo. *Neurosci Lett.* (1999) 259:149–52. doi: 10.1016/S0304-3940(98)00917-3
124. Anagnostou E, Stavropoulou G, Zachou A, Kararizou E. Spectral composition of body sway in persistent postural-perceptual dizziness. *Otol Neurotol.* (2021) 42:e1318–26. doi: 10.1097/MAO.0000000000003252
125. Creath R, Kiemel T, Horak F, Peterka R, Jeka JJ. A unified view of quiet and perturbed stance: simultaneous co-existing ankle and hip strategies. *Neurosci Lett.* (2005) 377:75–80. doi: 10.1016/j.neulet.2004.11.071
126. Winter DA, Prince F, Frank JS, Powell C, Zabjek KF. Unified theory regarding A/P and M/L balance in quiet stance. *J Neurophysiol.* (1996) 75:2334–43. doi: 10.1152/jn.1996.75.6.2334
127. Tarantola J, Nardone A, Tacchini E, Schieppati M. Human stance stability improves with the repetition of the task: effect of foot position and visual condition. *Neurosci Lett.* (1997) 228:75–8. doi: 10.1016/S0304-3940(97)00370-4
128. Mezzarane RA, Kohn AF. Control of upright stance over inclined surfaces. *Exp Brain Res.* (2007) 180:377–88. doi: 10.1007/s00221-007-0865-8
129. Cawsey RP, Chua R, Carpenter MG, Sanderson DJ. To what extent can increasing the magnification of visual feedback of the centre of pressure position change the control of quiet standing balance? *Gait Posture.* (2009) 29:280–4. doi: 10.1016/j.gaitpost.2008.09.007
130. Lubetzky-Vilnai A, McCoy SW, Price R, Ciol MA. Young adults largely depend on vision for postural control when standing on a

BOSU ball but not on foam. *J Strength Cond Res.* (2015) 29:2907–18. doi: 10.1519/JSC.0000000000000935
131. Thurrell A, Jáuregui-Renaud K, Gresty MA, Bronstein AM. Vestibular influence on the cardiorespiratory responses to whole-body oscillation after standing. *Exp Brain Res.* (2003) 150:325–31. doi: 10.1007/s00221-003-1422-8
132. Lackner JR, DiZio P, Jeka J, Horak F, Krebs D, Rabin E. Precision contact of the fingertip reduces postural sway of individuals with bilateral vestibular loss. *Exp Brain Res.* (1999) 126:459–66. doi: 10.1007/s002210050753
133. Creath R, Kiemel T, Horak F, Jeka JJ. The role of vestibular and somatosensory systems in intersegmental control of upright stance. *J Vestib Res.* (2008) 18:39–49. doi: 10.3233/VES-2008-18104
134. Honegger F, Tielkens RJ, Allum JH. Movement strategies and sensory reweighting in tandem stance: differences between trained tightrope walkers and untrained subjects. *Neuroscience.* (2013) 254:285–300. doi: 10.1016/j.neuroscience.2013.09.041
135. Chen FC, Tsai CL. The mechanisms of the effect of light finger touch on postural control. *Neurosci Lett.* (2015) 605:69–73. doi: 10.1016/j.neulet.2015.08.016
136. Johannsen L, Coward SRL, Martin GR, Wing AM, Casteren AV, Sellers WI, et al. Human bipedal instability in tree canopy environments is reduced by "light touch" fingertip support. *Sci Rep.* (2017) 7:1135. doi: 10.1038/s41598-017-01265-7
137. Clapp S, Wing AM. Light touch contribution to balance in normal bipedal stance. *Exp Brain Res.* (1999) 125:521–4. doi: 10.1007/s002210050711
138. Huang CY, Cherng RJ, Yang ZR, Chen YT, Hwang IS. Modulation of soleus H reflex due to stance pattern and haptic stabilization of posture. *J Electromyogr Kinesiol.* (2009) 19:492–9. doi: 10.1016/j.jelekin.2007.07.014
139. Bryanton MA, Chodan SDC, Vander Meulen J, Fenrich KK, Misiaszek JE. The effect of light touch on standing sway when the stability of the external touch reference becomes unreliable. *Exp Brain Res.* (2019) 237:663–72. doi: 10.1007/s00221-018-5455-4
140. Rabin E, Bortolami SB, DiZio P, Lackner JR. Haptic stabilization of posture: changes in arm proprioception and cutaneous feedback for different arm orientations. *J Neurophysiol.* (1999) 82:3541–9. doi: 10.1152/jn.1999.82.6.3541
141. Lee IC, Pacheco MM, Newell KM. Postural coordination and control to the precision demands of light finger touch. *Exp Brain Res.* (2019) 237:1339–46. doi: 10.1007/s00221-019-05513-2
142. Krishnamoorthy V, Slijper H, Latash ML. Effects of different types of light touch on postural sway. *Exp Brain Res.* (2002) 147:71–9. doi: 10.1007/s00221-002-1206-6
143. Conrad V, Vitello MP, Noppeney U. Interactions between apparent motion rivalry in vision and touch. *Psychol Sci.* (2012) 23:940–8. doi: 10.1177/0956797612438735
144. Janko M, Primerano R, Visell Y. On frictional forces between the finger and a textured surface during active touch. *IEEE Trans Haptics.* (2016) 9:221–32. doi: 10.1109/TOH.2015.2507583
145. Rogers MW, Wardman DL, Lord SR, Fitzpatrick RC. Passive tactile sensory input improves stability during standing. *Exp Brain Res.* (2001) 136:514–22. doi: 10.1007/s002210000615
146. Sozzi S, Decortes F, Schmid M, Crisafulli O, Schieppati M. Balance in blind subjects: cane and fingertip touch induce similar extent and promptness of stance stabilization. *Front Neurosci.* (2018) 12:639. doi: 10.3389/fnins.2018.00639
147. Goyal N, Lee Y, Luna G, Aruin AS. Individual and combined effects of a cognitive task, light finger touch, and vision on standing balance in older adults with mild cognitive impairment. *Aging Clin Exp Res.* (2020) 32:797–807. doi: 10.1007/s40520-019-01262-y
148. Andreopoulou G, Maaswinkel E, Cofré Lizama LE, van Dieën JH. Effects of support surface stability on feedback control of trunk posture. *Exp Brain Res.* (2015) 233:1079–87. doi: 10.1007/s00221-014-4185-5
149. Jergelová M, Podivinský F. Some conceptual remarks about supraspinal mechanisms in the control of voluntary and reflex motor activities. *Electromyogr Clin Neurophysiol.* (1992) 32:537–46.
150. Nardone A, Pasetti C, Schieppati M. Spinal and supraspinal stretch responses of postural muscles in early parkinsonian patients. *Exp Neurol.* (2012) 237:407–17. doi: 10.1016/j.expneurol.2012.07.003
151. Macaluso E, Maravita A. The representation of space near the body through touch and vision. *Neuropsychologia.* (2010) 48:782–95. doi: 10.1016/j.neuropsychologia.2009.10.010
152. Taube W, Schubert M, Gruber M, Beck S, Faist M, Gollhofer A. Direct corticospinal pathways contribute to neuromuscular control of perturbed stance. *J Appl Physiol.* (2006) 101:420–9. doi: 10.1152/japplphysiol.01447.2005
153. Bolton DA, Brown KE, McIlroy WE, Staines WR. Transient inhibition of the dorsolateral prefrontal cortex disrupts somatosensory modulation during standing balance as measured by electroencephalography. *Neuroreport.* (2012) 23:369–72. doi: 10.1097/WNR.0b013e328352027c
154. Mierau A, Pester B, Hülsdünker T, Schiecke K, Strüder HK, Witte H. Cortical correlates of human balance control. *Brain Topogr.* (2017) 30:434–46. doi: 10.1007/s10548-017-0567-x
155. Malcolm BR, Foxe JJ, Joshi S, Verghese J, Mahoney JR, Molholm S, et al. Aging-related changes in cortical mechanisms supporting postural control during base of support and optic flow manipulations. *Eur J Neurosci.* (2020). 1–19. doi: 10.1111/ejn.15004
156. Kim S, James TW. Enhanced effectiveness in visuo-haptic object-selective brain regions with increasing stimulus salience. *Hum Brain Mapp.* (2010) 31:678–93. doi: 10.1002/hbm.20897
157. Magre FL, Costa TDAD, Paiva ACS, Moraes R, Mauerberg-deCastro E. Does the level of difficulty in balancing tasks affect haptic sensitivity via light touch? *J Mot Behav.* (2020) 52:1–12. doi: 10.1080/00222895.2019.1565529
158. Kilby MC, Molenaar PC, Newell KM. Models of postural control: shared variance in joint and COM motions. *PLoS ONE.* (2015) 10:e0126379. doi: 10.1371/journal.pone.0126379
159. Sprenger A, Wojak JF, Jandl NM, Helmchen C. Postural control in bilateral vestibular failure: its relation to visual, proprioceptive, vestibular, and cognitive input. *Front Neurol.* (2017) 8:444. doi: 10.3389/fneur.2017.00444
160. Bacsi AM, Colebatch JG. Evidence for reflex and perceptual vestibular contributions to postural control. *Exp Brain Res.* (2005) 160:22–8. doi: 10.1007/s00221-004-1982-2
161. Carpenter MG, Murnaghan CD, Inglis JT. Shifting the balance: evidence of an exploratory role for postural sway. *Neuroscience.* (2010) 171:196–204. doi: 10.1016/j.neuroscience.2010.08.030
162. Reynard F, Christe D, Terrier P. Postural control in healthy adults: determinants of trunk sway assessed with a chest-worn accelerometer in 12 quiet standing tasks. *PLoS ONE.* (2019) 14:e0211051. doi: 10.1371/journal.pone.0211051
163. Knikou M, Rymer Z. Effects of changes in hip joint angle on H-reflex excitability in humans. *Exp Brain Res.* (2002) 43:149–59. doi: 10.1007/s00221-001-0978-4
164. Kiers H, Brumagne S, van Dieën J, van der Wees P, Vanhees L. Ankle proprioception is not targeted by exercises on an unstable surface. *Eur J Appl Physiol.* (2012) 112:1577–85. doi: 10.1007/s00421-011-2124-8
165. Ivanenko YP, Talis VL, Kazennikov OV. Support stability influences postural responses to muscle vibration in humans. *Eur J Neurosci.* (1999) 11:647–54. doi: 10.1046/j.1460-9568.1999.00471.x
166. Hatzitaki V, Pavlou M, Bronstein AM. The integration of multiple proprioceptive information: effect of ankle tendon vibration on postural responses to platform tilt. *Exp Brain Res.* (2004) 154:345–54. doi: 10.1007/s00221-003-1661-8
167. Franzén E, Gurfinkel VS, Wright WG, Cordo PJ, Horak FB. Haptic touch reduces sway by increasing axial tone. *Neuroscience.* (2011) 174:216–23. doi: 10.1016/j.neuroscience.2010.11.017
168. Warnica MJ, Weaver TB, Prentice SD, Laing AC. The influence of ankle muscle activation on postural sway during quiet stance. *Gait Posture.* (2014) 39:1115–21. doi: 10.1016/j.gaitpost.2014.01.019
169. van Dieën JH, van Drunen P, Happee R. Sensory contributions to stabilization of trunk posture in the sagittal plane. *J Biomech.* (2018) 70:219–27. doi: 10.1016/j.jbiomech.2017.07.016
170. Gandevia SC, Hall LA, McCloskey DI, Potter EK. Proprioceptive sensation at the terminal joint of the middle finger. *J Physiol.* (1983) 335:507–17. doi: 10.1113/jphysiol.1983.sp014547

171. Monteleone S, Feltroni L, Arbustini E, Bernardi E, Carenzio G, Dalla Toffola E Schieppati M. Balance in patients with Marfan syndrome. *Transl Sci Rare Dis.* (2018) 3:145–56. doi: 10.3233/TRD-180029
172. Yiou E, Hussein T, Larue J. Influence of temporal pressure on anticipatory postural control of medio-lateral stability during rapid leg flexion. *Gait Posture.* (2012) 35:494–9. doi: 10.1016/j.gaitpost.2011.11.015
173. Osoba MY, Rao AK, Agrawal SK, Lalwani AK. Balance and gait in the elderly: A contemporary review. *Laryngoscope Investig Otolaryngol.* (2019) 4:143–53. doi: 10.1002/lio2.252
174. Embrechts E, Van Criekinge T, Schröder J, Nijboer T, Lafosse C, Truijen S, et al. The association between visuospatial neglect and balance and mobility post-stroke onset: a systematic review. *Ann Phys Rehabil Med.* (2021) 64:101449. doi: 10.1016/j.rehab.2020.10.003
175. Shin S, Milosevic M, Chung CM, Lee Y. Contractile properties of superficial skeletal muscle affect postural control in healthy young adults: a test of the rambling and trembling hypothesis. *PLoS ONE.* (2019) 14:e0223850. doi: 10.1371/journal.pone.0223850
176. Michaud L, Richer N, Lajoie Y. Number of trials needed to assess postural control of young adults in single and dual-task. *J Mot Behav.* (2021) 53:30–9. doi: 10.1080/00222895.2020.1723479
177. Sozzi S, Nardone A, Schieppati M. Adaptation of balancing behaviour during continuous perturbations of stance. Supra-postural visual tasks and platform translation frequency modulate adaptation rate. *PLoS ONE.* (2020) 15:e0236702. doi: 10.1371/journal.pone.0236702
178. Keller M, Pfusterschmied J, Buchecker M, Müller E, Taube W. Improved postural control after slackline training is accompanied by reduced H-reflexes. *Scand J Med Sci Sports.* (2012) 22:471–7. doi: 10.1111/j.1600-0838.2010.01268.x
179. Kiss R, Brueckner D, Muehlbauer T. Effects of single compared to dual task practice on learning a dynamic balance task in young adults. *Front Psychol.* (2018) 9:311. doi: 10.3389/fpsyg.2018.00311
180. Beurskens R, Brueckner D, Muehlbauer T. Effects of motor versus cognitive task prioritization during dual-task practice on dual-task performance in young adults. *Front Psychol.* (2020) 11:581225. doi: 10.3389/fpsyg.2020.581225
181. Alsubaie SF, Whitney SL, Furman JM, Marchetti GF, Sienko KH, Sparto PJ. Reliability of postural sway measures of standing balance tasks. *J Appl Biomech.* (2018) 10:1–23. doi: 10.1123/jab.2017-0322
182. Fujimoto C, Kamogashira T, Kinoshita M, Egami N, Sugasawa K, Demura S, et al. Power spectral analysis of postural sway during foam posturography in patients with peripheral vestibular dysfunction. *Otol Neurotol.* (2014) 35:e317–23. doi: 10.1097/MAO.0000000000000554
183. Rasman BG, Forbes PA, Tisserand R, Blouin JS. Sensorimotor manipulations of the balance control loop-beyond imposed external perturbations. *Front Neurol.* (2018) 9:899. doi: 10.3389/fneur.2018.00899
184. Viseux F, Lemaire A, Barbier F, Charpentier P, Leteneur S, Villeneuve P. How can the stimulation of plantar cutaneous receptors improve postural control? Review and clinical commentary. *Neurophysiol Clin.* (2019) 49:263–8. doi: 10.1016/j.neucli.2018.12.006
185. Tremblay F, Mireault AC, Dessureault L, Manning H, Sveistrup H. Postural stabilization from fingertip contact: I. Variations in sway attenuation, perceived stability and contact forces with aging. *Exp Brain Res.* (2004) 157:275–85. doi: 10.1007/s00221-004-1830-4
186. Tremblay F, Mireault AC, Dessureault L, Manning H, Sveistrup H. Postural stabilization from fingertip contact II. Relationships between age, tactile sensibility and magnitude of contact forces. *Exp Brain Res.* (2005) 164:155–64. doi: 10.1007/s00221-005-2238-5
187. Fujimoto C, Egami N, Demura S, Yamasoba T, Iwasaki S. The effect of aging on the center-of-pressure power spectrum in foam posturography. *Neurosci Lett.* (2015) 585:92–7. doi: 10.1016/j.neulet.2014.11.033
188. Pauelsen M, Jafari H, Strandkvist V, Nyberg L, Gustafsson T, Vikman I, et al. Frequency domain shows: fall-related concerns and sensorimotor decline explain inability to adjust postural control strategy in older adults. *PLoS One.* (2020) 15:e0242608. doi: 10.1371/journal.pone.0242608
189. Yoneda S, Tokumasu K. Frequency analysis of body sway in the upright posture. Statistical study in cases of peripheral vestibular disease. *Acta Otolaryngol.* (1986) 102:87–92. doi: 10.3109/00016488609108650
190. Baloh RW, Jacobson KM, Beykirch K, Honrubia V. Static and dynamic posturography in patients with vestibular and cerebellar lesions. *Arch Neurol.* (1998) 55:649–54. doi: 10.1001/archneur.55.5.649
191. Fino PC, Horak FB, El-Gohary M, Guidarelli C, Medysky ME, Nagle SJ, et al. Postural sway, falls, and self-reported neuropathy in aging female cancer survivors. *Gait Posture.* (2019) 69:136–42. doi: 10.1016/j.gaitpost.2019.01.025
192. Nagy E, Feher-Kiss A, Barnai M, Domján-Preszner A, Angyan L, Horvath G. Postural control in elderly subjects participating in balance training. *Eur J Appl Physiol.* (2007) 100:97–104. doi: 10.1007/s00421-007-0407-x

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Human Neuroscience

ORIGINAL RESEARCH
published: 09 December 2021
doi: 10.3389/fnhum.2021.777776

Kinematic Changes in the Uninjured Limb After a Traumatic Brachial Plexus Injury

*Lidiane Souza[1,2], Luiggi Lustosa[1,2], Ana Elisa Lemos Silva[2], José Vicente Martins[2], Thierry Pozzo[3] and Claudia D. Vargas[1,2]**

[1] Laboratório de Neurobiologia do Movimento, Instituto de Biofísica Carlos Chagas Filho – Universidade Federal Rio de Janeiro, Rio de Janeiro, Brazil, [2] Núcleo de Pesquisa em Neurociências e Reabilitação, Instituto de Neurologia Deolindo Couto – Universidade Federal Rio de Janeiro, Rio de Janeiro, Brazil, [3] INSERM UMR 1093-CAPS, Université Bourgogne Franche-Comté, UFR des Sciences du Sport, Dijon, France

Background: Traumatic brachial plexus injury (TBPI) typically causes sensory, motor and autonomic deficits of the affected upper limb. Recent studies have suggested that a unilateral TBPI can also affect the cortical representations associated to the uninjured limb.

Objective: To investigate the kinematic features of the uninjured upper limb in participants with TBPI.

Methods: Eleven participants with unilateral TBPI and twelve healthy controls matched in gender, age and anthropometric characteristics were recruited. Kinematic parameters collected from the index finger marker were measured while participants performed a free-endpoint whole-body reaching task and a cup-to-mouth task with the uninjured upper limb in a standing position.

Results: For the whole-body reaching task, lower time to peak velocity ($p = 0.01$), lower peak of velocity ($p = 0.003$), greater movement duration ($p = 0.04$) and shorter trajectory length ($p = 0.01$) were observed in the TBPI group compared to the control group. For the cup-to-mouth task, only a lower time to peak velocity was found for the TBPI group compared to the control group ($p = 0.02$). Interestingly, no differences between groups were observed for the finger endpoint height parameter in either of the tasks. Taken together, these results suggest that TBPI leads to a higher cost for motor planning when it comes to movements of the uninjured limb as compared to healthy participants. This cost is even higher in a task with a greater postural balance challenge.

Conclusion: This study expands the current knowledge on bilateral sensorimotor alterations after unilateral TBPI and should guide rehabilitation after a peripheral injury.

Keywords: kinematic analysis, motor planning, brachial plexus, uninjured limb, upper limb, peripheral nerve injury

OPEN ACCESS

Edited by:
Paolo Cavallari, University of Milan, Italy

Reviewed by:
Milad Nazarahari, University of Waterloo, Canada
Noureddin Nakhostin Ansari, Tehran University of Medical Sciences, Iran

***Correspondence:**
Claudia D. Vargas
cdvargas@biof.ufrj.br

Specialty section:
This article was submitted to Motor Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *15 September 2021*
Accepted: *18 November 2021*
Published: *09 December 2021*

Citation:
Souza L, Lustosa L, Silva AEL, Martins JV, Pozzo T and Vargas CD (2021) Kinematic Changes in the Uninjured Limb After a Traumatic Brachial Plexus Injury. Front. Hum. Neurosci. 15:777776. doi: 10.3389/fnhum.2021.777776

INTRODUCTION

The brachial plexus comprises a dense network of spinal nerves originating from vertebrae C5 to T1. Traumatic brachial plexus injury (TBPI) is more commonly found in young adults involved in motorcycle accidents (Faglioni et al., 2014), and typically causes sensory, motor and autonomic deficits of the affected upper limb (Resnick, 1995). The injury can partially or entirely affect

the brachial plexus nerve roots (C5-T1) (Dubuisson and Kline, 2002; Moran et al., 2005). As a consequence, proximal shoulder and elbow flexor muscles are those most susceptible to paralysis and sensory loss (Özkan and Aydin, 2001), with the degree of sensorimotor dysfunction varying as a function of the lesion extent and severity (Crouch et al., 2016). Although complete reconstruction of the damaged peripheral nerve pathways is not possible, complex reconstructive surgeries (Noland et al., 2019) and physical therapy (Kinlaw, 2005; Milicin and Sîrbu, 2018; Rich et al., 2019; Chagas et al., 2021) are often performed to restore the motor function of the affected upper limb.

Employing posturographic measurement, Souza et al. (2016) found that TBPI affects body balance, suggesting that the consequences of TBPI on motor control are not restricted to the injured upper limb. Webber et al. (2019) showed that TBPI patients display a greater range of motion of the trunk accompanied by limited shoulder external rotation while performing activities of daily living with the injured arm. In a similar way, Nazarahari et al. (2020) found increased trunk motion when the injured shoulder was performing flexion/extension and abduction/adduction as compared with the uninjured side. These results point toward plastic modifications of the motor plan after a TBPI in respect of upper limb movements, presenting a potential challenge to postural balance.

In another line of evidence, several studies have demonstrated that TBPI is capable of promoting structural and functional modifications in the sensory (S1) and motor (M1) primary cortices contralateral and ipsilateral to the affected side (Mano et al., 1995; Malessy et al., 1998; Beaulieu et al., 2006; Anastakis et al., 2008; Taylor et al., 2009; Davis et al., 2011; Jaggi and Singh, 2011; Yoshikawa et al., 2012; Liu et al., 2013; Fraiman et al., 2016; Lu et al., 2016; Amini et al., 2018; Torres et al., 2018; Fischmeister et al., 2020). Liu et al. (2013) observed changes in interhemispheric connectivity between motor areas, while Fraiman et al. (2016) observed reduced functional connectivity in the representation of the trunk and upper limbs bilaterally in M1, suggesting that TBPI might result in alterations of motor control beyond the affected limb. Recently, Rangel et al. (2021) investigated the occurrence of prediction markers in anticipation of observed sensorimotor events in individuals with upper trunk TBPI. The results showed that TBPI specifically affected the ability to predict upcoming tactile events for the dominant limb. Furthermore, TBPI blurred the prediction markers of upcoming movements in the sensorimotor cortex contralateral to the uninjured limb, indicating that higher order plastic effects might occur following a peripheral sensorimotor loss. This evidence therefore suggests that kinematic changes in the uninjured limb occur after a TBPI.

Kinematic parameters of goal-directed actions have long been shown to reflect their motor plan (Bernstein, 1967; Soechting and Lacquaniti, 1981; Marteniuk et al., 1987; Papaxanthis et al., 1998; Desmurget et al., 1999; Svoboda and Li, 2018). The motor plan encodes where the reach will land on average (the endpoint) and the expected movement duration (Wolpert and Landy, 2012). Several studies have shown that reaching movements display regularities such as typical straight trajectories and bell-shaped velocity profiles (Bernstein, 1967; Atkeson and Hollerbach, 1985; Flash and Hogan, 1985; Marteniuk et al., 1987; Soechting and Flanders, 1991). Duration is an important kinematic component because of the speed-accuracy tradeoff, with movements that take more time to execute being spatially more accurate (Wolpert and Landy, 2012). In addition, Marteniuk et al. (1987) showed that when the task demands greater precision (grasping versus pointing, for example), the duration of the deceleration phase of the trajectory is increased as a consequence of the greater demand for sensory feedback to perform the task.

Motion analysis after TBPI has been used in the clinical context in order to quantify compensatory trunk movements and shoulder dysfunction, and thus help prioritize secondary surgical targets (Webber et al., 2019; Nazarahari et al., 2020). Webber et al. (2019) identified compensatory trunk movements accompanied by limited external rotation of the shoulder when individuals with TBPI performed feeding and dressing tasks. The authors concluded that the restoration of external rotation of the shoulder would be a beneficial secondary target of surgical recovery of motor function. In addition to being a tool for objective outcome evaluation of TBPI and its biomechanical consequences, motion analysis also allows inferences about motor planning aspects to be made through calculation of spatiotemporal variables. Kinematic analysis can thus be profitably used to explore further changes in motor planning after a TBPI. Since bilateral alterations in the sensorimotor cortex have been reported to occur after a TBPI (Liu et al., 2013; Fraiman et al., 2016; Ramalho et al., 2019) our conjecture is that an unilateral TBPI might lead to changes in the motor plan of both limbs. To our knowledge no investigation has focused specifically on the kinematics of the uninjured limb. Measuring the kinematics of the uninjured limb might reveal changes in the motor plan of the upper limbs induced by TBPI and help to guide rehabilitation programs.

The main objective of this cross-sectional study was to investigate the kinematic features of the uninjured upper limb in participants with TBPI. Specifically, we analyzed the kinematic parameters of movement performed with the uninjured upper limb of individuals with TBPI in a free-endpoint whole-body reaching task. This task allows the subjects to freely choose their final hand position, introducing a spatial ambiguity and exposing the subject to a number of subjective choices (Haggard, 2008; Andersen and Cui, 2009; Berret et al., 2011; Hilt et al., 2016). Furthermore, this task presents a postural challenge that allows the investigation of the individual strategies used to choose a suitable hand trajectory toward the target while conserving postural balance (Flanders et al., 1999; Hilt et al., 2016). In addition, we introduced a new task (bringing a cup to the mouth) to investigate the association between the postural component and motor planning in individuals with TBPI, as this task requires minimal trunk displacement. We hypothesized that kinematic features of the uninjured upper limb would be affected by a unilateral TBPI as compared to healthy individuals.

MATERIALS AND METHODS

Participants

Patients with TBPI were recruited from a database (Patroclo et al., 2019) maintained by the Laboratory of Neuroscience

and Rehabilitation of the Institute of Neurology Deolindo Couto of the Federal University of Rio de Janeiro from June 2018 to September 2019. This database contains patients' epidemiological, physical and clinical information collected by a multidisciplinary team through digital questionnaires. The following inclusion criteria were applied: age between 18 and 50 years, right-handed (Oldfield, 1971) before the lesion and with unilateral TBPI, diagnosed by clinical evaluation and/or complementary exams. Individuals were excluded if they presented other neurological injuries, a Mini-Mental State Exam (Folstein et al., 1975; Brucki et al., 2003) score below 24, visual loss or uncorrected visual impairment. Upper extremity function after a TBPI was measured using the version of the Disabilities of the Arm, Shoulder and Hand questionnaire (DASH) adapted to Brazilian Portuguese (Orfale et al., 2005). The DASH is composed of 30 questions that address the ability to perform upper extremity activities and the severity of symptoms (Hudak et al., 1996). Each question is scored on a scale from 1 to 5, with a total score rate from 0 to 100. A higher score reflects greater disability.

All participants were informed about the experimental procedures and provided a written consent form before the tests. The procedures were approved by the ethics committee of the Institute of Neurology Deolindo Couto, the Federal University of Rio de Janeiro (process number: 1.375.64).

Experimental Procedure

Whole-Body Reaching Task

The experimental protocol was adapted from the study by Hilt et al. (2016). From a standing position, the participants were asked to perform a series of reaching movements toward a homogenous surface upon which no specific endpoint was drawn. This surface (2.0 m high × 0.9 m wide) consisted of a white plastic screen positioned at an angle of 15° from the vertical, located at a distance of 120% of the arm's length from the surface of their shoulder (measured from the acromion to the apex of the index finger). The distance and angle were chosen to allow a significant reaching distance, requiring the controlled maintenance of equilibrium without placing subjects beyond the limits of their balance (**Figure 1A**; Hilt et al., 2016). Thus, changes in the kinematic metrics could be attributed to the combined motions of the uninjured limb and trunk. The participants were positioned on a rigid surface while their feet were positioned hip-width apart and parallel to the sagittal plane. Reflective markers (15 mm in diameter) were placed in the apex of the right and the left index fingers.

Participants were instructed to remain facing forward, without turning their body, and with their arms relaxed at their sides. The task was to point toward the apparatus using their arm (left and right) starting from three different initial positions: position 1 (P1), arm relaxed next to the body; position 2 (P2), elbow flexed at 90° forward from the side of the body; position 3 (P3), elbow flexed with the hand at shoulder height. Starting from each of the initial postures the participant was instructed to point toward the apparatus with their index finger at a comfortable speed when they heard a "beep" (**Figure 1C**).

Six trials (2 per position) were performed as training and the data were not included in the analysis. The reaching tasks were separated into blocks: two blocks were performed with the right upper limb and two blocks were performed with the left upper limb. For TBPI participants, the first two blocks were performed with the uninjured limb, and the last two blocks with the injured limb. Each block contained 24 trials (8 for each start position), totaling 96 trials for each participant.

The initial position sequence could be fixed or variable within a block. We defined as a fixed sequence the consecutive order: P1, P2, and P3. In the variable sequence there was a 20% chance of P3 being altered by P2. The participants performed the task in the following order: 1 block of fixed sequence and 1 block of a variable sequence. TBPI patients only performed the task with their injured upper limb if they were able to adopt and maintain the initial positions. To avoid muscle fatigue participants had intervals of 5 mins between blocks.

The Cup-to-Mouth Task

We performed a supplementary experiment to investigate if a simple plastic cup-to-mouth task in a standing position might also cause changes in the kinematic profile in individuals with TBPI. From a standing position, with both arms relaxed by their sides and holding a plastic cup in the moving hand, the participants were asked to perform a series of three different tasks illustrated by showing them a picture projected (Epson PowerLit S18+®, Epson, Japan) onto a white wall of an actor doing the following tasks: task 1, keep the arm straight close to the body while holding the cup; task 2, flex the elbow at 90° while holding the cup without any pause in the movement and return to the position in task 1; and task 3, bring the cup to the mouth and immediately return to the position in task 1 (**Figure 1B**). The picture illustrating the task was shown to the participant for 5 s, in which time they were told to perform the task. They then had to wait for the next picture, which was shown after the exhibition of a fixation cross for 5 s (**Figure 1D**).

These tasks were also separated into two blocks performed with the right/uninjured upper limb and two blocks performed with the left/injured upper limb for both sequence conditions. Each block contained 24 trials (8 for each task), totaling 96 trials for each participant. Only the data collected in task 3 will be considered in this study, as our goal was to compare the kinematic results of this task with those found in the whole-body reaching task.

Data Acquisition and Analysis

Movements in three axes (mediolateral, X, antero-posterior, Y and vertical, Z) were recorded at 100 Hz using Vicon Nexus software version 2.2 (Vicon Motion Systems Ltd, Vicon, United States) and a seven-camera motion capture system with 1 Megapixel resolution (Vicon Bonita 10, Vicon, United States). The triaxial coordinate time series of the index finger reflective markers were recorded. The sequence of initial positions was generated using the software Presentation® (Neurobehavioral System, United States). Data acquisition was synchronized with the stimulus presentation through a synchronizer (Vicon Lock).

Pre-processing was performed using Vicon Nexus 2.2 software. The index finger marker triaxial coordinates were

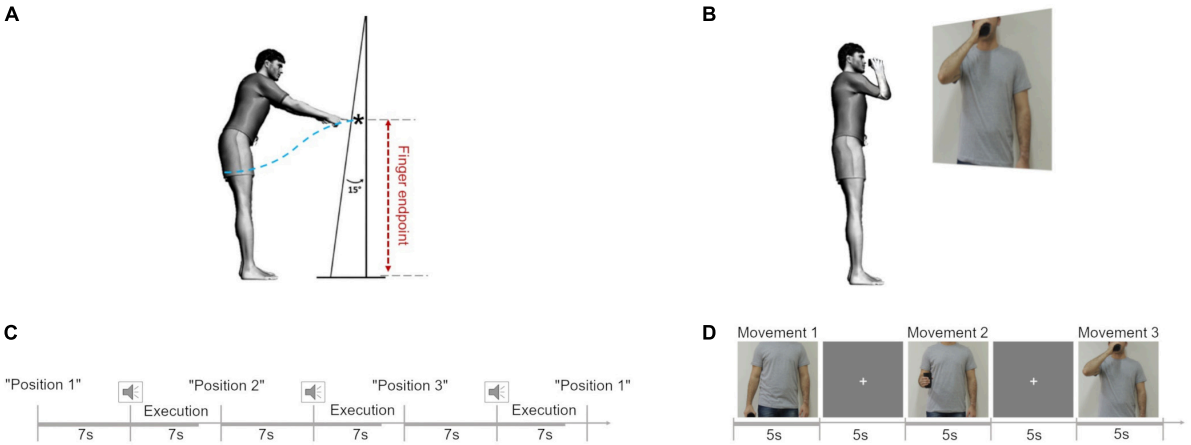

FIGURE 1 | Experimental protocol. **(A)** Movement trajectory length (blue dotted line) and finger endpoint (black star) during the reaching in position 1 (P1). Adapted from Hilt et al. (2016). **(B)** Cup-to-mouth task. **(C)** Schematic representation of the fixed stimuli sequence in the reaching task. **(D)** Schematic representation of the sequence of stimuli in the cup-to-mouth task.

reconstructed and analyzed offline using Matlab software (R2015a, Mathworks Inc., Natick, MA, United States). As the index finger describes a curved trajectory, we estimated index finger speed by its tangential velocity ($\vec{v}$) in relation to the path. For each instant of time, the tangential velocity ($\vec{v}(t)$) is calculated by multiplying the sampling frequency (f_s) to the magnitude of index finger displacement vector ($|\Delta\vec{r}|$), which corresponds to the index finger displacement in 3-D space.

$$\vec{v}\,(t) \;=\; |\Delta\vec{r}| \;\cdot\; f_s$$

The 3-D reconstruction of the tangential velocity profile was estimated and subsequently filtered with a 5th-order low pass filter at 10 Hz cutoff. The movement was divided in two phases: (I) from the initial position to the target (apparatus or mouth) and (II) returning from the target to initial position. The onset of each phase was calculated using 5% of peak velocity (PV) as a threshold value. The same threshold was used to detect the end of each phase, i.e., when the tangential velocity dropped below the 5% of peak velocity (Esteves et al., 2016). Peaks and valleys were detected and marked along the velocity profile of each trial, and each phase of the movement consisted of two valleys and a peak. Phase I was separated for analysis and the tangential velocity profile was time-normalized by a linear interpolation of 200 points. Discrepant velocity profile shapes in each trial for each condition were detected through visual inspection, marked and excluded from the analysis.

Outcome Measures

The following dependent variables were calculated for the index finger marker:

- **Vertical Finger Endpoint (VFE)**: index finger endpoint measured on the vertical axis normalized by the height of the participant.
- **Horizontal Finger Endpoint (HFE)**: index finger endpoint measured on the horizontal axis normalized by the upper limb length.
- **Movement Duration (MD)**: the time interval between the onset and offset of the reach movement.
- **Trajectory Length (TL)**: the distance traveled by the index finger marker during the reaching movement.
- **Peak Velocity (PV)**: the maximal velocity attained for each participant in the reaching movement.
- **Time to Peak Velocity (TPV)**: the ratio between the acceleration duration and movement duration. A TPV index greater than 0.5 indicates that acceleration duration was longer than the deceleration duration for the reach movement; conversely, a TPV index less than 0.5 indicates that deceleration duration was longer than the acceleration duration for the reach movement. TPV is the kinematic parameter of the movement considered as providing optimal information about motor plans (Marteniuk et al., 1987; Sartori et al., 2011).

Statistical Analysis

All the analyzed kinematic variables displayed normal distribution (Kolmogorov-Smirnov calculated $p \leq 0.05$). A paired T test was performed to compare the kinematic parameters collected from the right versus the left upper limb in the control group. No significant difference was observed ($p > 0.05$). Therefore, the kinematic values obtained for each arm (i.e., left and right) were averaged per control subject to perform statistical analysis. Kinematic analysis of the TBPI group corresponds to the uninjured upper limb recording, since only three participants succeeded in performing the tasks with the injured limb. A Mann Whitney U test was applied by comparing the kinematic measures of left and right uninjured sides to verify the existence of injury side effects.

A three-way mixed model ANOVA was performed with event sequence (fixed sequence vs. variable sequence), initial position

(P1 vs. P2 vs. P3) and group (TBPI vs. control) as independent variables for each kinematic parameter. The level of significance was set at 5%. No main effects were observed for event sequence, so they were removed from the model, leaving a two-way model with the other two factors. A two-way mixed model ANOVA was applied with group and initial position as factors. Tukey's post-hoc analysis was subsequently applied. All statistical analyses were performed using STATISTICA version 10 (Statsoft Inc., United States). Post-hoc power analyses were conducted using G*Power software (Erdfelder et al., 1996), with $\alpha = 0.05$, two-tailed, to check the statistical power of our results.

RESULTS

Participants

From an initial group of 12 participants with TBPI, 11 individuals (2 females) matched the pre-established criteria. The TBPI group exhibited the following characteristics: median age, 35 years of age (range 22–43); median height 174 cm (range 152–184); and median weight 75 kg (range 39–105). Four participants had left arm and seven right arm TBPI (**Table 1**). A control group of 12 healthy individuals matched in gender, age and physical characteristics was recruited for the study with the following characteristics: median age, 28 years of age (range 19–48); median height 178 (153–190); and median weight 77 kg (52–101). Anthropometric measures and age were similar between the groups (Mann-Whitney tests $p > 0.05$ for all comparisons).

The characteristics of the individuals with TBPI are presented in **Table 1**. From eleven participants included in the TBPI group, four had complete (C5–T1) and seven had partial TBPI. Ten participants with TBPI had undergone surgical reconstruction of the brachial plexus and only one had not undergone any surgical procedure. The median time elapsed from the injury to participation in the experimental protocol was 48 (range: 4–116) months. The median DASH score was 45.0 (range: 25.0–59.5; **Table 1**). Only three individuals in the TBPI group were able to perform the tasks with the injured arm (data not analyzed).

Kinematic Parameters for Whole-Body Reaching Task

The kinematic analysis of the uninjured upper limb of the TBPI vs. control participants was evaluated by means of a two-way ANOVA. This analysis was performed with group (TBPI patients vs. control) and initial position (P1, P2, and P3) as independent variables for each kinematic parameter. The group comparison results are shown for the tangential velocity profile, movement duration, trajectory length and index finger end-point parameters.

Peak Velocity

Peak velocity was significantly lower for the TBPI group when compared to the control group [$F(1, 63) = 9.75$, $p = 0.003$; **Figure 2A** and **Table 2**]. Moreover, as expected, the PV differed in respect of the initial position [$F(2, 63) = 25.69$, $p < 0.001$; **Table 2**]. Post-hoc comparisons showed that all positions differed ($p < 0.01$). No significant interaction between group and initial position was found [$F(2, 63) = 0.1$, $p = 0.91$; **Table 2**]. With our sample size and effect size estimate for the PV variable, the post-hoc power analysis revealed a 51% power to detect a large effect size ($d = 0.87$) between groups.

Time to Peak Velocity

The TPV analysis revealed that the TBPI group had significantly lower values for this parameter than the control group [$F(1, 63) = 6.64$, $p = 0.01$], which means that the duration of the acceleration phase was shorter for the TBPI group when compared to the control group (**Figure 2A** and **Table 2**). Differences between the initial position for the TPV parameter were also observed [$F(2, 63) = 13.83$, $p < 0.001$]. Post-hoc analysis showed that P2 differed from the others (P1 and P3, $p < 0.01$; **Table 2**). No significant interaction between group and initial position was found [$F(2, 63) = 0.8$, $p = 0.46$; **Table 2**]. With our sample size and effect size estimate for the TPV variable, the post-hoc power analysis revealed a 75% power to detect a large effect size ($d = 1.17$) between groups.

TABLE 1 | Traumatic brachial plexus injury (TBPI) individual characteristics.

ID	Age	T1	Injured side	Diagnosis	T2	T3	Surgical Procedure	DASH
TBPI01	37	14	Left	C5–C7	5/8	9/6	Ac-SE/Oberlin	50.8
TBPI02	28	35	Left	C5–C7	3	32	Oberlin	27.5
TBPI03	42	41	Left	C5–C8, T1	3	38	INT–MSC, Ac–SE	43.3
TBPI04	35	51	Right	C5–C7	3	48	Ac–SE, Oberlin	59.5
TBPI05	39	54	Right	C5–C8, T1	11/13	43/41	INT–MSC/Ac–SE	30.0
TBPI06	27	27	Right	C5–C7	15	12	Ac–SE	–
TBPI07	38	116	Right	C5–C8, T1	6/15	110/101	INT–MSC/Ac–SE	59.2
TBPI08	43	53	Right	C5–C6	5	48	Ph-SE, Oberlin, and Tr-Ax	45.0
TBPI09	30	48	Right	C5–C8, T1	6	42	Ac-MSC	45.7
TBPI10	29	70	Left	C5–C7	5	65	Ac-SE and Oberlin	25.0
TBPI11	20	4	Right	Posterior Cord	–	–	None	–

Age in years; T1, time between the injury and the kinematic assessment in months; T2, time between the injury and the surgery in months; T3, time between the surgery and the kinematic assessment in months; Oberlin, ulnar nerve transfer to musculocutaneous nerve; INT–MSC, intercostal nerve transfer to musculocutaneous nerve; Ac–SE, accessory nerve transfer to suprascapular nerve; Ph-SE, phrenic nerve transfer to suprascapular nerve; Tr-Ax, medial triceps transfer to axillary nerve; Ac-MSC, accessory nerve transfer to musculocutaneous nerve; Disabilities of the Arm, Shoulder and Hand (DASH) was collected in 9 of the 11 participants.

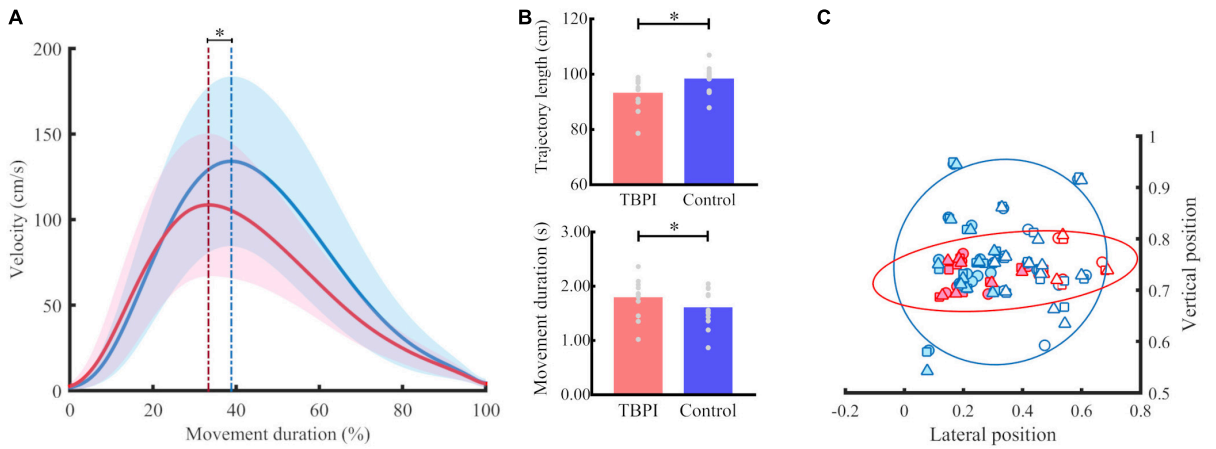

FIGURE 2 | Kinematic performance for groups. **(A)** Tangential velocity profile. Mean (continuous line) and standard deviation (shaded area) for the TBPI group in red and the control group in blue in the reaching phase. The blue dotted line indicates the peak of velocity of the control group and the red dotted line marks the peak velocity of the TBPI group. *$p < 0.05$. **(B)** Trajectory length and movement duration for TBPI (red bar) and control (blue bar) groups. The average of trials per subject is displayed as a gray dot. *$p < 0.05$. **(C)** Normalized finger endpoint in vertical and horizontal planes. The symbols represent the normalized average position of the index finger at the end of reaching per subject (TBPI in red, and control in blue) and per starting position (position 1 – circle, position 2 – square, position 3 – triangle). Left finger endpoints are plotted with colored dots, and the right ones with white dots. No significant differences between TBPI and control groups were found for normalized finger endpoint in vertical ($p = 0.99$) and horizontal planes ($p = 1.00$). The covariance data are shown through the 95% confidence ellipse for each group (TBPI – smallest diameter: 0.15, largest diameter: 0.90; Controls – smallest diameter: 0.40; largest diameter: 0.72).

TABLE 2 | Mean and standard deviation of the TBPI and control groups per initial position in the reaching task.

Kinematic parameters	TBPI group ($n = 11$)			Control group ($n = 12$)		
	P1	P2	P3	P1	P2	P3
Movement duration (s)	1.78 (0.40)	1.77 (0.36)	1.86 (0.37)	1.56 (0.35)	1.59 (0.35)	1.62 (0.36)
Trajectory length (cm)	111.40 (8.56)	69.27 (5.51)	96.07 (7.68)	120.10 (9.85)	73.67 (5.20)	99.68 (10.62)
Peak velocity (cm/s)	154.20 (36.21)	84.38 (21.80)	120.80 (27.51)	187.60 (40.27)	107.60 (30.22)	149.60 (48.34)
Time to peak velocity	0.30 (0.06)	0.42 (0.06)	0.33 (0.06)	0.37 (0.06)	0.44 (0.06)	0.38 (0.07)
Finger endpoint (V) (%H)	0.74 (0.03)	0.73 (0.03)	0.74 (0.03)	0.75 (0.08)	0.76 (0.08)	0.75 (0.09)
Finger endpoint (H) (%UL)	0.34 (0.18)	0.34 (0.19)	0.34 (0.19)	0.32 (0.15)	0.33 (0.15)	0.33 (0.15)

Vertical Finger Endpoint (VFE) expressed as a percentage of participant's height (%H); Horizontal Finger Endpoint (HFE) expressed as a percentage of participant's upper limb length (%UL).

Movement Duration

A main effect was found for the group [$F(1, 63) = 4.38$, $p = 0.04$]. The TBPI group showed greater MD compared to the control group (**Figure 2B** and **Table 2**). No other effects were observed for this parameter (see **Table 2**). With our sample size and effect size estimate for the MD variable, the post-hoc power analysis revealed a 27% power to detect a medium effect size ($d = 0.58$) between groups.

Trajectory Length

The TBPI group showed significantly shorter TL [$F(1, 63) = 6.3$, $p = 0.01$] compared to the control group (**Figure 2B** and **Table 2**). As expected, the TL differed between the initial position [$F(2,63) = 171.36$, $p < 0.001$] for all positions ($p < 0.01$; **Table 2**). No significant interaction between group and initial position was found [$F(2, 63) = 0.5$, $p = 0.61$; **Table 2**]. With our sample size and effect size estimate for the TL variable, the post-hoc power analysis revealed a 58% power to detect a large effect size ($d = 0.94$) between groups.

Finger Endpoint

No significant differences were found for the FE parameters for both the vertical [$F(1, 63) = 1.40$, $p = 0.24$] and horizontal [$F(1, 63) = 0.23$, $p = 0.63$] planes (**Figure 2C** and **Table 2**), although the TBPI participants seemed to exhibit a smaller variability in FE when compared to controls. No differences for initial position comparison were found for the VFE [$F(2, 63) = 0.01$, $p = 0.99$] and HFE [$F(2, 63) = 0$, $p = 1$] parameters (see **Table 2**).

Injury Side Effects

No difference was observed between left and right sides of TBPI except for the TPV parameter in P3 ($U = 0.00$, $p = 0.003$). With our sample size and effect size estimate for the TPV variable in the P3, the post-hoc power analysis revealed a 88% power to detect a large effect size ($d = 2.25$) between groups.

Kinematic Parameters for the Cup-to-Mouth Task

One-Way ANOVA was applied to compare those same kinematic parameters between the control and the TBPI groups in the cup-to-mouth task (**Supplementary Table 2**). The TBPI group was composed of the same eleven patients described in **Table 1**, and the control group was composed of nine out of the same twelve individuals tested in the pointing task. The TBPI group showed lower TPV (0.34 ± 0.04) compared to the control group (0.37 ± 0.02) [$F(1, 18) = 6.91$, $p = 0.02$]. No significant differences between groups were found for PV [$F(1, 18) = 3.3$, $p = 0.09$], MD [$F(1, 18) = 3.68$, $p = 0.07$], TL [$F(1, 18) = 2.65$, $p = 0.12$] and VFE [$F(1, 18) = 0.12$, $p = 0.73$]. With our sample size and effect size estimate for the TPV variable, the post-hoc power analysis revealed a 51% power to detect a large effect size ($d = 0.95$) between groups. No effect of injury side for the cup-to-mouth task was observed for any kinematic parameters.

DISCUSSION

We aimed to describe the kinematic features of the uninjured upper limb in participants with TBPI. As the free endpoint whole-body reaching task involves a greater postural challenge (Flanders et al., 1999; Hilt et al., 2016) compared to a simple cup-to-mouth task, we hypothesized that the effects of TBPI on the kinematics of the uninjured limb would be more evident in the former than in the latter task. Indeed, whereas lower TPV values were found in the TBPI group compared to the control group for both tasks, lower PV values, greater MD and shorter TLs were found in the TBPI group only for the reaching task.

Kinematic Changes in the Uninjured Limb: Time to Peak Velocity

For both tasks, a reduced TPV of the uninjured limb was found in the TBPI group compared to the control group. Shorter TPV values translate into a shorter period of acceleration followed by a longer deceleration period while performing the movement. This ratio provides information about the motor strategies used to control actions (Marteniuk et al., 1987; Papaxanthis et al., 1998; Sartori et al., 2011), since the deceleration phase duration increases with the task demand (Marteniuk et al., 1987). Rangel et al. (2021) have suggested that the plastic reorganization after TBPI is associated with modifications in motor planning. Changes in trunk representation, occurring bilaterally in M1 (Fraiman et al., 2016), in addition to balance impairment in adults with TBPI (Souza et al., 2016), could translate as greater motor cost to TBPI participants in performing both tasks in a standing position.

Hilt et al. (2016) showed that in healthy participants reducing the base of support leads to an increased deceleration phase in the TPV parameter. In the same way, the shortening of the acceleration phase and the lengthening of the deceleration phase in the TPV parameter found for both tasks in the present study could relate to the negative impact of TBPI on balance (Souza et al., 2016). A reduced TPV, favoring a lengthened control of the final portion of the reaching movement, could occur as a consequence of postural balance prioritization. Since the reduced TPV was also observed in the TPBI group in the cup-to-mouth task, then the mere control of upright posture could be challenging enough to impact the kinematics of the uninjured upper limb. In fact, although both tasks are performed in a standing posture, there are differences when it comes to their postural challenges.

The two tasks clearly differ in terms of the specific role of the trunk. In the whole-body task, there is a dynamic role for the trunk in assisting the upper limb movement (Hilt et al., 2016), whereas in the cup-to-mouth task the trunk functions rather as a stabilizer, allowing a relative independence of the upper limb movement (Flanders et al., 1999; Hilt et al., 2016). Crucially, the two tasks also clearly differ in the task demand imposed over postural control, being much higher for the whole-body task (Hilt et al., 2016). Thus, the augmented need of postural control imposed by the whole-body task could explain the higher number of altered kinematic parameters observed amongst TBPI participants.

Since a reduced TPV was found for both tasks in the TBPI group, it is reasonable to suppose that the longer deceleration phase would reflect an alteration in the motor plan related more generically to movements of the uninjured limb. Conversely, for the whole-body reaching task there could be a postural balance component associated more specifically with the other kinematic alterations, as discussed below.

Kinematic Changes in Uninjured Upper Limb: Other Kinematic Parameters

In the whole-body reaching task, the participant has to choose a suitable hand trajectory toward the target while keeping postural balance (Flanders et al., 1999; Hilt et al., 2016). These task constraints can affect both movement planning and execution compared to reaching from a standing position without trunk displacement. Marteniuk et al. (1987) observed that reaching tasks demanding higher precision were executed with longer movement duration and a prolonged deceleration phase (when compared to the acceleration phase). Considering that reaching movements show an initial ballistic phase and a subsequent controlling phase in which fine adjustments are made to successfully achieve the task goal (Desmurget and Grafton, 2000), it is reasonable to think that tasks with higher precision requirements demand more sensory feedback control during the movement deceleration phase (Marteniuk et al., 1987).

Besides the effects of TBPI on the TPV parameter, we found lower PV values and longer MD in the TBPI group compared to the control group when performing the whole-body reaching task. These results are similar to those found

by Callegari et al. (2018) who reported that during an upper limb pointing task, individuals in postural positions with less trunk stability showed longer movement duration and lower peak velocity. These effects might indicate greater difficulty in planning upper limb movements (Callegari et al., 2018).

Individuals with TBPI have also exhibited a reduction in TL of the index finger. A reduced trajectory length might reflect detriment in the correlation between trunk and limbs angular displacement (Stapley et al., 1999; Berret et al., 2009). This possibility seems supported by the fact that, although not statistically significant, TPBI end point appeared more compact and more precise than controls, suggesting that the task goal (virtual target to reach) is achieved despite a deterioration of coordination between the arm and the trunk. Moreover, upper limb kinematics was shown to be equilibrium-dependent (Stapley et al., 1999; Berret et al., 2009). For instance, Paizis et al. (2008) found a reduction of wrist trajectory length in young adults in equilibrium restriction conditions similar to those observed in older adult individuals without postural restrictions. The authors proposed that such a strategy becomes dominant in the motor plan of older adults (Paizis et al., 2008). Hilt et al. (2016) observed that the "optimizing balance" strategy was preferred when healthy individuals performed a whole-body-reaching task under reduced postural stability. According to the optimal control theory, motor control will always prioritize a lower cost to achieve the task goal (Todorov, 2004). Our results suggest that the cost to optimize motor planning to achieve the task goal successfully with the uninjured limb was greater for the TBPI group than for the control group.

Target Specificity

In a free-endpoint whole-body reaching task the participants are free to choose their final hand position, which results in the greater involvement of implicit variables to guide action selection (Haggard, 2008; Andersen and Cui, 2009; Berret et al., 2011; Hilt et al., 2016). Interestingly, participants with TBPI were able to reach the final position as precisely as the control group, independently of the motor strategy used to achieve it. Furthermore, no significant differences were observed between the groups in respect of the finger endpoint parameter in the cup-to-mouth task.

Finger endpoint consistency for both groups, and the differences between the TBPI and control groups for the velocity and trajectory profiles in the reaching task could reflect the motor system's efficacy in controlling the numerous degrees of freedom involved in the intended movement in order to achieve a same goal (Bernstein, 1967; Turvey et al., 1982; Schöner and Kelso, 1988; Latash et al., 2002; Bizzi et al., 2008). Chang et al. (2009) observed similar results in an animal model of peripheral nerve injury in the ankle extensor muscle; Although there was an alteration in the trajectories of individual joint kinematics, those of limb orientation and limb length remained largely invariant, even when considering the paralyzed ankle extensor muscles. These results suggest that changes in mean joint angles were coordinated as part of a long-term compensation strategy to minimize change in whole limb kinematics (Chang et al., 2009). This strategy may represent a fundamental compensation principle after peripheral injuries that allows the adaptation to the new condition with a minimal effect on overall motor function.

Differences in Starting Position

The differences observed between the starting positions in the whole-body reaching task for the majority of kinematic parameters confirm that they offer different mechanical constraints for movement planning and execution. Previous studies have shown that the differences in the initial positions of the upper limb in free-endpoint reaching tasks in sitting (Berret et al., 2011) or standing posture (Hilt et al., 2016) did not influence the target choice in healthy subjects. Similar results were observed in our present study, in which a small variability in the target choice was found for both groups independently of the initial mechanical constraints of the upper limb.

Consequences for Rehabilitation

Current TBPI therapeutic objectives consist of improving muscle strength, range of motion and functionality (Milicin and Sîrbu, 2018; Rich et al., 2019; Chagas et al., 2021), as well as reducing the pain (Lovaglio et al., 2019) of the injured upper limb. Kinematic alterations shown here for the uninjured upper limb in the whole-body task in comparison to the cup-to-mouth task suggest, however, that the greater the postural challenge of the task, the greater is the motor cost to plan and perform it. Indeed, Souza et al. (2016) had already warned about the need to prevent and treat balance impairment in TBPI patients. The present work furthers this proposal by providing evidence in favor of including whole body and uninjured arm movements in TBPI rehabilitation programs. A better understanding of the motor plans changes after a TBPI upon the uninjured limb may help to improve the development of more accurate kinematic measures and more effective and customized rehabilitation programs.

Study Limitations

The main limitations of the current study were the small sample size as well as its heterogeneity regarding the extent of the injury, the occurrence and type of surgical intervention and the time elapsed since the injury. We have reproduced a very well characterized task to impose trunk displacement (Hilt et al., 2016). This said, a higher number of participants might help to confirm the kinematic results. Also, a direct measurement of the trunk motion would be helpful to identify more precisely its contribution to the altered kinematic parameters found for the uninjured limb as compared to controls.

CONCLUSION

This is the first study to show kinematic changes in the uninjured upper limb of adults with TBPI. Our results indicate a higher cost to perform the tasks, reflecting the greater impairment in motor planning and motor control of the individuals with TBPI. These findings expand the current knowledge on bilateral sensorimotor alterations after unilateral TBPI (Liu et al., 2013; Fraiman et al., 2016; Souza et al., 2016; Ramalho et al., 2019).

Also, they indicate that treatment after a brachial plexus injury should not be restricted to the affected upper limb and that the postural difficulty of the task should be considered in a treatment program. This study provides important information that could be helpful to guide the rehabilitation program after peripheral injuries. Future research must be performed to better understand the neural mechanisms involved in the kinematic modifications in the uninjured upper limb induced by TBPI.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institute of Neurology Deolindo Couto, Federal University of Rio de Janeiro (process number: 1.375.64). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

LS, TP, and CV conceived and designed the study. LS and JM recruited and made clinical assessment of participants. LS, LL, and AS collected kinematic data from participants involved in the study. LS and LL organized the database. LS performed the statistical analysis and created manuscript tables. LL and AS designed the figures and legends. LS, AS, LL, and CV wrote the first draft of manuscript. CV and TP provided the mentorship for LS, LL, and AS. All authors gave contributions to different sections in the manuscript, revised, read, and approved the submitted version.

FUNDING

This research was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico, CNPq (grant number 309560/2017-9), Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro FAPERJ (grants E26/010002474/2016, CNE 202.785/2018, and E-26/010.002418/2019) and Financiadora de Estudos e projetos FINEP (PROINFRA HOSPITALAR grant 18.569-8). This research was also supported by CAPES-COFECUB (project n°819-14, and is also part of the activities of the Fundação de Amparo à Pesquisa do Estado de São Paulo FAPESP's Research, Innovation and Dissemination Center for Neuromathematics-NeuroMat (FAPESP grant 2013/07699-0).

ACKNOWLEDGMENTS

The authors would like to thank Gabriel Freire Miranda, José Magalhães de Oliveira, Yves Ballay, and Ghislain Saunier for their contribution to this work.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnhum.2021.777776/full#supplementary-material

REFERENCES

Amini, A., Fischmeister, F. P. S., Matt, E., Schmidhammer, R., Rattay, F., and Beisteiner, R. (2018). Peripheral nervous system reconstruction reroutes cortical motor output-brain reorganization uncovered by effective connectivity. *Front. Neurol.* 9:1116. doi: 10.3389/fneur.2018.01116

Anastakis, D. J., Malessy, M. J. A., Chen, R., Davis, K. D., and Mikulis, D. (2008). Cortical plasticity following nerve transfer in the upper extremity. *Hand Clin.* 24, 425–444, vi–vii. doi: 10.1016/j.hcl.2008.04.005

Andersen, R. A., and Cui, H. (2009). Intention, action planning, and decision making in parietal-frontal circuits. *Neuron* 63, 568–583. doi: 10.1016/j.neuron.2009.08.028

Atkeson, C. G., and Hollerbach, J. M. (1985). Kinematic features of unrestrained vertical arm movements. *J. Neurosci.* 5, 2318–2330. doi: 10.1523/JNEUROSCI.05-09-02318.1985

Beaulieu, J.-Y., Blustajn, J., Teboul, F., Baud, P., De Schonen, S., Thiebaud, J.-B., et al. (2006). Cerebral plasticity in crossed C7 grafts of the brachial plexus: an fMRI study. *Microsurgery* 26, 303–310. doi: 10.1002/micr.20243

Bernstein, N. A. (1967). *The Co-Ordination and Regulation of Movements*. Oxford: Pergamon Press.

Berret, B., Bonnetblanc, F., Papaxanthis, C., and Pozzo, T. (2009). Modular control of pointing beyond arm's length. *J. Neurosci.* 29, 191–205. doi: 10.1523/JNEUROSCI.3426-08.2009

Berret, B., Chiovetto, E., Nori, F., and Pozzo, T. (2011). Manifold reaching paradigm: how do we handle target redundancy? *J. Neurophysiol.* 106, 2086–2102. doi: 10.1152/jn.01063.2010

Bizzi, E., Cheung, V. C. K., d'Avella, A., Saltiel, P., and Tresch, M. (2008). Combining modules for movement. *Brain Res. Rev.* 57, 125–133. doi: 10.1016/j.brainresrev.2007.08.004

Brucki, S. M. D., Nitrini, R., Caramelli, P., Bertolucci, P. H. F., and Okamoto, I. H. (2003). Sugestões para o uso do mini-exame do estado mental no Brasil. *Arq. Neuro Psiquiatr.* 61, 777–781. doi: 10.1590/S0004-282X2003000500014

Callegari, B., Saunier, G., Duarte, M. B., Almeida, G. C., da, S., Amorim, C. F., et al. (2018). Anticipatory postural adjustments and kinematic arm features when postural stability is manipulated. *PeerJ* 6:e4309. doi: 10.7717/peerj.4309

Chagas, A. C., de, S., Wanderley, D., Barboza, P. J. M., Martins, J. V. P., de Moraes, A. A., et al. (2021). Proprioceptive neuromuscular facilitation compared to conventional physiotherapy for adults with traumatic upper brachial plexus injury: a protocol for a randomized clinical trial. *Physiother. Res. Int.* 26:e1873. doi: 10.1002/pri.1873

Chang, Y.-H., Auyang, A. G., Scholz, J. P., and Nichols, T. R. (2009). Whole limb kinematics are preferentially conserved over individual joint kinematics after peripheral nerve injury. *J. Exp. Biol.* 212, 3511–3521. doi: 10.1242/jeb.033886

Crouch, D. L., Santago, A. C., Plate, J. F., Li, Z., and Saul, K. R. (2016). Relationship between maximum isometric joint moment and functional task performance in patients with brachial plexus injury: a pilot study. *Gait Posture* 44, 238–244. doi: 10.1016/j.gaitpost.2015.12.038

Davis, S. F., Abdel Khalek, M., Giles, J., Fox, C., Lirette, L., and Kandil, E. (2011). Detection and prevention of impending brachial plexus injury secondary to arm positioning using ulnar nerve somatosensory evoked potentials during

transaxillary approach for thyroid lobectomy. *Am. J. Electroneurodiagnostic Technol.* 51, 274–279.

Desmurget, M., Epstein, C. M., Turner, R. S., Prablanc, C., Alexander, G. E., and Grafton, S. T. (1999). Role of the posterior parietal cortex in updating reaching movements to a visual target. *Nat. Neurosci.* 2, 563–567. doi: 10.1038/9219

Desmurget, M., and Grafton, S. (2000). Forward modeling allows feedback control for fast reaching movements. *Trends Cogn. Sci.* 4, 423–431. doi: 10.1016/s1364-6613(00)01537-0

Dubuisson, A. S., and Kline, D. G. (2002). Brachial plexus injury: a survey of 100 consecutive cases from a single service. *Neurosurgery* 51, 673–682; discussion682–683.

Erdfelder, E., Faul, F., and Buchner, A. (1996). GPOWER: a general power analysis program. *Behav. Res. Methods Instr. Comput.* 28, 1–11. doi: 10.3758/BF03203630

Esteves, P. O., Oliveira, L. A. S., Nogueira-Campos, A. A., Saunier, G., Pozzo, T., Oliveira, J. M., et al. (2016). Motor planning of goal-directed action is tuned by the emotional valence of the stimulus: a kinematic study. *Sci. Rep.* 6:28780. doi: 10.1038/srep28780

Faglioni, W., Siqueira, M. G., Martins, R. S., Heise, C. O., and Foroni, L. (2014). The epidemiology of adult traumatic brachial plexus lesions in a large metropolis. *Acta Neurochir.* 156, 1025–1028. doi: 10.1007/s00701-013-1948-x

Fischmeister, F. P. S., Amini, A., Matt, E., Reinecke, R., Schmidhammer, R., and Beisteiner, R. (2020). A new rehabilitative mechanism in primary motor cortex after peripheral trauma. *Front. Neurol.* 11:125. doi: 10.3389/fneur.2020.00125

Flanders, M., Daghestani, L., and Berthoz, A. (1999). Reaching beyond reach. *Exp. Brain Res.* 126, 19–30. doi: 10.1007/s002210050713

Flash, T., and Hogan, N. (1985). The coordination of arm movements: an experimentally confirmed mathematical model. *J. Neurosci.* 5, 1688–1703. doi: 10.1523/JNEUROSCI.05-07-01688.1985

Folstein, M. F., Folstein, S. E., and McHugh, P. R. (1975). "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J. Psychiatr. Res.* 12, 189–198. doi: 10.1016/0022-3956(75)90026-6

Fraiman, D., Miranda, M. F., Erthal, F., Buur, P. F., Elschot, M., Souza, L., et al. (2016). Reduced functional connectivity within the primary motor cortex of patients with brachial plexus injury. *Neuroimage Clin.* 12, 277–284. doi: 10.1016/j.nicl.2016.07.008

Haggard, P. (2008). Human volition: towards a neuroscience of will. *Nat. Rev. Neurosci.* 9, 934–946. doi: 10.1038/nrn2497

Hilt, P. M., Berret, B., Papaxanthis, C., Stapley, P. J., and Pozzo, T. (2016). Evidence for subjective values guiding posture and movement coordination in a free-endpoint whole-body reaching task. *Sci. Rep.* 6:23868. doi: 10.1038/srep23868

Hudak, P. L., Amadio, P. C., and Bombardier, C. (1996). Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand) [corrected]. The Upper Extremity Collaborative Group (UECG). *Am. J. Ind. Med.* 29, 602–608. doi: 10.1002/(SICI)1097-0274(199606)29:6<602::AID-AJIM4<3.0.CO;2-L

Jaggi, A. S., and Singh, N. (2011). Role of different brain areas in peripheral nerve injury-induced neuropathic pain. *Brain Res.* 1381, 187–201. doi: 10.1016/j.brainres.2011.01.002

Kinlaw, D. (2005). Pre-/postoperative therapy for adult plexus injury. *Hand Clin.* 21, 103–108, vii. doi: 10.1016/j.hcl.2004.10.003

Latash, M. L., Scholz, J. F., Danion, F., and Schöner, G. (2002). Finger coordination during discrete and oscillatory force production tasks. *Exp. Brain Res.* 146, 419–432. doi: 10.1007/s00221-002-1196-4

Liu, B., Li, T., Tang, W.-J., Zhang, J.-H., Sun, H.-P., Xu, W.-D., et al. (2013). Changes of inter-hemispheric functional connectivity between motor cortices after brachial plexuses injury: a resting-state fMRI study. *Neuroscience* 243, 33–39. doi: 10.1016/j.neuroscience.2013.03.048

Lovaglio, A. C., Socolovsky, M., Di Masi, G., and Bonilla, G. (2019). Treatment of neuropathic pain after peripheral nerve and brachial plexus traumatic injury. *Neurol. India* 67, S32–S37. doi: 10.4103/0028-3886.250699

Lu, Y., Liu, H., Hua, X., Xu, J.-G., Gu, Y.-D., and Shen, Y. (2016). Attenuation of brain grey matter volume in brachial plexus injury patients. *Neurol. Sci.* 37, 51–56. doi: 10.1007/s10072-015-2356-1

Malessy, M. J., Thomeer, R. T., and van Dijk, J. G. (1998). Changing central nervous system control following intercostal nerve transfer. *J. Neurosurg.* 89, 568–574. doi: 10.3171/jns.1998.89.4.0568

Mano, Y., Nakamuro, T., Tamura, R., Takayanagi, T., Kawanishi, K., Tamai, S., et al. (1995). Central motor reorganization after anastomosis of the musculocutaneous and intercostal nerves following cervical root avulsion. *Ann. Neurol.* 38, 15–20. doi: 10.1002/ana.410380106

Marteniuk, R. G., MacKenzie, C. L., Jeannerod, M., Athenes, S., and Dugas, C. (1987). Constraints on human arm movement trajectories. *Can. J. Psychol.* 41, 365–378. doi: 10.1037/h0084157

Milicin, C., and Sîrbu, E. (2018). A comparative study of rehabilitation therapy in traumatic upper limb peripheral nerve injuries. *Neurorehabilitation* 42, 113–119. doi: 10.3233/NRE-172220

Moran, S. L., Steinmann, S. P., and Shin, A. Y. (2005). Adult brachial plexus injuries: mechanism, patterns of injury, and physical diagnosis. *Hand Clin.* 21, 13–24. doi: 10.1016/j.hcl.2004.09.004

Nazarahari, M., Chan, K. M., and Rouhani, H. (2020). A novel instrumented shoulder functional test using wearable sensors in patients with brachial plexus injury. *J. Shoulder Elbow Surg.* 30, e493–e502. doi: 10.1016/j.jse.2020.10.025

Noland, S. S., Bishop, A. T., Spinner, R. J., and Shin, A. Y. (2019). Adult traumatic brachial plexus injuries. *J. Am. Acad. Orthop. Surg.* 27, 705–716. doi: 10.5435/JAAOS-D-18-00433

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9, 97–113. doi: 10.1016/0028-3932(71)90067-4

Orfale, A. G., Araújo, P. M. P., Ferraz, M. B., and Natour, J. (2005). Translation into Brazilian Portuguese, cultural adaptation and evaluation of the reliability of the Disabilities of the Arm, Shoulder and Hand Questionnaire. *Braz. J. Med. Biol. Res.* 38, 293–302. doi: 10.1590/s0100-879x2005000200018

Özkan, T., and Aydin, A. (2001). "Physical examination," in *Brachial Plexus Injury*, ed. A. Gilbert (London: Martin Dunitz Ltd), 17–29.

Paizis, C., Papaxanthis, C., Berret, B., and Pozzo, T. (2008). Reaching beyond arm length in normal aging: adaptation of hand trajectory and dynamic equilibrium. *Behav. Neurosci.* 122, 1361–1370. doi: 10.1037/a0013280

Papaxanthis, C., Pozzo, T., Vinter, A., and Grishin, A. (1998). The representation of gravitational force during drawing movements of the arm. *Exp. Brain Res.* 120, 233–242. doi: 10.1007/s002210050397

Patroclo, C. B., Ramalho, B. L., Maia, J. S., Rangel, M. L., Torres, F. F., Souza, L., et al. (2019). A public database on traumatic brachial plexus injury. *bioRxiv* [Preprint]. doi: 10.1101/399824

Ramalho, B. L., Rangel, M. L., Schmaedeke, A. C., Erthal, F. S., and Vargas, C. D. (2019). Unilateral brachial plexus lesion impairs bilateral touch threshold. *Front. Neurol.* 10:872. doi: 10.3389/fneur.2019.00872

Rangel, M. L., Souza, L., Rodrigues, E. C., Oliveira, J. M., Miranda, M. F., Galves, A., et al. (2021). Predicting upcoming events occurring in the space surrounding the hand. *Neural Plast.* 2021:6649135. doi: 10.1155/2021/6649135

Resnick, D. (1995). *Diagnosis of Bone and Joint Disorders*, 3rd Edn. California, CA: WB Saunders Company.

Rich, J. A., Newell, A., and Williams, T. (2019). Traumatic brachial plexus injury rehabilitation using neuromuscular electrical muscle stimulation in a polytrauma patient. *BMJ Case Rep.* 12:e232107. doi: 10.1136/bcr-2019-232107

Sartori, L., Becchio, C., and Castiello, U. (2011). Cues to intention: the role of movement information. *Cognition* 119, 242–252. doi: 10.1016/j.cognition.2011.01.014

Schöner, G., and Kelso, J. A. (1988). Dynamic pattern generation in behavioral and neural systems. *Science* 239, 1513–1520. doi: 10.1126/science.3281253

Soechting, J. F., and Flanders, M. (1991). "Kinematic transformations for arm movements in three-dimensional space," in *Tutorials in Motor Neuroscience* NATO ASI Series, eds J. Requin and G. E. Stelmach (Dordrecht: Springer Netherlands), 435–442. doi: 10.1007/978-94-011-3626-6_34

Soechting, J. F., and Lacquaniti, F. (1981). Invariant characteristics of a pointing movement in man. *J. Neurosci.* 1, 710–720. doi: 10.1523/JNEUROSCI.01-07-00710.1981

Souza, L., Lemos, T., Silva, D. C., de Oliveira, J. M., Guedes Corrêa, J. F., Tavares, P. L., et al. (2016). Balance impairments after brachial plexus injury as assessed through clinical and posturographic evaluation. *Front. Hum. Neurosci.* 9:715. doi: 10.3389/fnhum.2015.00715

Stapley, P. J., Pozzo, T., Cheron, G., and Grishin, A. (1999). Does the coordination between posture and movement during human whole-body reaching ensure center of mass stabilization? *Exp. Brain Res.* 129, 134–146. doi: 10.1007/s002210050944

Svoboda, K., and Li, N. (2018). Neural mechanisms of movement planning: motor cortex and beyond. *Curr. Opin. Neurobiol.* 49, 33–41. doi: 10.1016/j.conb.2017.10.023

Taylor, K. S., Anastakis, D. J., and Davis, K. D. (2009). Cutting your nerve changes your brain. *Brain* 132, 3122–3133. doi: 10.1093/brain/awp231

Todorov, E. (2004). Optimality principles in sensorimotor control. *Nat. Neurosci.* 7, 907–915. doi: 10.1038/nn1309

Torres, F. F., Ramalho, B. L., Patroclo, C. B., Souza, L., Guimaraes, F., Martins, J. V., et al. (2018). "Plasticity in the brain after a traumatic brachial plexus injury in adults," in *Treatment of Brachial Plexus Injury*, ed. IntechOpen (London: IntechOpen), 1–16. doi: 10.5772/intechopen.77133

Turvey, M., Fitch, H., and Tuller, B. (1982). "The Bernstein perspective, I: the problems of degrees of freedom and context-conditioned variability," in *Human Motor Behavior: An Introduction*, ed. J. A. S. Kelso (Hillsdale, NJ: Lawrence Erlbaum Associates), 239–252.

Webber, C. M., Shin, A. Y., and Kaufman, K. R. (2019). Kinematic profiles during activities of daily living in adults with traumatic brachial plexus injuries. *Clin. Biomech.* 70, 209–216. doi: 10.1016/j.clinbiomech.2019.10.010

Wolpert, D. M., and Landy, M. S. (2012). Motor control is decision-making. *Curr. Opin. Neurobiol.* 22, 996–1003. doi: 10.1016/j.conb.2012.05.003

Yoshikawa, T., Hayashi, N., Tajiri, Y., Satake, Y., and Ohtomo, K. (2012). Brain reorganization in patients with brachial plexus injury: a longitudinal functional MRI study. *Sci. World J.* 2012:501751. doi: 10.1100/2012/501751

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

frontiers in Human Neuroscience

ORIGINAL RESEARCH
published: 17 December 2021
doi: 10.3389/fnhum.2021.762450

Gait Adaptation to a Phase-Specific Nociceptive Electrical Stimulation Applied at the Ankle: A Model to Study Musculoskeletal-Like Pain

*Michaël Bertrand-Charette[1], Renaud Jeffrey-Gauthier[1], Jean-Sébastien Roy[1,2] and Laurent J. Bouyer[1,2]**

[1] Center for Interdisciplinary Research in Rehabilitation and Social Integration, Quebec City, QC, Canada, [2] Department of Rehabilitation, Faculty of Medicine, Université Laval, Quebec City, QC, Canada

Introduction: Lower limb pain, whether induced experimentally or as a result of a musculoskeletal injury, can impair motor control, leading to gait adaptations such as increased muscle stiffness or modified load distribution around joints. These adaptations may initially reduce pain but can also lead to longer-term maladaptive plasticity and to the development of chronic pain. In humans, many current experimental musculoskeletal-like pain models are invasive, and most don't accurately reproduce the movement-related characteristics of musculoskeletal pain. The main objective of this study was to measure pain adaptation strategies during gait of a musculoskeletal-like experimental pain protocol induced by phase-specific, non-invasive electrical stimulation.

Methods: Sixteen healthy participants walked on a treadmill at 4 km/h for three consecutive periods (BASELINE, PAIN, and POST-PAIN). Painful electrical stimulations were delivered at heel strike for the duration of heel contact (HC) using electrodes placed around the right lateral malleolus to mimic ankle sprains. Gait adaptations were quantified bilaterally using instrumented pressure-sensitive insoles. One-way ANOVAs and group time course analyses were performed to characterize the impact of electrical stimulation on heel and forefoot contact pressure and contact duration.

Results: During the first few painful strides, peak HC pressure decreased on the painful side (8.6 ± 1.0%, $p < 0.0001$) and increased on the non-stimulated side (11.9 ± 0.9%, $p < 0.0001$) while HC duration was significantly reduced bilaterally (painful: 12.1 ± 0.9%, $p < 0.0001$; non-stimulated: 4.8 ± 0.8%, $p < 0.0001$). No clinically meaningful modifications were observed for the forefoot. One minute after the onset of painful stimulation, perceived pain levels stabilized and peak HC pressure remained significantly decreased on the painful side, while the other gait adaptations returned to pre-stimulation values.

Discussion: These results demonstrate that a non-invasive, phase-specific pain can produce a stable painful gait pattern. Therefore, this protocol will be useful to study musculoskeletal pain locomotor adaptation strategies under controlled conditions.

Keywords: pain, pain protocol, gait, adaptation, ankle, musculoskeletal

OPEN ACCESS

Edited by:
Teddy Caderby, Université de la Réunion, France

Reviewed by:
Nicolas Alain Turpin, Université de la Réunion, France
Alessio Gallina, University of Birmingham, United Kingdom
Anthony Chen, University of British Columbia, Canada

****Correspondence:***
Laurent J. Bouyer
laurent.bouyer@rea.ulaval.ca

Specialty section:
This article was submitted to Motor Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *21 August 2021*
Accepted: *30 November 2021*
Published: *17 December 2021*

Citation:
Bertrand-Charette M, Jeffrey-Gauthier R, Roy J-S and Bouyer LJ (2021) Gait Adaptation to a Phase-Specific Nociceptive Electrical Stimulation Applied at the Ankle: A Model to Study Musculoskeletal-Like Pain. Front. Hum. Neurosci. 15:762450. doi: 10.3389/fnhum.2021.762450

INTRODUCTION

In the presence of acute pain, whether induced experimentally or as a result of a musculoskeletal injury, various sensorimotor modifications are often present. They include proprioceptive deficits, altered patterns of neuromuscular activations and/or altered movement kinetics/kinematics (Sterling et al., 2001; Bank et al., 2013). For example, after an ankle sprain, increased knee valgus at heel contact (HC) and reduced hip extension at toe-off (TO) can be observed in the injured limb (Crosbie et al., 1999; Doherty et al., 2015; Punt et al., 2015). Effects on the non-injured joints are also reported, such as reductions in ankle plantar flexion at HC and TO (Doherty et al., 2015). Similarly, a decrease in motor performance can even be seen in both limbs, as shown with the Star Excursion Balance Test (Bertrand-Charette et al., 2020).

While some of these changes are associated with the injured anatomical structure and affect mechanical joint stability (Laskowski et al., 2000), others lead to the protection of the painful limb, and to immediate pain reduction. According to Hodges and Tucker (2011), the repeated use of "protective" pain-avoidance motor strategies, while beneficial in the short-term, can become detrimental in the longer-term, and lead to pain chronicization. Indeed, the presence of pain can modify muscle stiffness and/or muscle recruitment, thereby changing the way load is applied on articular surfaces and lead to early wear of the locomotor apparatus. Transforming an initial pain-avoidance motor strategy into a regular motor pattern therefore represents a form of maladaptive learning (Hodges and Tucker, 2011) that should be avoided to prevent chronic pain development (Henriksen et al., 2011).

As inadequate management of acute pain could potentially increase the risk of developing chronic pain (Sinatra, 2010), it is of the utmost importance to better understand the impact of acute pain on lower limb motor control. In order to assess this impact, a valid musculoskeletal (MSK) pain model to study pain adaptation strategies must induce lasting effects, not only immediate withdrawal effects. Unfortunately, many current acute MSK pain models are invasive [e.g., intramuscular injections of hypertonic saline or adenosine (Madeleine et al., 1999; Henriksen et al., 2011)] and most don't accurately represent the movement-related (or phasic) nature of MSK pain. For example, hypertonic saline or adenosine injections and ischemic contractions have been described as producing a tonic, continuous pain (Stohler et al., 1996; Bennell et al., 2004) that can induce both local and referred (widespread) pain (Graven-Nielsen et al., 2003). Regarding the latter, MSK injuries such as ankle sprain tend to generate mainly local pain around the injury site (Dubin et al., 2011). To better represent this aspect, previous pain models, such as the steel beads model of Levins et al. (1998), were designed to generate localized pain in order to alter gait pattern and study gait adaptations. The reduction in single-limb support on the painful limb is similar to what Hodges and Tucker (2011) suggested, however, this protocol cannot control parameters such as pain timing, duration, or intensity.

Gallina et al. (2021) have recently proposed a pain protocol using low-frequency sinusoidal electrical stimuli and showed that this type of electrical stimulation can induce knee pain of constant intensity for 60 s. However, the stimulation used was continuous. A protocol using nociceptive electrical stimulation that would be phase-specific (i.e., having adjustable pain intensity and present only at an MSK-pain relevant moment of the gait cycle), and being described as an acute MSK-like pain, would be more ecological to study the effects of experimental acute pain on gait motor control. Therefore, to avoid some of these limitations, an experimental pain model using electrical stimulation was developed. Pain induced by electrical stimulation is non-invasive, can produce a pain sensation of adjustable intensity, has the potential of being focal to the site around electrode location, and can be triggered at a specific moment of the gait cycle (Duysens et al., 1992).

The main objective of this study was therefore to characterize the impact of a phase-specific, painful electrical stimulation on gait adaptations. As gait is a complex multi-articular movement, we decided to focus the analysis of this study on two functionally important movement outputs during gait: the HC phase representing the initial contact and weight acceptance phases of the gait cycle, and push-off, a key part of the pre-swing phase associated with the control of gait speed (Dean et al., 2000). Vertical force magnitude and support duration were measured in these two regions of interest (ROIs) using pressure-sensitive insoles. As pain perception can be quite diverse, the secondary objective of this study was therefore to qualify the nociceptive stimulus perceived by the participants in order to highlights the potential similarities between "MSK" aspects of a real acute pain and the actual electrical nociceptive stimulation delivered.

Our main hypothesis was that electrically evoked phasic pain (and not a non-painful stimulation) would modify the gait into a pain-avoidance strategy, leading to a gait pattern modification beyond an initial pain-avoidance strategy (as reported clinically; O'Connor et al., 2013). This would therefore be a good experimental model to later study MSK-like pain during gait. In addition, we hypothesized that the pain generated would have similar qualities to acute MSK-like pain, i.e., local at the application site, phase-specific and qualified mainly by sensory pain descriptors, such as those reported in the Short-Form McGill Pain Questionnaire-2 (SF-MPQ-2).

MATERIALS AND METHODS

Participants

A convenience sample of 16 young healthy participants (28.2 $\pm$ 4.8 years old; 8 females) was recruited from *Université Laval* student population for this single-day, repeated measures design study. Participants had to be naïve to the task and present no self-reported pain. The exclusion criteria were self-reported symptoms or movement limitations at the lower limb or any neurological impairment that could affect task performance. All participants read and signed a consent form describing the experimental procedure and their involvement in the study. This protocol was approved by the local Ethics Review Board (CIUSSS-CN, #2010-212). The experimental procedures were in accordance with the Declaration of Helsinki.

General Protocol

Participants took part in a 2-h laboratory session. After filling the Waterloo Footedness Questionnaire (WFQ; Elias et al., 1998), they walked at 4 km/h on a motorized treadmill (Biodex Gait Trainer 2) for four periods: a 5-min PRE-BASELINE period to familiarize with treadmill walking and to set individual painful stimulation intensity, a 3-min BASELINE period, where they walked without any stimulation, a 3-min PAIN period with stimulation on every gait cycle, and a 3-min POST-PAIN period with no stimulation. Short rest moments (<30 s) were given between the four walking periods. Participants wore shoes instrumented with pressure-sensitive insoles (Tekscan F-Scan, South Boston, MA, United States) to collect dynamic pressure distribution under the foot and temporal gait parameters. They were instructed to walk on the treadmill normally, and to keep walking as they would normally in the presence of pain.

During the PAIN period, they verbally rated ankle pain intensity every 15 s using a numeric Visual Analog Scale (VAS; range 0–10). Immediately after the PAIN period, they rated their global unpleasantness intensity using a modified numeric VAS incorporating the anchors "not bad at all" and "the most unpleasant imaginable" (Duncan et al., 1989), painful region size by pointing at circles of different diameters (Bennell et al., 2004), and pain location by pointing on a schematic shank and foot chart (Bennell et al., 2004). Upon completion of the treadmill walking test, participants completed the SF-MPQ-2. The SF-MPQ-2 consists of 22 pain descriptors divided into four sub-scales: continuous pain, intermittent pain, predominantly neuropathic pain, and affective (Dworkin et al., 2015).

Painful Electrical Stimulation

Real-time heel-contact duration was measured using a pressure-sensitive foot switch located under the right heel. It served as stimulus trigger and stimulus duration control. There was no time delay between HC and actual electrical stimulus onset. A home-made electronic circuit interfaced the foot switch with two Grass s-88 stimulators (Grass Instruments, Quincy, MA, United States) wired in-series for signal generation, and a Digitimer DS7A stimulator (Hertfordshire, United Kingdom) for stimulus delivery to the participants. The painful electrical stimulation consisted of series of five pulses (pulse width: 500 μs; pulse frequency: 200 Hz) delivered in bursts at 30 Hz, for the duration of individual right HCs (**Figure 1A**). Kendall 2.2 cm^2 H69P disposable electrodes were placed on the right lateral malleolus and 2 cm further along the distal end of the fibula and used for stimulus delivery. Intensity required to reach 3/10 on the VAS was determined for each participant during the PRE-BASELINE period (steps of 5 mA increased every 10 s) and maintained constant throughout the experiment.

Non-painful Electrical Stimulation Controls

In a subgroup of five participants, a second walking test was performed on a separate day in the presence of non-painful stimulation, to assess the contribution of stimulation distraction on the gait biomechanical parameters. Walking periods duration, order, etc., remained the same except for stimulation intensity that was set at 1.4× perceptual threshold (PT), compared to approximately 3.0× PT for the pain experiment.

Gait Adaptations Characterization

F-Scan pressure-sensitive insoles (Tekscan, South Boston, MA, United States) were used to collect dynamic pressure distribution under the foot and temporal gait parameters. Peak foot pressure magnitude and duration in the heel and metatarsal regions (see section "Materials and Methods" and **Figure 1B**) were quantified for each stride of the BASELINE, PAIN, and POST-PAIN walking periods, bilaterally.

Data Analysis

Stride-to-stride duration of the nociceptive electrical stimulation was measured off-line from recordings of the pulse trains using a custom-made program written in MATLAB (Version R2018b, MathWorks, United States). The Tekscan data analysis software (F-Scan Research V7.5; Tekscan, United States) was used to set the ROIs on the pressure data from the insoles around the heels and the metatarsals for each participant (**Figure 1B**). These two ROIs were selected as they represent two functionally important outputs of movement strategies during gait: HC representing the initial contact at heel strike, weight acceptance and mid-stance phases of the gait cycle, and push-off a key part of the pre-swing phase associated with gait speed (Dean et al., 2000). These functional ROIs will be referred to as heel and metatarsal regions throughout this paper, respectively. Both peak pressure magnitude and contact duration of these ROIs were extracted and analyzed with a custom-made MATLAB program.

Statistics

To measure the effects of pain on gait adaptations, two complementary analyses were performed; (1) evolution over time for the group data (Fortin et al., 2009; Bertrand-Charette et al., 2021) of the time course (Cumming and Finch, 2005); (2) multi-epochs (see below) for statistical comparisons (see Bertrand-Charette et al., for details).

Multi-Epochs Analysis

The following epochs were defined:

(1) BASELINE late: mean of the last 50 strides of the group BASELINE period;
(2) PAIN early: mean of the first 5 strides of the group PAIN period;
(3) PAIN late: mean of the last 50 strides of the group PAIN period;
(4) POST-PAIN early: mean of the first 5 strides of the group POST-PAIN period;

One-way ANOVA with Dunnett's multiple comparisons test were performed to compare these epochs using GraphPad Prism (version 9.0.0). The level of significance was set at 0.05.

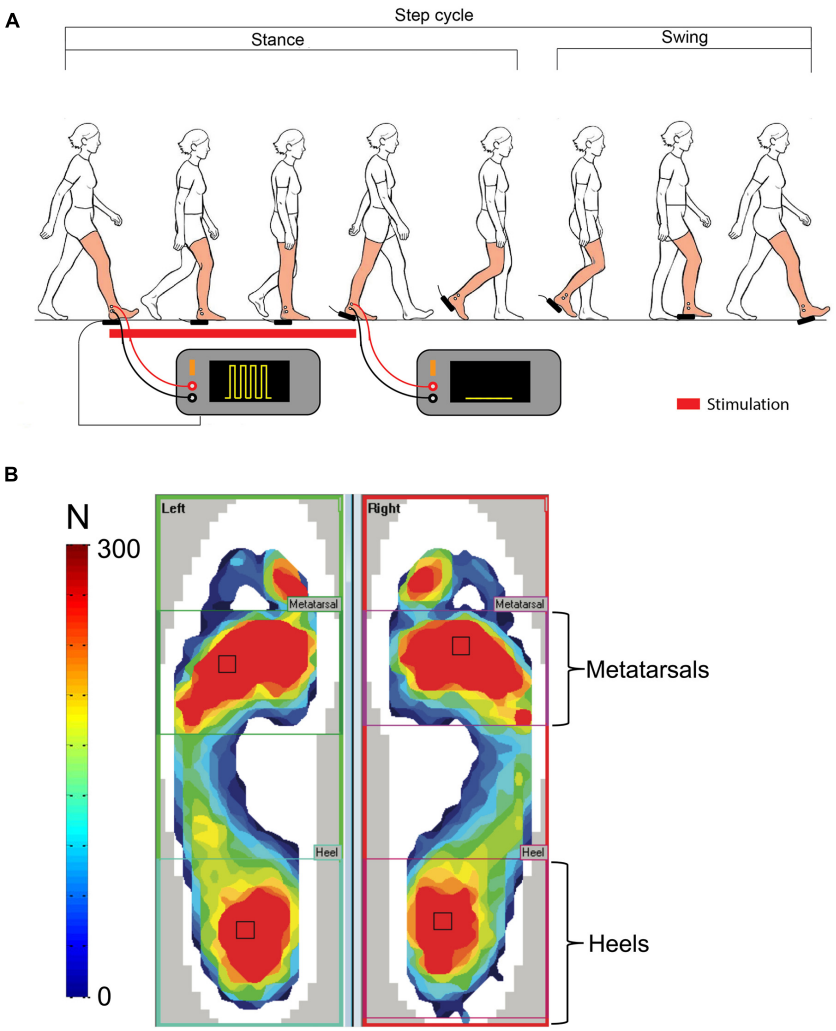

FIGURE 1 | Regions of interest. **(A)** Schematic representation of the pain-generating set-up and electrical stimulus waveform. **(B)** Representation of the two functional regions of interest: heels and metatarsals.

Group Time Course Analysis

A 95% confidence interval ($CI_{95\%}$) was calculated from the last 50 baseline strides to represent normal stride-to-stride variability observed during BASELINE walking. PAIN and POST-PAIN data were then compared to this $CI_{95\%}$ using an 11-points moving average line as a visual reference. Moving average values outside of the $CI_{95\%}$ were considered as significantly different from baseline.

Questionnaires

Individual scores on the WFQ and SF-MPQ-2 were extracted and pooled to report the footedness and frequency of perceived pain qualities.

General Unpleasantness, Painful Area Size, and Location

Data collected for each participant were extracted and pooled to report the group painful area size and location on the ankle.

Duration of the Nociceptive Stimulation

The duration of each stimulation was extracted for each participant and pooled to report mean duration and standard deviation.

RESULTS

Participants' Characteristics

The group was composed of 16 participants (mean age: 28.2 ± 4.8 years; 8 females; see **Table 1** for participants' characteristics).

Stimulus Intensity, Duration, and Pain Level During Gait

The mean stimulus intensity necessary to obtain a phasic painful stimulation of 3/10 on the VAS during gait at the onset of the pain period was 14.4 ± 5.2 mA. While stimulus

TABLE 1 | Participants' characteristics.

Characteristics	
Age	28.2 ± 4.8
Sex	
• Male	8
• Female	8
Footedness	
• Right	14
• Left	2
Stimulation intensity (mA)	14.4 ± 5.2
Mean VAS score (range 0-10)	2.5 ± 0.1
Unpleasantness score (range 0-10)	4.3 ± 1.7

mA, milliamps; VAS, Visual Analog Scale.

intensity was maintained fixed throughout the PAIN period, pain intensity perceived by the participants slightly decreased over the first 60 s, and then stabilized at 2.5 ± 0.4/10 (time course shown in **Figure 2A**). Pain tended to be centered on the right lateral malleolus with a mean diameter of 3.3 ± 1.3 cm. No radiating pain was reported by participants. The mean duration of the nociceptive stimulation was 300.7 ± 59 ms, 112.1 ± 12.1 ms shorter than the total HC phase measured with the insoles (**Figure 3A**).

Perceived Pain Qualities of the Nociceptive Electrical Stimulation

Participants rated the general unpleasantness of the stimulation session at 4.3 ± 1.7/10. According to the results of their SF-MPQ-2 (**Figure 2B**), the electrical stimulus was described as throbbing (n = 10/16), sharp (n = 13/16), tender (n = 10/16), electric-shock (n = 16/16), and tingling (n = 15/16). Other qualities of pain reported were stabbing and numbness (n = 7/16). All perceived qualities of pain are presented in **Figure 2B**.

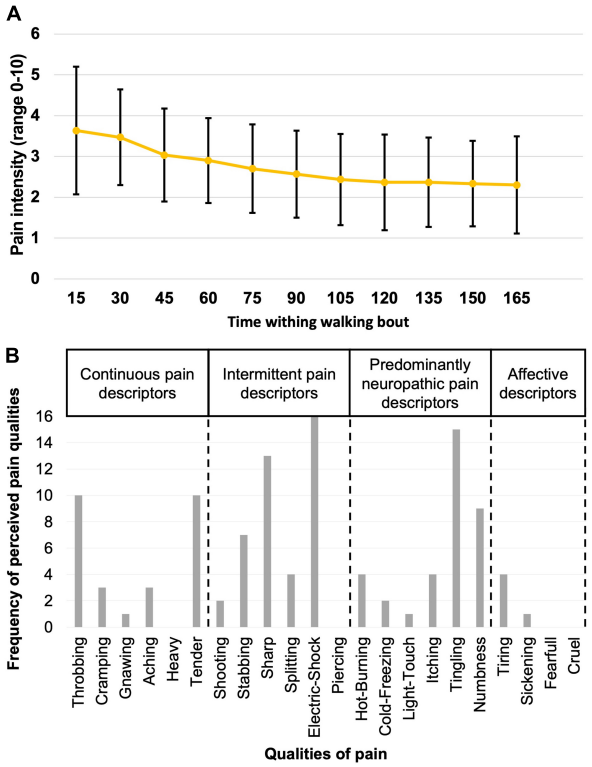

FIGURE 2 | Description of the perceived pain. **(A)** The mean score and standard deviation (black lines) on the Visual Analog Scale for pain intensity as measured every 15 s for all participants while walking during the PAIN period. **(B)** Frequency of perceived pain qualities, as assessed using the Short-Form McGill Pain Questionnaire-2.

Effect of Painful Electrical Stimulation on Gait Adaptations

As mentioned in section "Materials and Methods," gait is a complex multi-articular movement resulting in various movement strategies. Therefore, this section will present our results according to the two functionally important movement outputs identified by our ROIs (heel for weight acceptance; metatarsals for push-off), separately for peak pressure and contact duration.

Epoch Analysis for Peak Pressure Magnitude

Regarding the heel ROIs, on the stimulated side, HC peak pressure magnitude was significantly reduced by 8.6 ± 1.0% ($p < 0.0001$) and 8.1 ± 0.4% ($p < 0.0001$) during the PAIN early and PAIN late, respectively, compared to BASELINE late. During the PAIN early, on the non-stimulated side, HC peak pressure magnitude significantly increased by 11.9 ± 0.9% ($p < 0.0001$). For the metatarsal ROIs, significant changes can be found on the stimulated side for PAIN early (1.9 ± 0.7% reduction; $p < 0.05$), PAIN late (2.3 ± 0.3% increase; $p < 0.0001$), and POST-PAIN early (3.8 ± 0.7% reduction; $p < 0.0001$) compared to BASELINE late. On the non-stimulated side, a significant reduction of 5.5 ± 0.7% ($p < 0.0001$) can be observed during PAIN early when compared to BASELINE late. Overall, 10 participants reduced their HC peak pressure magnitude on the stimulated side during the PAIN early period, while 9 of them increased their HC peak pressure magnitude on the non-stimulated side. There was no relationship between pain intensity and HC peak pressure magnitude (see **Supplementary Figure 1**).

Epoch Analysis for Contact Duration

Regarding HC duration, a significant reduction was observed during PAIN early (mean duration reduction of 12.1 ± 0.9%; $p < 0.0001$) and PAIN late (mean duration reduction of 4.4 ± 0.4%; $p < 0.0001$) while an increase can be observed in POST-PAIN early (mean duration increase of 3.4 ± 0.9%; $p < 0.001$) for the right heel ROI. For the non-stimulated side, a mean reduction of 4.8 ± 0.8% ($p < 0.0001$) was present for the PAIN early epoch. For the metatarsal ROIs, a significant mean reduction of 9.3 ± 1.4% (PAIN early, $p < 0.0001$) was present on the stimulated side, but nothing during PAIN late and POST-PAIN early. On the non-stimulated side, a significant 2.7 ± 0.6% ($p < 0.0001$) reduction can be observed for PAIN early only. There was no relationship between pain intensity and contact duration. Overall, HC duration was reduced for 12 participants

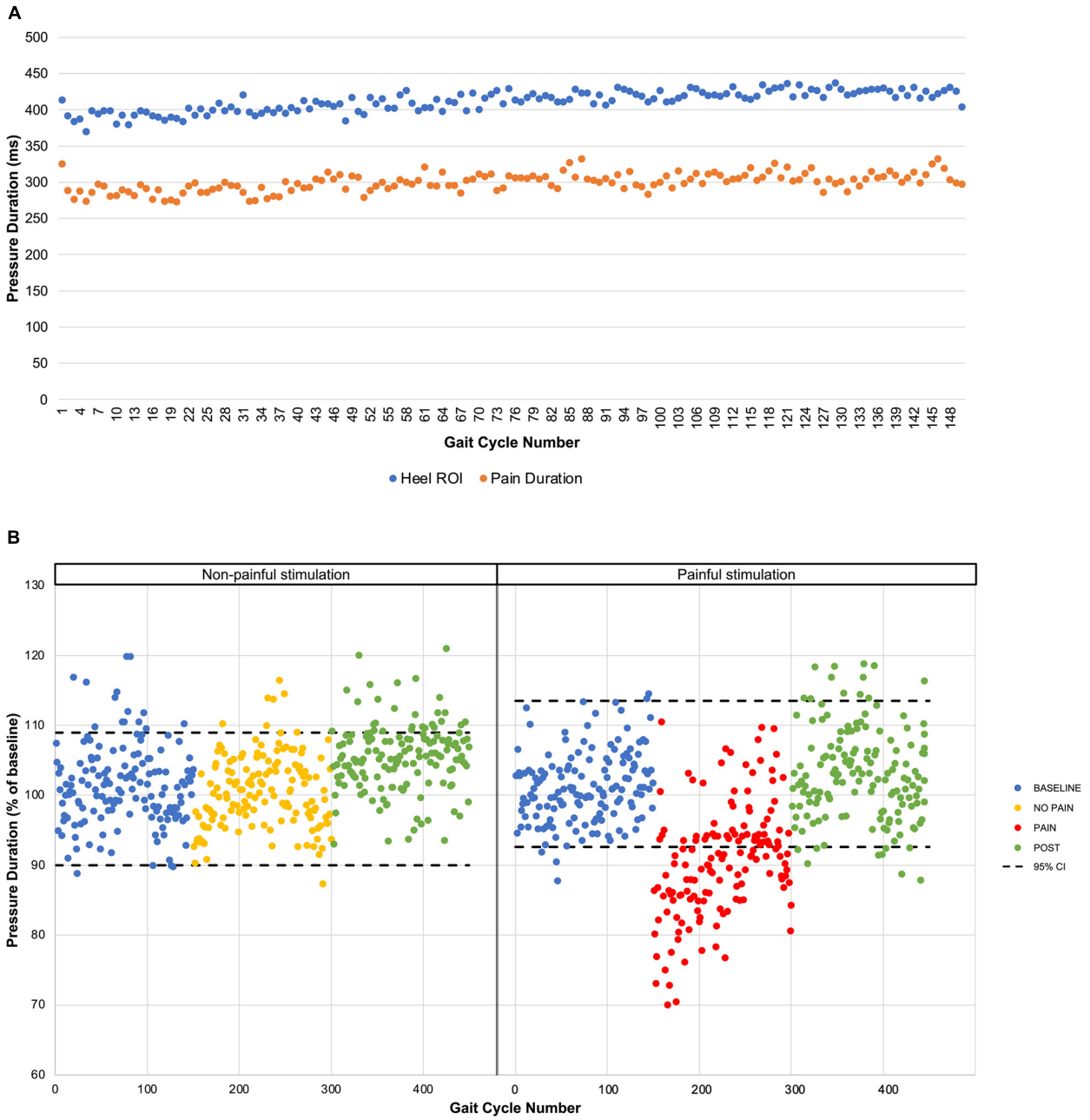

FIGURE 3 | Pressure duration time course. **(A)** The mean pressure durations for each gait cycle during PAIN period are presented for the heel ROI extracted from the pressure-sensitive insoles (blue dots) and for the pressure-sensitive foot switch located under the right heel (orange dots). **(B)** Results from the non-painful stimulation control experiment. Mean pressure durations are presented for the five participants for each period with the 95% confidence interval (black dashed line) based on the BASELINE.

on the stimulated side and 11 participants on the non-stimulated side during PAIN early.

Peak Pressure Magnitude Time Course

A statistically significant drop in peak pressure during HC was observed for the PAIN period on the stimulated side only (**Figure 4A**). Peak HC pressure decreased to a mean 90.6 ± 4.0% of baseline value for the first five strides (PAIN early, $p < 0.0001$) and stabilized under the lower $CI_{95\%}$ of BASELINE for the remaining of the painful period.

In contrast, the non-stimulated side had a significant increase in HC peak pressure magnitude, that can be seen at the beginning of the painful period (mean maximal increase of 12.0 ± 3.8% of baseline values for PAIN early, $p < 0.0001$). Thereafter, the HC peak pressure moving average line remained around the upper $CI_{95\%}$ for the rest of PAIN period.

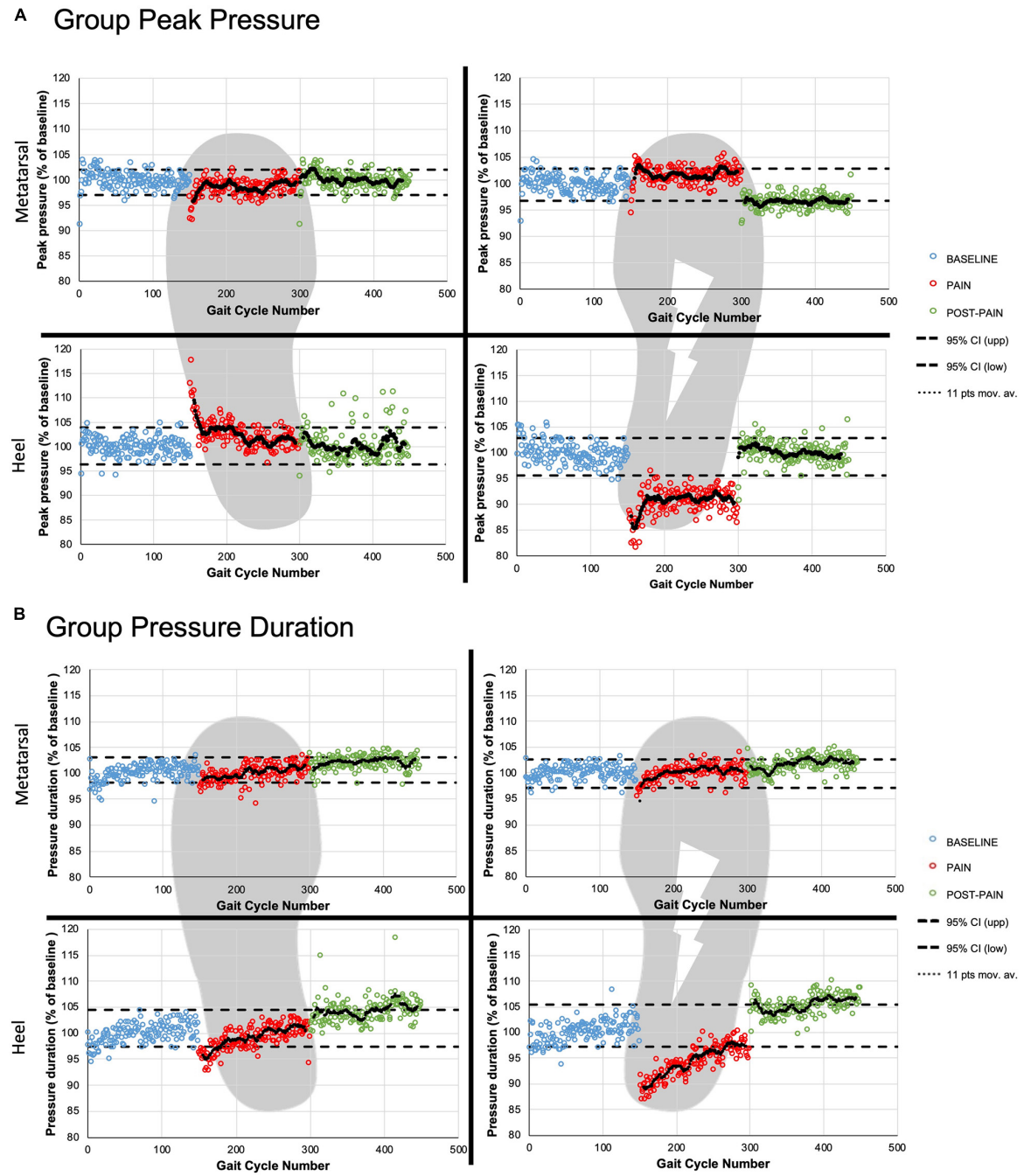

FIGURE 4 | Group time courses. The three periods are presented for group peak pressure magnitude **(A)** and group contact duration **(B)** with the 95% confidence interval (black dashed line) based on the BASELINE. The two ROIs are presented for the right (painful) and the left (non-stimulated) foot. The black dotted lines represent the 11-points moving average for the PAIN and POST-PAIN periods.

For the metatarsal ROIs, the moving average line remained most of the time within the $CI_{95\%}$ for both pain periods: less than 25 strides were over the upper $CI_{95\%}$ for the painful side, and below the lower $CI_{95\%}$ for the non-stimulated side.

For the heel ROIs during POST-PAIN period, participants returned to their normal HC peak pressure. Only the right metatarsal ROI showed peak pressure values around the lower $CI_{95\%}$ (POST-PAIN late: 96.8 ± 1.7% vs. lower $CI_{95\%}$: 96.7%).

Contact Duration Time Course

Regarding HC duration on the painful side, the moving average line was below the $CI_{95\%}$ for most of the painful period (**Figure 4B**). Mean duration spent on the right heel for PAIN

early was 391.0 ± 7.2 ms compared to 443.8 ± 8.9 ms during BASELINE late value ($p < 0.0001$), showing a 12.1 ± 0.9% reduction. When looking at the non-stimulated side, a transient significant reduction in contact duration was observed for the first 43 steps of the PAIN period when compared to the baseline HC duration.

For the metatarsal ROIs, the moving average lines remained within the $CI_{95\%}$ most of the time during PAIN.

Regarding the POST-PAIN period, all ROIs values tend to vary around to the upper $CI_{95\%}$, with the right metatarsal ROI being the only ROI significantly increased compared to baseline values. This increase represents a 3.4 ± 0.9% ($p < 0.001$) of BASELINE late.

Non-painful Stimulation Control Experiment

The effect of non-painful electrical stimulation on heel-contact duration was also tested in a subgroup of five participants on a different day. Results show that the non-painful stimulation did not affect HC duration (see **Figure 3B**).

DISCUSSION

The present study demonstrates that a painful phasic electrical stimulation applied at the ankle can modify the gait pattern beyond an initial pain-avoidance response in healthy participants. By assessing peak pressure magnitude and contact duration of the heel and metatarsal ROIs bilaterally as a means of quantifying the presence of gait adaptations, our results suggest that this protocol can recreate pain-avoidance reactions during the first few strides for duration and peak pressure magnitude. Moreover, the results suggest that this painful stimulation generates a modified painful gait pattern with a persistent reduction in HC peak pressure magnitude for the remaining of pain exposure. As a control, five of the participants returned to the lab for a similar experiment, in the presence of non-nociceptive stimulation. No change in contact duration was observed during the non-nociceptive stimulation, suggesting that the effect seen here is pain-specific.

Gait Adaptations With Electrical Pain

Participants modified their gait pattern in the presence of phasic nociceptive electrical stimulation. It is important to notice that not only did they modify their gait (HC duration and peak pressure) during the initial phase of the PAIN period (PAIN early), as hypothesized, but they also showed a persisting reduction of their HC peak pressure magnitude that stabilized for the rest of the stimulated period (PAIN late). These two periods will be discussed separately below.

During PAIN early, there was a significant reduction in HC peak pressure and HC contact duration, indicative of an unloading of the painful limb. Even though the stimulation protocol was not designed to generate a complete withdrawal response on the stimulated side (withdrawal caused by higher stimulus intensities such as those presented in Spaich et al. (2004), this unloading suggests that stimulation was painful enough to alter the gait pattern. This effect on the painful side was associated with an increased HC peak pressure on the non-stimulated side, indicative of a dynamic increase in weight transfer to that limb (loading). This bilateral change in motor strategy could be interpreted as a protective response, based on Hodges and Tucker (2011).

After approximatively 25 strides into the PAIN period, HC peak pressure stabilized below the lower $CI_{95\%}$, i.e., at a significantly lower level than before PAIN period. This pressure level was then maintained stable for the rest of the pain period, i.e., for approximately 125 more strides (**Figure 4A**). Participants therefore showed a persisting reduction in HC peak pressure on the painful side. HC contact duration continued to tend toward baseline values until the end of the pain period. On the non-stimulated side, both pressure magnitude and contact duration returned to BASELINE values. Together these results suggest that the electrical nociceptive stimulus not only generated acute pain-avoidance gait modifications (as mentioned above), but also lead to the development of a persistent modification in gait pattern for the duration of the pain exposure. It is this modified gait pattern that will enable further studies on sensorimotor control or gait modifications with a well-controlled nociceptive stimulus in the future. The current protocol therefore brings a simple and powerful tool to further our knowledge in this field of research.

During the POST-PAIN period, statistically significant changes were observed, mainly for HC duration on the stimulated side. However, these changes were fairly small compared to the main effect observed during the PAIN period. As an example, on the painful side, an increase of 3.4 ± 0.9% relative to baseline duration is measured, compared to the 12.1 ± 0.9% decrease observed for PAIN early. Such small changes are therefore unlikely to be functionally or clinically meaningful.

Link Between Heel Contact Pressure Duration and Stimulation Duration

Even if participants modified their contact duration to modulate pain duration (similar to what has been seen in Gallina et al. (2021) with task-relevant modulation of perceived pain intensity), they still maintained their unloading of the painful limb (reduced HC peak pressure) to possibly continue to "protect" the painful limb. We suggest that this persistent behavior could represent a maladaptive gait modification, according to Hodges and Tucker (2011). Using nociceptive electrical stimulation is therefore a powerful pain model that mimics possible adaptation to modulate pain as shown in Gallina et al. (2021) and by our results.

Perceived Qualities of the Nociceptive Stimulus

Regarding painful area size and location, the electrical stimulation used in our protocol was localized around the stimulation site (3.3 ± 1.3 cm), similar to the result of Gallina et al. (2021). This is a major improvement compared to saline or adenosine injections and ischemic block (Graven-Nielsen et al., 2003), with participants reporting pain in various location below their knee.

As a means of further describing the qualities of the pain generated, previous studies using other experimental pain models

simulating lower limb MSK pain (saline injections, ischemic block) have used the McGill Pain Questionnaire (versions 1 or 2). They have reported various qualities from the sensory subgroups of the SF-MPQ-2 including *Aching* and *Throbbing* (Bennell et al., 2004; Smith et al., 2020) or *Stabbing*, *Cramping*, *Burning*, *Heavy*, and *Exhausting* (Graven-Nielsen et al., 2003).

In the present study, *Throbbing*, *Sharp*, *Tender*, *Electric-shock*, and *Tingling* were the most frequently reported pain qualities. *Sharp* and *Electric-shock* have been categorized as *intermittent* pain descriptors, *Throbbing* and *Tender* as *continuous*, and *Tingling* as *predominantly neuropathic* (Dworkin et al., 2009). These subcategories were suggested by Dworkin et al. (2009, 2015), for participants suffering from chronic pain and acute low back pain. It has been shown that people suffering from acute pain tend to use sensory subgroups (continuous, intermittent, and predominantly neuropathic descriptors) more frequently compared to participants with chronic pain, that tend to score more frequently the affective descriptors (Reading, 1982). Due to the electrical nature of the pain used in our protocol, it is not surprising to have a higher number of participants reporting *Electric-shock* and *Tingling* over *Burning* or *Cramping* (frequent with the other models). However, in the present study, participants mainly reported sensory subgroups pain descriptors, and only rarely affective ones. This further supports the fact that the electrical nociceptive stimulation represents a good acute pain model.

Comparisons to Other Pain Models

Similarities in Term of Motor Response to Pain

The electrically evoked phasic ankle pain protocol led to effects similar to those of other pain models used to study gait modifications. Regarding HC peak pressure reduction on the painful side, Madeleine et al. (1999) noted similar modifications following saline injections in the tibialis anterior, where participants tended to put less weight on the injected leg. Also, Seeley et al. (2013) noticed a decrease in peak vertical impact ground reaction force of 3–4% following injection in the infrapatellar fat pad. Regarding the decrease in HC duration, Levins et al. (1998) also noted a decrease in single limb support duration while using steel beads under the heel to create the painful stimulus. Such similarities with other experimental pain models further support the validity of our electrically evoked phasic ankle pain model during gait. One main difference, however, is that injections create a tonic continuous pain that rapidly increases and then gradually reduces (Madeleine et al., 1999; Graven-Nielsen et al., 2003). On the contrary, painful electrical stimulation can be triggered at a specific moment of the gait cycle as shown in this study and the pain intensity can be modulated by participants (Gallina et al., 2021). Our model therefore leads to the same effect observed throughout their experiment. However, since time-courses aren't available to compare their results to ours, it is difficult to further conclude in terms of initial vs. late effects.

Previous work with electrical stimulation showed some similarities with our phase-specific ankle pain model. Studies investigating painful electrical stimulation at the lower back (Moseley et al., 2004; Moseley and Hodges, 2005) and at the knee (Tucker et al., 2012; Gallina et al., 2021) showed an altered motor response in the assessed muscles. Even if these studies used movement to trigger pain [for example arm movement to elicit painful stimulation of the lower back (Moseley and Hodges, 2005) or shifting body weight to modulate pain perception at the knee (Gallina et al., 2021)], none of them used a functional activity such as walking to trigger a painful stimulation. This phase-specific aspect of our pain model made it possible to study how pain can alter motor response during a task involving sensory gating and sensorimotor processing (Nielsen, 2003).

Advantages of the Electrically-Evoked *Phasic* Pain

In addition to the similarities with previous experimental pain models, using electrical stimulation allowed us to generate a local, phase-specific, non-invasive pain. Importantly, the mild to moderate pain level of 3–4/10 on the VAS (Boonstra et al., 2014) was easily reached for all participants at relatively low stimulation intensities (maximal intensity: 27 mA). Furthermore, this corresponds to what is typically reported during gait following grade I or II lateral ankle sprains (LASs) (Ivins, 2006). Electrode placement alongside the distal end of the lateral malleolus evoked a localized pain while avoiding radiating pain toward the foot. This is an improvement over other pain models, such as saline injections or ischemic block (Graven-Nielsen et al., 2003), where radiating pain was reported to a larger region than targeted. Only one of our participants felt pain from the lateral malleolus to the lateral side of the calcaneum. Moreover, electrical stimulation is less invasive and no flares are present hours after initial exposure to the stimulus (Petersen and Rowbotham, 1999).

A major advantage of this painful stimulation protocol is that it can be adjusted in its timing of application to target a specific moment in the gait cycle, i.e., it is phase-specific. Unlike other pain models such as capsaicin, saline, or ischemic block, which are described as a tonic continuous pain (Graven-Nielsen et al., 2003; Bouffard et al., 2014), the painful stimulus used in this study was present only during HC and lasted less than 500 ms.

This phasic aspect is closer to what is experienced during actual MSK pain. Levins et al. (1998) used steel beads to create a phasic plantar heel pain experimentally. Similar to our results, Levins et al. (1998) reported that participants reduced the amount of time spent on the painful limb. However, unlike the electrical stimulation proposed here, they could not precisely set the pain timing, duration, or intensity, as it could vary across participants depending on their mass, gait speed, and gait pattern (initial and adapted). The electrically evoked phasic ankle pain protocol presented in this study also shows direct similarities with actual ankle injuries. Regarding HC peak pressure, Doherty et al. (2015) suggested that, following a first acute ankle sprain, patients tend to use a "*compensatory mechanism*" that consists of attenuating impact forces at HC. Similar results can be seen during other movements, such as a drop vertical jump, where participants with an acute ankle sprain are offloading the injured limb or increasing the load on the non-injured limb (Doherty et al., 2014).

Strengths and Limitations of the Study

This study has some limitations. First, the relatively young adult group and relatively small sample size that was recruited

might limit the generalizability of the results. Also, participants walked on a treadmill, which may not be as functional as walking overground, but was necessary for our stimulation setup. Regarding the pain intensity, following the first minute of pain exposure, the perceived pain level stabilized around 2.5/10 (compared to the 3/10 initially reached). This could be partly explained by the electrical nature and parameters of the stimulation, close to what is used for transcutaneous electrical nerve stimulation (TENS), known for its hypoalgesic effects in healthy participants (Chesterton et al., 2002, 2003). Using monophasic square waveform at 300 Hz with an intensity of 14.4 ± 5.2 mA [compared to the 7.4 ± 2.2 mA sinusoidal waveform at 4 Hz in Gallina et al. (2021)] show similarities to usual TENS parameters (Chesterton et al., 2003). Importantly, this 0.5-point reduction in pain score had no major impact on the objectives of the study, that were to study gait modifications in the presence of pain. Now knowing that these stimulation parameters can induce changes in pain intensity, it will be possible to conduct future studies using parameters similar to Gallina et al. (2021). In addition, adjusting pain intensity to reflect the amount of pressure on the heel could be an improvement to even better represent the MSK-like aspect of our protocol. Finally, collecting electromyographic data would've made it possible to determine if flexion reflex were elicited following painful stimulation.

This study also has several strengths. It presents an original protocol to elicit pain experimentally that shares characteristics similar to actual MSK pain, in order to study human adaptation to nociceptive stimulation. One of the highlights of this phase-specific pain model is its easily adjustable nature (in terms of phase, duration, and intensity at any moment of the experiment), that allowed being present at a functionally relevant moment of the gait cycle. Another highlight is the longer-lasting gait modifications that quickly stabilized to obtain a robust modified gait pattern during the painful condition. Moreover, this model is non-invasive making it safe and easy to use in many settings and populations. Finally, it is possible to recreate gait adaptations that are found in other validated pain models and actual MSK injuries.

CONCLUSION

These results support the use of the proposed phase-specific electrically evoked phasic ankle pain protocol to study gait adaptations in the presence of MSK-like pain. This protocol is an attractive MSK-like pain model, as it is non-invasive and can target specific, functionally relevant moments of the gait cycle, and shows similarities with actual MSK pain adaptation strategies. Future studies will use this protocol to further investigate the similarities of persisting gait adaptations to those observed during actual MSK pain, and thereby advance our understanding of the effects of MSK pain on global motor control.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Centre Intégré Universitaire de Santé et de Services Sociaux de la Capitale-Nationale Ethics Review Board. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

MB-C, J-SR, and LJB contributed to study conception and design. MB-C, RJ-G, and LJB conducted the data collection and performed the data validation and analysis. MB-C wrote the draft of the manuscript and prepared the figures. All authors provided substantive feedback on the manuscript, contributed to the final manuscript, and read and approved the final manuscript.

FUNDING

This study was supported by an operating grant to LJB from the Natural Sciences and Engineering Research Council of Canada (NSERC; grant #RGPIN-2018-06184) (https://www.nserc-crsng.gc.ca). These funding bodies had no role in the design of the study, data collection, analysis, and interpretation nor did they have a role in writing the manuscript. J-SR was supported by a salary award from the Fonds de Recherche du Québec – Santé (FRQ-S). MB-C received a studentship from the Fonds de Recherche du Québec – Santé (FRQ-S).

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnhum.2021.762450/full#supplementary-material

Supplementary Figure 1 | Individual time courses for the pain intensity (red line), pressure duration (pressure-sensitive insoles; blue line), and foot switch located under the right heel (orange line) for each participant.

REFERENCES

Bank, P. J., Peper, C. E., Marinus, J., Beek, P. J., and van Hilten, J. J. (2013). Motor consequences of experimentally induced limb pain: a systematic review. *Eur. J. Pain* 17, 145–157. doi: 10.1002/j.1532-2149.2012.00186.x

Bennell, K., Hodges, P., Mellor, R., Bexander, C., and Souvlis, T. (2004). The nature of anterior knee pain following injection of hypertonic saline into the infrapatellar fat pad. *J. Orthop. Res.* 22, 116–121. doi: 10.1016/S0736-0266(03)00162-1

Bertrand-Charette, M., Dambreville, C., Bouyer, L. J., and Roy, J.-S. (2020). Systematic review of motor control and somatosensation assessment tests for

the ankle. *BMJ Open Sport Exerc. Med.* 6:e000685. doi: 10.1136/bmjsem-2019-000685

Bertrand-Charette, M., Nielsen, J. B., and Bouyer, L. J. (2021). A simple, clinically applicable motor learning protocol to increase push-off during gait: a proof-of-concept. *PLoS One* 16:e0245523. doi: 10.1371/journal.pone.0245523

Boonstra, A. M., Schiphorst Preuper, H. R., Balk, G. A., and Stewart, R. E. (2014). Cut-off points for mild, moderate, and severe pain on the visual analogue scale for pain in patients with chronic musculoskeletal pain. *Pain* 155, 2545–2550. doi: 10.1016/j.pain.2014.09.014

Bouffard, J., Bouyer, L. J., Roy, J.-S., and Mercier, C. (2014). Tonic pain experienced during locomotor training impairs retention despite normal performance during acquisition. *J. Neurosci.* 34:9190. doi: 10.1523/JNEUROSCI.5303-13.2014

Chesterton, L. S., Barlas, P., Foster, N. E., Lundeberg, T., Wright, C. C., and Baxter, D. G. (2002). Sensory stimulation (TENS): effects of parameter manipulation on mechanical pain thresholds in healthy human subjects. *Pain* 99, 253–262. doi: 10.1016/s0304-3959(02)00118-5

Chesterton, L. S., Foster, N. E., Wright, C. C., Baxter, D. G., and Barlas, P. (2003). Effects of TENS frequency, intensity and stimulation site parameter manipulation on pressure pain thresholds in healthy human subjects. *Pain* 106, 73–80. doi: 10.1016/s0304-3959(03)00292-6

Crosbie, J., Green, T., and Refshauge, K. (1999). Effects of reduced ankle dorsiflexion following lateral ligament sprain on temporal and spatial gait parameters. *Gait Posture* 9, 167–172. doi: 10.1016/s0966-6362(99)00010-7

Cumming, G., and Finch, S. (2005). Inference by eye: confidence intervals and how to read pictures of data. *Am. Psychol.* 60:170. doi: 10.1037/0003-066x.60.2.170

Dean, C. M., Richards, C. L., and Malouin, F. (2000). Task-related circuit training improves performance of locomotor tasks in chronic stroke: a randomized, controlled pilot trial. *Arch. Phys. Med. Rehabil.* 81, 409–417.

Doherty, C., Bleakley, C., Hertel, J., Caulfield, B., Ryan, J., and Delahunt, E. (2015). Lower extremity function during gait in participants with first time acute lateral ankle sprain compared to controls. *J. Electromyogr. Kinesiol.* 25, 182–192.

Doherty, C., Bleakley, C., Hertel, J., Sweeney, K., Caulfield, B., Ryan, J., et al. (2014). Lower extremity coordination and symmetry patterns during a drop vertical jump task following acute ankle sprain. *Hum. Mov. Sci.* 38, 34–46.

Dubin, J. C., Comeau, D., McClelland, R. I., Dubin, R. A., and Ferrel, E. (2011). Lateral and syndesmotic ankle sprain injuries: a narrative literature review. *J. Chiropr. Med.* 10, 204–219.

Duncan, G. H., Catherine Bushnell, M., and Lavigne, G. J. (1989). Comparison of verbal and visual analogue scales for measuring the intensity and unpleasantness of experimental pain. *Pain* 37, 295–303. doi: 10.1016/0304-3959(89)90194-2

Duysens, J., Tax, A. A., Trippel, M., and Dietz, V. (1992). Phase-dependent reversal of reflexly induced movements during human gait. *Exp. Brain Res.* 90, 404–414. doi: 10.1007/BF00227255

Dworkin, R. H., Turk, D. C., Revicki, D. A., Harding, G., Coyne, K. S., Peirce-Sandner, S., et al. (2009). Development and initial validation of an expanded and revised version of the Short-form McGill Pain Questionnaire (SF-MPQ-2). *Pain* 144, 35–42. doi: 10.1016/j.pain.2009.02.007

Dworkin, R. H., Turk, D. C., Trudeau, J. J., Benson, C., Biondi, D. M., Katz, N. P., et al. (2015). Validation of the Short-form McGill Pain Questionnaire-2 (SF-MPQ-2) in acute low back pain. *J. Pain* 16, 357–366. doi: 10.1016/j.jpain.2015.01.012

Elias, L. J., Bryden, M. P., and Bulman-Fleming, M. B. (1998). Footedness is a better predictor than is handedness of emotional lateralization. *Neuropsychologia* 36, 37–43. doi: 10.1016/s0028-3932(97)00107-3

Fortin, K., Blanchette, A., McFadyen, B. J., and Bouyer, L. J. (2009). Effects of walking in a force field for varying durations on aftereffects and on next day performance. *Exp. Brain Res* 199, 145–155. doi: 10.1007/s00221-009-1989-9

Gallina, A., Abboud, J., and Blouin, J.-S. (2021). A task-relevant experimental pain model to target motor adaptation. *J. Physiol.* 599, 2401–2417. doi: 10.1113/JP281145

Graven-Nielsen, T., Jansson, Y., Segerdahl, M., Kristensen, J. D., Mense, S., Arendt-Nielsen, L., et al. (2003). Experimental pain by ischaemic contractions compared with pain by intramuscular infusions of adenosine and hypertonic saline. *Eur. J. Pain* 7, 93–102. doi: 10.1016/s1090-3801(02)00069-1

Henriksen, M., Rosager, S., Aaboe, J., and Bliddal, H. (2011). Adaptations in the gait pattern with experimental hamstring pain. *J. Electromyogr. Kinesiol.* 21, 746–753. doi: 10.1016/j.jelekin.2011.07.005

Hodges, P. W., and Tucker, K. (2011). Moving differently in pain: a new theory to explain the adaptation to pain. *Pain* 152(3 Suppl):, S90–S98. doi: 10.1016/j.pain.2010.10.020

Ivins, D. (2006). Acute ankle sprain: an update. *Am. Fam. Physician* 74, 1714–1720.

Laskowski, E. R., Newcomer-Aney, K., and Smith, J. (2000). Proprioception. *Phys. Med. Rehabil.Clin. N. Am.* 11, 323–340.

Levins, A. D., Skinner, H. B., and Caiozzo, V. J. (1998). Adaptive gait responses to plantar heel pain. *J. Rehabil. Res. Dev.* 35, 289–293.

Madeleine, P., Voigt, M., and Arendt-Nielsen, L. (1999). Reorganisation of human step initiation during acute experimental muscle pain. *Gait Posture.* 10, 240–247. doi: 10.1016/s0966-6362(99)00036-3

Moseley, G. L., and Hodges, P. W. (2005). Are the changes in postural control associated with low back pain caused by pain interference? *Clin. J. Pain* 21, 323–329. doi: 10.1097/01.ajp.0000131414.84596.99

Moseley, G. L., Nicholas, M. K., and Hodges, P. W. (2004). Does anticipation of back pain predispose to back trouble? *Brain* 127, 2339–2347. doi: 10.1093/brain/awh248

Nielsen, J. B. (2003). How we walk: central control of muscle activity during human walking. *Neuroscientist* 9, 195–204. doi: 10.1177/1073858403009003012

O'Connor, S. R., Bleakley, C. M., Tully, M. A., and McDonough, S. M. (2013). Predicting functional recovery after acute ankle sprain. *PLoS One* 8:e72124. doi: 10.1371/journal.pone.0072124

Petersen, K. L., and Rowbotham, M. C. (1999). A new human experimental pain model: the heat/capsaicin sensitization model. *Neuroreport* 10, 1511–1516. doi: 10.1097/00001756-199905140-00022

Punt, I. M., Ziltener, J.-L., Laidet, M., Armand, S., and Allet, L. (2015). Gait and physical impairments in patients with acute ankle sprains who did not receive physical therapy. *PM R* 7, 34–41. doi: 10.1016/j.pmrj.2014.06.014

Reading, A. E. (1982). A comparison of the McGill Pain Questionnaire in chronic and acute pain. *Pain* 13, 185–192. doi: 10.1016/0304-3959(82)90028-8

Seeley, M. K., Park, J., King, D., and Hopkins, J. T. A. (2013). Novel experimental knee-pain model affects perceived pain and movement biomechanics. *J. Athl. Train.* 48, 337–345. doi: 10.4085/1062-6050-48.2.02

Sinatra, R. (2010). Causes and consequences of inadequate management of acute pain. *Pain Med.* 11, 1859–1871. doi: 10.1111/j.1526-4637.2010.00983.x

Smith, S. A., Micklewright, D., Winter, S. L., and Mauger, A. R. (2020). Muscle pain induced by hypertonic saline in the knee extensors decreases single-limb isometric time to task failure. *Eur. J. Appl. Physiol.* 120, 2047–2058. doi: 10.1007/s00421-020-04425-2

Spaich, E. G., Arendt-Nielsen, L., and Andersen, O. K. (2004). Modulation of lower limb withdrawal reflexes during gait: a topographical study. *J. Neurophysiol.* 91, 258–266. doi: 10.1152/jn.00360.2003

Sterling, M., Jull, G., and Wright, A. (2001). The effect of musculoskeletal pain on motor activity and control. *J. Pain.* 2, 135–145. doi: 10.1054/jpai.2001.19951

Stohler, C. S., Zhang, X., and Lund, J. P. (1996). The effect of experimental jaw muscle pain on postural muscle activity. *Pain* 66, 215–221. doi: 10.1016/0304-3959(96)03026-6

Tucker, K., Larsson, A.-K., Oknelid, S., and Hodges, P. (2012). Similar alteration of motor unit recruitment strategies during the anticipation and experience of pain. *Pain* 153, 636–643. doi: 10.1016/j.pain.2011.11.024

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Neurology

OPINION
published: 24 December 2021
doi: 10.3389/fneur.2021.812342

Tai Chi Training as a Primary Daily Care Plan for Better Balance Ability in People With Parkinson's Disease: An Opinion and Positioning Article

Ting Zhang[1,2], *Zhenyu Lv*[3] *and Song Gao*[1*]

[1] College of Physical Education and Health Sciences, Zhejiang Normal University, Jinhua, China, [2] University Hospital, Zhejiang Normal University, Jinhua, China, [3] Department of Chinese Medicine, Naval Special Medical Center, Naval Medical University, Shanghai, China

Keywords: Parkinson's disease, fall, tai chi, balance ability, limitations

INTRODUCTION

Parkinson's disease (PD) is a common degenerative disease of the central nervous system. Clinically, its incidence is second only to Alzheimer's disease, which seriously harms the health of middle-aged and elderly people (1). Main clinical manifestations of this disease include balance disorder, resting tremor, bradykinesia, and muscle stiffness, and this disease has a high incidence and disability rate. However, initial symptoms of PD are different, and the early symptoms are often ignored by people, which delays the optimal time to manage the disease. PD is closely related to age. Epidemiological surveys showed that the global prevalence of PD is 0.3%, among which the population over 65 years old accounts for 1–2%, and the prevalence rate over 85 years old increases to 3–5% (2, 3). A meta-analysis of people, both genders, with PD showed that men are at higher risk of PD than women (4). The progression of PD is unpredictable and may suddenly worsen. People with PD often complain that their symptoms clearly worsen within one year.

Fall is a balance disorder that often occurs in the late stage of PD. However, some studies have found that abnormal body swings occur in the early stages of PD, that is, mild balance dysfunction, which gradually worsens as the course of the disease progresses (5). Some researchers have found that people with Hoehn-Yahr stageII PD have balance adjustment disorders when they turn around (6). Newly diagnosed unmedicated people with PD have abnormal balance (7). Ultrasound of abnormal brain substantia nigra shows mild balance wobble in high-risk people with PD (8). Therefore, people with PD can have mild balance dysfunction in the early stage (9). As the course of the disease progresses, people with PD will inevitably show signs of abnormal dynamic balance, and even fall, leading to fractures and disability.

Although the apoptosis of dopaminergic cells in the substantia nigra striatum is the main cause of motor symptoms of PD, the balance disorder cannot be explained by lack of dopamine alone. Application of PET-CT found that apoptosis of the substantia nigra is closely related to motor retardation, but it has little to do with postural balance. It is well known that Medoba cannot alleviate or partially alleviate the symptoms of balance disorders in people with PD. Levodopa is the first-line drug for the treatment of PD. It has a good therapeutic effect on muscle stiffness and motor retardation, but there is no consensus on whether it can improve the symptoms of instability in PD (10, 11). In addition, long-term use of drugs can cause adverse drug reactions, such as nausea, vomiting, and orthostatic hypotension. Deep brain stimulation (DBS) is a surgical treatment for movement disorders such as PD (12). A study found that DBS stimulation of bilateral pontine nuclei can provide an effective treatment for alleviating gait and balance abnormalities in people with PD (13). In other studies, the effect of DBS on gait and balance disorders has been

OPEN ACCESS

Edited by:
Eric Yiou,
Université Paris-Saclay, France

Reviewed by:
Arnaud Delafontaine,
CIAMS, Université Paris-Saclay, France

****Correspondence:***
Song Gao
1811516014@sus.edu.cn

Specialty section:
This article was submitted to Neurorehabilitation, a section of the journal Frontiers in Neurology

Received: *10 November 2021*
Accepted: *03 December 2021*
Published: *24 December 2021*

Citation:
Zhang T, Lv Z and Gao S (2021) Tai Chi Training as a Primary Daily Care Plan for Better Balance Ability in People With Parkinson's Disease: An Opinion and Positioning Article. Front. Neurol. 12:812342. doi: 10.3389/fneur.2021.812342

less successful and may even lead to freezing and increased gait imbalance (14). For the symptoms of PD, management rather than treatment is considered a more realistic strategy. Therefore, it is particularly important to actively seek safe and effective complementary and alternative therapies to improve the balance disorder in PD. Since 2002, Complementary and alternative therapy has been widely used in the United States and has attracted the attention of patients with neurological diseases (15). Short-term muscle stretching and functional electrical stimulation have also been shown to be effective in improving the gait of patients with PD (16, 17). Exercise therapy is considered to be an adjunct to medical and surgical treatments designed to maximize function, improve quality of life, and minimize or reduce complications (18). Although exercise therapy is recommended as an effective treatment for persons with PD, there is no uniform standard for specific exercise patterns (19, 20).

Fear of falling, decreased muscle strength, and decreased proprioception are the main factors that cause falls. A study reported that the elderly showed lower muscle use efficiency and greater postural swings in standing balance tasks, which means that the elderly has a greater risk of falls (21). Lelard et al. (22) considered that any form of physical activities can increase confidence in maintaining balance, and that strength and proprioception training is the most suitable balance exercises for healthy elderly people. However, due to practical considerations, the elderly, especially elderly people with PD, have a low chance of participating in special strength training.

Tai chi, a popular traditional Chinese martial art, has gradually developed into an exercise therapy. As we all know, tai chi is a form of exercise that requires long-term practice and continuous improvement, and Yang tai chi is the most popular (23). Tai chi can increase muscle strength and improve body coordination. Unlike other complementary and alternative therapies, tai chi training is very economical, and there is no need to consider whether the state can provide subsidies. According to a report, each tai chi class in the United States is worth USD 3.5, which is acceptable to most practitioners (24). Practitioners can choose actions that improve balance and flexibility rather than the entire set of actions. In recent years, tai chi has been proven to improve many diseases, such as chronic obstructive pulmonary disease, heart failure, and knee osteoarthritis (25). In the tai chi training process, participants continuously adjust their center of gravity while moving slowly in multiple directions to maintain their body balance. A meta-analysis showed that tai chi has a promoting effect on balance, and it is believed that it has a good effect on the strengthening of proprioception (26, 27). A study by Guo et al. (28) found that compared with a control group who had not practiced tai chi, the elderly who had practiced tai chi for an average of 9 years or more had a great advantage in proprioception of the knee and ankle joints. This shows that long-term tai chi exercise helps maintain or strengthen the proprioception of the elderly.

The balance and stability of people with PD are seriously threatened, and tai chi training has potential healing effects. Therefore, this article aims to outline the key role of tai chi training in enhancing balance ability and preventing falls in people with PD. Moreover, the authors emphasize the limitations and challenges of this research on tai chi to improve balance ability in PD.

TAI CHI PROMOTES THE BALANCE ABILITY OF PEOPLE WITH PD

Human daily activities cannot be performed without balance ability. Studies have shown that elderly people with PD are more likely to be admitted to a hospital for fractures due to falls (29). Therefore, seeking active and effective exercise methods to enhance the balance ability of elderly people with PD is particularly important for improving their quality of life. Tai chi has slow rhythm and continuous movements. It enhances the balance ability of people with PD by constantly shifting the center of gravity. The decreased balance ability of people with PD is closely related to loss of posture control. Tai chi training finely controls joints through muscle coordination. In addition, tai chi training can strengthen the sensory stimulation of the limbs and lower limb muscles, which is very important for the improvement of the movement and balance ability of people with PD.

In order to investigate how tai chi reduces the risk of falls, Rahal et al. (30) compared the balance ability between healthy elderly people who practiced Tai Chi and ballroom dancers. They found that the tai chi group had faster walking speed and shorter transfer time, and that in the sit-to-stand test the tai chi group had better balance performance in the final standing posture. Besides, Zhou et al. (31) reported the influence of tai chi training on posture control of elderly women. When the tai chi group shifted the center of gravity as quickly as possible to complete the special orientation posture, and remain stable without falling, the overall, lateral, and anteroposterior diameter swing paths of the center of gravity were smaller than those of the control group. The study by Holmes et al. (32) found that tai chi can reduce the swing of the body's center of gravity caused by respiratory disturbance, thereby reducing the instability of the body. Zhou et al. (33) found that Tai Chi can effectively increase muscle strength of the lower limbs for elderly people. Furthermore, crossing obstacles is a behavior that occurs in daily life, which requires better dynamic balance ability. Chang et al. (34) reported that when crossing obstacles, the flexion angle of the hip joint in a tai chi group was significantly greater when raising the leg, and that the tai chi group had a larger stride, faster stepping speed, and shorter time required to cross an obstacle. Therefore, tai chi training has a positive effect on maintaining balance when crossing obstacles. Another research by Zou et al. (35) showed that both the 24-style tai chi and the modified Chen-style tai chi can effectively enhance the balance function and adaptability of body posture control in elderly people with PD. Recent studies have shown that tai chi exercise can better promote balance function, and that it is significantly better than stretching exercises and multi-modal exercises in reducing the incidence of moderate injury falls and severe injury falls (36, 37). However, the results of this study cannot determine whether

Tai Chi is suitable for elderly PD patients since the participants were not PD patients though over 65 years old.

Tai Chi can effectively improve the static balance ability of middle-aged and elderly people, but there is no direct evidence to improve PD patients' static balance ability (38). In tai chi movements, such as "brushing keen and twisting step" and "parting the wild horse's mane," the legs should be open to a larger and suitable angle, and the maximum swing should be emphasized when doing the movements (39, 40). The knees should be bent and squat with the knee joints on the frontal axis. The angle between the sagittal axis and the sagittal axis is increased, and this posture can improve the control ability of the practitioner's lower limbs. This may be the key reason for long-term tai chi training to improve posture control ability and reduce the ellipse area that represents the static balance ability.

The significance of tai chi for the treatment of PD is mainly to improve gait and strengthen neuromuscular control to reduce the risk of falls. Characteristics of the included studies are shown in **Table 1**. A research study by Li et al. (39) found that tai chi can maintain and improve various body functions of elderly people with PD and that it is a very effective exercise therapy. In its follow-up study (41), 195 patients with PD, Hoehn-Yahr stages 1 to 4, were randomly divided into tai chi group, resistance training group, and stretching training group, each for 60 min/time, 2 times/week, for a total of 24 weeks of intervention. The results showed that the tai chi group performed better than the resistance group in terms of maximum excursion, with a difference of 5.55 percentage points between the groups (95% confidence interval [CI], 1.12–9.97, $P = 0.01$). In terms of directional control, the difference between groups was 10.45 percentage points (95% CI, 3.89–17, $P = 0.002$). Compared with the stretching group, the tai chi group had more obvious differences between the groups in maximum excursion and direction control. This showed that tai chi has significant effects on improving postural stability and functional ability of people with mild to moderate PD. Liu (42) et al. showed that tai chi exercise-assisted balance and gait training can reduce the occurrence of falls in people with PD, and that the improvement of traction in the tai chi training group was significantly better than that of the control group. A study by Gao et al. (43) found that the 12-week Yang Style tai chi was better than the control group in improving the Berg balance scale ($p < 0.05$), and that the number of falls in the Tai Chi group during the 6-month follow-up period was significantly less than that in the control group. The number of falls in the tai chi group was 0.3 ± 0.62 times, and in the control group it was $= 0.64 \pm 0.74$ times ($p < 0.05$). In a preliminary experiment conducted by Hackney et al. (44), 30 people with PD were randomly divided into a tai chi group and a control group. The tai chi group intervened for 1 h a day twice a week, for a total of 10 weeks. The control group did not intervene. The results showed that before and after exercise, the tai chi group had significant changes in the Berg Balance Scale, Unified Parkinson's Disease Rating Scale (UPDRS), Timed Up and Go, tandem stance test, 6-minute walk, and backward walking compared with the control group.

However, there are only few studies that believe tai chi has no significant effect on reducing falls in people with PD (45, 46). Amano et al. (47) found that tai chi training had no effect on the gait and posture control of people with PD, and that no improvement in people's balance ability was observed. It was speculated that the reason could be the short duration of training, which was only 16 weeks and only 2 to 3 practice sessions per week.

LIMITATIONS OF CURRENT TAI CHI RESEARCH

There are some limitations in the research on Tai Chi improving the balance ability of people with PD. This may be attributed to the following reasons: at present, most clinical control studies recruit subjects who have no foundation in tai chi training. After randomization, the trial group will be given tai chi training and practice for not more than 6 months to evaluate the difference with the control group (46, 47). Therefore, the reason for the diverse conclusions is the difference in the standard degree of tai chi movement and length of training. Moreover, when formulating tai chi to improve the balance ability of people with PD, the characteristics of different tai chi categories should be considered, and unified Tai Chi training movements should be performed. The selection and modification of Tai Chi actions for PD needs to focus on the severity of the disease of people with PD to enhance the reproducibility and generalization of the research results.

Tai Chi, as a medium-intensity aerobic exercise, with frequency of training of three times a week, can meet the recommended standards of American College of Sports Medicine (ACSM). Furthermore, tai chi is a kind of physical and mental exercise. During exercise, breathing and soothing music should be used to effectively improve the mood of people with PD, and it is beneficial to overcome the fear of falling. Compared with the rehabilitation training content of modern medicine, tai chi training improves the abnormal gait and balance disorders of elderly people with PD. It does not require special equipment and venues, and the exercise intensity and difficulty are not challenging, which is convenient for people with PD to practice. Tai chi improves the movement and balance abilities of people with PD, effectively reducing physical and psychological burdens of caregivers, and it has high social and economic benefits.

CONCLUSION

The authors of this article point out that tai chi can improve balance ability and reduce the risk of falls in people with mild to moderate PD. It is an effective non-drug intervention. In addition, in view of the differences in research results, the existing problems of Tai Chi intervention in PD should be deeply analyzed. This is also a key issue that needs attention and

TABLE 1 | Characteristics of the included studies.

Study	Participants	Interventions	Outcomes
Li et al. (39)	*n* = 17 Age: 71.51 (± 5.4) y HY scale1–3 stage ability to walk with/without aids	Yang style Tai Chi-based stepping exercises vs. no intervention 90min, 5 times/week, 5 weeks	50-ft walk, TUGT, FRT
Li et al. (41)	*n* = 195 Age: 40–85y HY scale scale1–4 stage ability to walk with/without aids	Tai Chi vs. resistance training vs. stretching 60 min, 2 times/week, 24 weeks	Falls, TUG, UPDRS-III, limit-of stability, FRT, gait, strength
Gao et al. (43)	*n* = 76 Age>40 y Independent walking≥1 fall during past 1 y	Yang style Tai Chi vs. no intervention 60 min, 3 times/week, 12 weeks	Occurrences of falls, BBS, TUGT, UPDRS-III
Amano et al. (47)	*n* = 45 Age: 50–7 0y HY scale 2–3 stage ability to walk with/without aids	Tai Chi vs. Qigong vs. no intervention 60 min, 2 times/week, 16 weeks	GI, gait, UPDRS-III
Hackney et al. (44)	*n* = 26 Age > 40 y HY scale 1.5–3 stageindependent walking with/without aids for 3 m	Yang short style Tai Chi vs. no intervention 60 min, 2 times/week, 20 sessions	BBS, TUG, TS, UPDRS-III,OLS, GAITRite, 6MWT

HY scale, Hoehn and Yahr scale; TUGT, timed up and go test; FRT, functional reach test; UPDRS, Unified Parkinson's Disease Rating Scale; BBS, Berg Balance Scale; GI, gait initiation; TS, tandem stance; OLS, one-leg stance; 6MWT, 6-min walk test.

consideration in the future research. However, more evidence-based research is needed to prove the effectiveness of tai chi in improving balance ability and preventing falls of people with PD. Researchers designing tai chi movements should take into full consideration the special physical conditions of people with PD, movements that are simple and easy to learn while having good effects on improving balance ability. Based on a good mass foundation, tai chi movement will be more widely used and promoted as a daily care plan for people with PD.

AUTHOR CONTRIBUTIONS

TZ and ZL conceived the manuscript and revised the drafts. SG wrote the first draft. All authors contributed to the article and approved the submitted version.

FUNDING

This study was supported by the College of Physical Education and Health Sciences, Zhejiang Normal University, Jinhua, China.

REFERENCES

1. Arii Y, Sawada Y, Kawamura K, Miyake S, Taichi Y, Izumi Y, et al. Immediate effect of spinal magnetic stimulation on camptocormia in Parkinson's disease. *J Neurol Neurosurg Psychiatry.* (2014) 85:1221–6. doi: 10.1136/jnnp-2014-307651
2. de Lau LML, Breteler MMB. Epidemiology of Parkinson's disease. *Lancet Neurol.* (2006) 5:525–35 doi: 10.1016/S1474-4422(06)70471-9
3. Elbaz A, Carcaillon L, Kab S, Moisan F. Epidemiology of Parkinson's disease. *Rev Neurol (Paris).* (2016) 172:14–26. doi: 10.1016/j.neurol.2015.09.012
4. Taylor KSM, Cook JA, Counsell CE. Heterogeneity in male to female risk for Parkinson's disease. *J Neurol Neurosurg Psychiatry.* (2007) 78:905–6 doi: 10.1136/jnnp.2006.104695
5. Kim SD, Allen NE, Canning CG, Fung VSC. Postural instability in patients with Parkinson's disease. epidemiology, pathophysiology and management. *CNS Drugs.* (2013) 27:97–112. doi: 10.1007/s40263-012-0012-3
6. Song J, Sigward S, Fisher B, Salem GJ. Altered dynamic postural control during step turning in persons with early-stage parkinson's disease. *Parkinsons Dis.* (2012) 2012:386962. doi: 10.1155/2012/386962
7. Mancini M, Horak FB, Zampieri C, Carlson-Kuhta P, Nutt JG, Chiari L. Trunk accelerometry reveals postural instability in untreated Parkinson's disease. *Parkinsonism Relat Disord.* (2011) 17:557–62. doi: 10.1016/j.parkreldis.2011.05.010
8. Maetzler W, Mancini M, Liepelt-Scarfone I, Müller K, Becker C, van Lummel RC, et al. Impaired trunk stability in individuals at high risk for Parkinson's disease. *PLoS ONE.* (2012) 7:e32240. doi: 10.1371/journal.pone.0032240
9. Delafontaine A, Hansen C, Marolleau I, Kratzenstein S, Gouelle A. Effect of a concurrent cognitive task, with stabilizing visual information and withdrawal, on body sway adaptation of Parkinsonian's patients in an off-medication state: a controlled study. *Sensors (Basel).* (2020) 20:18. doi: 10.3390/s20185059
10. Nova IC, Perracini MR, Ferraz HB. Levodopa effect upon functional balance of Parkinson's disease patients. *Parkinsonism Relat Disord.* (2004) 10:411–5 doi: 10.1016/j.parkreldis.2004.04.004
11. Rocchi L, Chiari L, Horak FB. Effects of deep brain stimulation and levodopa on postural sway in Parkinson's disease. *J Neurol Neurosurg Psychiatry.* (2002) 73:267–74 doi: 10.1136/jnnp.73.3.267
12. Fukaya C, Yamamoto T. Deep brain stimulation for Parkinson's disease: recent trends and future direction. *Neurol Med Chir.* (2015) 55:422–31. doi: 10.2176/nmc.ra.2014-0446
13. Stefani A, Lozano AM, Peppe A, Stanzione P, Galati S, Tropepi D, et al. Bilateral deep brain stimulation of the pedunculopontine and subthalamic nuclei in severe Parkinson's disease. *Brain.* (2007) 130(Pt 6):1596–607 doi: 10.1093/brain/awl346
14. Collomb-Clerc A, Welter ML. Effects of deep brain stimulation on balance and gait in patients with Parkinson's disease: A systematic neurophysiological review. *Neurophysiol Clin.* (2015) 45:371–88. doi: 10.1016/j.neucli.2015.07.001

15. Du S, Dong J, Zhang H, Jin S, Xu G, Liu Z, et al. Taichi exercise for self-rated sleep quality in older people: a systematic review and meta-analysis. *Int J Nurs Stud.* (2015) 52:368–79. doi: 10.1016/j.ijnurstu.2014.05.009
16. Delafontaine A, Fourcade P, Zemouri A, Diakhaté DG, Saiydoun G, Yiou E. In patients with parkinson's disease in an off-medication state, does bilateral electrostimulation of tibialis anterior improve anticipatory postural adjustments during gait initiation? *Front Hum Neurosci.* (2021) 15:692651. doi: 10.3389/fnhum.2021.692651
17. Vialleron T, Delafontaine A, Millerioux I, Memari S, Fourcade P, Yiou E. Acute effects of short-term stretching of the triceps surae on ankle mobility and gait initiation in patients with Parkinson's disease. *Clin Biomech.* (2021) 89:105449. doi: 10.1016/j.clinbiomech.2021.105449
18. Abbruzzese G, Marchese R, Avanzino L, Pelosin E. Rehabilitation for Parkinson's disease: Current outlook and future challenges. *Parkinsonism Relat Disord.* (2016) 22 Suppl 1:S60–S4. doi: 10.1016/j.parkreldis.2015.09.005
19. Luan X, Tian X, Zhang H, Huang R, Li N, Chen P, et al. Exercise as a prescription for patients with various diseases. *J Sport Health Sci.* (2019) 8:422–1. doi: 10.1016/j.jshs.2019.04.002
20. Guo S, Huang Y, Zhang Y, Huang H, Hong S, Liu T. Impacts of exercise interventions on different diseases and organ functions in mice. *J Sport Health Sci.* (2020) 9:53–73. doi: 10.1016/j.jshs.2019.07.004
21. Donath L, Kurz E, Roth R, Zahner L, Faude O. Leg and trunk muscle coordination and postural sway during increasingly difficult standing balance tasks in young and older adults. *Maturitas.* (2016) 91:60–8. doi: 10.1016/j.maturitas.2016.05.010
22. Lelard T, Ahmaidi S. Effects of physical training on age-related balance and postural control. *Neurophysiol Clin.* (2015) 45:357–69. doi: 10.1016/j.neucli.2015.09.008
23. Huang Z-G, Feng Y-H, Li Y-H, Lv C-S. Systematic review and meta-analysis: Tai Chi for preventing falls in older adults. *BMJ Open.* (2017) 7:e013661. doi: 10.1136/bmjopen-2016-013661
24. Li F, Harmer P, McAuley E, Duncan TE, Duncan SC, Chaumeton N, et al. An evaluation of the effects of Tai Chi exercise on physical function among older persons: a randomized contolled trial. *Ann Behav Med.* (2001) 23:139–46 doi: 10.1207/S15324796ABM2302_9
25. Lan C, Lai J-S, Chen S-Y. Tai Chi Chuan: an ancient wisdom on exercise and health promotion. *Sports Med.* (2002) 32:217–24 doi: 10.2165/00007256-200232040-00001
26. Winser SJ, Tsang WW, Krishnamurthy K, Kannan P. Does Tai Chi improve balance and reduce falls incidence in neurological disorders? a systematic review and meta-analysis. *Clin Rehabil.* (2018) 32:1157–68. doi: 10.1177/0269215518773442
27. Zou L, Han J, Li C, Yeung AS, Hui SS-C, Tsang WWN, et al. Effects of tai chi on lower limb proprioception in adults aged over 55: a systematic review and meta-analysis. *Arch Phys Med Rehabil.* (2019) 100:1102–13. doi: 10.1016/j.apmr.2018.07.425
28. Guo L-y, Yang C-p, You Y-l, Chen S-k, Yang C-h, Hou Y-y, et al. Underlying mechanisms of Tai-Chi-Chuan training for improving balance ability in the elders. *Chin J Integr Med.* (2014) 20:409–15. doi: 10.1007/s11655-013-1533-4
29. Lan C, Chen S-Y, Lai J-S, Wong AM-K. Tai chi chuan in medicine and health promotion. *Evid Based Complement Alternat Med.* (2013) 2013:502131. doi: 10.1155/2013/502131
30. Rahal MA, Alonso AC, Andrusaitis FR, Rodrigues TS, Speciali DS, Greve JMDA, et al. Analysis of static and dynamic balance in healthy elderly practitioners of Tai Chi Chuan versus ballroom dancing. *Clinics (São Paulo).* (2015) 70:157–61. doi: 10.6061/clinics/2015(03)01
31. Zhou J, Chang S, Cong Y, Qin M, Sun W, Lian J, et al. Effects of 24 weeks of Tai Chi Exercise on postural control among elderly women. *Res Sports Med.* (2015) 23:302–14. doi: 10.1080/15438627.2015.1040918
32. Holmes ML, Manor B, Hsieh W-h, Hu K, Lipsitz LA, Li L. Tai Chi training reduced coupling between respiration and postural control. *Neurosci Lett.* (2016) 610:60–5. doi: 10.1016/j.neulet.2015.10.053
33. Zhou M, Peng N, Dai Q, Li H-W, Shi R-G, Huang W. Effect of Tai Chi on muscle strength of the lower extremities in the elderly. *Chin J Integr Med.* (2016) 22:861–6 doi: 10.1007/s11655-015-2104-7
34. Chang Y-T, Huang C-F, Chang J-H. The effect of tai chi chuan on obstacle crossing strategy in older adults. *Res Sports Med.* (2015) 23:315–29. doi: 10.1080/15438627.2015.1040920
35. Zou L, Loprinzi PD, Yu JJ, Yang L, Li C, Yeung AS, et al. Superior effects of modified chen-style tai chi versus 24-style tai chi on cognitive function, fitness, and balance performance in adults over 55. *Brain Sci.* (2019) 9:5. doi: 10.3390/brainsci9050102
36. Moreland B, Kakara R, Henry A. Trends in nonfatal falls and fall-related injuries among adults aged ≥65 Years - United States, 2012-2018. *MMWR Morb Mortal Wkly Rep.* (2020) 69:875–81. doi: 10.15585/mmwr.mm6927a5
37. Li F, Harmer P, Eckstrom E, Fitzgerald K, Chou L-S, Liu Y. Effectiveness of tai ji quan vs multimodal and stretching exercise interventions for reducing injurious falls in older adults at high risk of falling: follow-up analysis of a randomized clinical trial. *JAMA Netw Open.* (2019) 2:e188280. doi: 10.1001/jamanetworkopen.2018.8280
38. Li Y, Devault CN, Van Oteghen S. Effects of extended Tai Chi intervention on balance and selected motor functions of the elderly. *Am J Chin Med.* (2007) 35:383–91 doi: 10.1142/S0192415X07004904
39. Li F, Harmer P, Fisher KJ, Xu J, Fitzgerald K, Vongjaturapat N. Tai Chi-based exercise for older adults with Parkinson's disease: a pilot-program evaluation. *J Aging Phys Act.* (2007) 15:139–51 doi: 10.1123/japa.15.2.139
40. Schleicher MM, Wedam L, Wu G. Review of Tai Chi as an effective exercise on falls prevention in elderly. *Res Sports Med.* (2012) 20:37–58. doi: 10.1080/15438627.2012.634697
41. Li F, Harmer P, Fitzgerald K, Eckstrom E, Stock R, Galver J, et al. Tai chi and postural stability in patients with Parkinson's disease. *N Engl J Med.* (2012) 366:511–9. doi: 10.1056/NEJMoa1107911
42. Liu H-H, Yeh N-C, Wu Y-F, Yang Y-R, Wang R-Y, Cheng F-Y. Effects of Tai Chi exercise on reducing falls and improving balance performance in parkinson's disease: a meta-analysis. *Parkinsons Dis.* (2019) 2019:9626934. doi: 10.1155/2019/9626934
43. Gao Q, Leung A, Yang Y, Wei Q, Guan M, Jia C, et al. Effects of Tai Chi on balance and fall prevention in Parkinson's disease: a randomized controlled trial. *Clin Rehabil.* (2014) 28:748–53 doi: 10.1177/0269215514521044
44. Hackney ME, Earhart GM. Tai Chi improves balance and mobility in people with Parkinson disease. *Gait Posture.* (2008) 28:456–60. doi: 10.1016/j.gaitpost.2008.02.005
45. Taylor-Piliae RE, Hoke TM, Hepworth JT, Latt LD, Najafi B, Coull BM. Effect of Tai Chi on physical function, fall rates and quality of life among older stroke survivors. *Arch Phys Med Rehabil.* (2014) 95:816–24. doi: 10.1016/j.apmr.2014.01.001
46. Kurlan R, Evans R, Wrigley S, McPartland S, Bustami R, Cotter A. Tai Chi in Parkinson!s Disease: a preliminary randomized, controlled, and rater-blinded study. *Adv Parkinson's Dis.* (2015) :9-12. doi: 10.4236/apd.2015.41002
47. Amano S, Nocera JR, Vallabhajosula S, Juncos JL, Gregor RJ, Waddell DE, et al. The effect of Tai Chi exercise on gait initiation and gait performance in persons with Parkinson's disease. *Parkinsonism Relat Disord.* (2013) 19:955–60. doi: 10.1016/j.parkreldis.2013.06.007

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Neurology

ORIGINAL RESEARCH
published: 13 January 2022
doi: 10.3389/fneur.2021.789176

Startle Increases the Incidence of Anticipatory Muscle Activations but Does Not Change the Task-Specific Muscle Onset for Patients After Subacute Stroke

Nan Xia[1,2], *Chang He*[3], *Yang-An Li*[1,2], *Minghui Gu*[1,2], *Zejian Chen*[1,2], *Xiupan Wei*[1,2], *Jiang Xu*[1,2*] *and Xiaolin Huang*[1,2*]

[1] *Department of Rehabilitation Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China,* [2] *World Health Organization Collaborating Centre for Training and Research in Rehabilitation, Wuhan, China,* [3] *State Key Lab of Digital Manufacturing Equipment and Technology, Institute of Rehabilitation and Medical Robotics, Huazhong University of Science and Technology, Wuhan, China*

OPEN ACCESS

Edited by:
Eric Yiou,
Université Paris-Saclay, France

Reviewed by:
Ann Hallemans,
University of Antwerp, Belgium
William P. Berg,
Miami University, United States
Yun-Ju Lee,
National Tsing Hua University, Taiwan

***Correspondence:**
Jiang Xu
xujiang@hust.edu.cn
Xiaolin Huang
xiaolinh2006@tjh.tjmu.edu.cn

Specialty section:
This article was submitted to Neurorehabilitation, a section of the journal Frontiers in Neurology

Received: *04 October 2021*
Accepted: *13 December 2021*
Published: *13 January 2022*

Citation:
Xia N, He C, Li Y-A, Gu M, Chen Z, Wei X, Xu J and Huang X (2022) Startle Increases the Incidence of Anticipatory Muscle Activations but Does Not Change the Task-Specific Muscle Onset for Patients After Subacute Stroke. Front. Neurol. 12:789176. doi: 10.3389/fneur.2021.789176

Objectives: To demonstrate the task-specificities of anticipatory muscle activations (AMAs) among different forward-reaching tasks and to explore the StartleReact Effect (SE) on AMAs in occurrence proportions, AMA onset latency or amplitude within these tasks in both healthy and stroke population.

Methods: Ten healthy and ten stroke subjects were recruited. Participants were asked to complete the three forward-reaching tasks (reaching, reaching to grasp a ball or cup) on the left and right hand, respectively, with two different starting signals (warning-Go, 80 dB and warning-startle, 114 dB). The surface electromyography of anterior deltoid (AD), flexor carpi radialis (FCR), and extensor carpi radialis (ECR) on the moving side was recorded together with signals from bilateral sternocleidomastoid muscles (SCM), lower trapezius (LT), latissimus dorsi (LD), and tibialis anterior (TA). Proportions of valid trials, the incidence of SE, AMA incidence of each muscle, and their onset latency and amplitude were involved in analyses. The differences of these variables across different move sides (healthy, non-paretic, and paretic), normal or startle conditions, and the three tasks were explored. The ECR AMA onset was selected to further explore the SE on the incidence of AMAs.

Results: Comparisons between move sides revealed a widespread AMA dysfunction in subacute stroke survivors, which was manifested as lower AMA onset incidence, changed onset latency, and smaller amplitude of AMAs in bilateral muscles. However, a significant effect of different tasks was only observed in AMA onset latency of muscle ECR ($F = 3.56$, $p = 0.03$, $\eta^2_p = 0.011$), but the significance disappeared in the subsequent analysis of the stroke subjects only ($p > 0.05$). Moreover, the following *post-hoc* comparison indicated significant early AMA onsets of ECR in task cup when comparing with reach ($p < 0.01$). For different stimuli conditions, a significance was only revealed on shortened premotor reaction time under startle for all participants ($F = 60.68$, $p < 0.001$, $\eta^2_p = 0.056$). Furthermore, stroke survivors had a significantly lower incidence

of SE than healthy subjects under startle ($p < 0.01$). But all performed a higher incidence of ECR AMA onset ($p < 0.05$) than with normal signal. In addition, the incidence of ECR AMAs of both non-paretic and paretic sides could be increased significantly *via* startle ($p \leq 0.02$).

Conclusions: Healthy people have task-specific AMAs of muscle ECR when they perform forward-reaching tasks with different hand manipulations. However, this task-specific adjustment is lost in subacute stroke survivors. SE can improve the incidence of AMAs for all subjects in the forward-reaching tasks involving precision manipulations, but not change AMA onset latency and amplitude.

Keywords: startle, stroke, anticipatory muscle activation, rehabilitation, anticipatory postural adjustments

INTRODUCTION

Anticipatory muscle activations (AMAs) are considered as unconscious muscular activities to prevent the upcoming external disturbance to posture brought by the focal movement (1). For example, when we sit at the table and prepare to enjoy a glass of wine, we raise our right shoulder and arm to accurately grasp the glass in front of us. Before the arms are raised, our body will first move back to offset the disturbance of the forward movement, and approximately 50 ms before or at the same time, the muscles of the trunk and limbs have also been activated to prevent disturbance caused by voluntary movement and ensure the precision of grasp action. Such posture adjustments and muscle activation of the trunk and proximal joints are called anticipatory postural adjustments (APAs) and AMAs, respectively. As one motor control strategy, such anticipations are integrated into motor programing in a feed-forward way to both maintain postural stability and improve the focal motor performance (2, 3). The APAs could be observed and evaluated by the displacement of the body center of mass *via* postural graphic analysis and AMAs *via* surface electromyography (sEMG) (3–5) in the corresponding time window (6). In coping with disturbances and task accuracy (7), the AMAs show orderly activations and adjustments of systemic bilateral muscles and were further depicted as a servo-system responding to external or internal disturbance (2).

Compared with the displacement of the body center of mass, which represents the feedforward trunk movements, the AMAs of the whole body can provide more abundant muscle onset information, and it has been used for the movement prediction (3, 8). Related researches on the upper-limb movement at a sitting position indicated that AMA order, the amplitude of contraction, and duration could be used as predictive factors for the forthcoming action (3). The changes in AMA patterns brought about by the limb movements in different directions and speeds are easy to understand due to the different amplitude and directions of the disturbances. Indeed, even at the forearm level, the AMA tune of limb muscles could be opposite when performing finger taps with hand prone or supine (9). This phenomenon suggests that the AMAs are involved in the precision movement of the hand (9), and the timing and sequence of muscle activations can be specifically adjusted according to the position of the forearm. And this intra-limb AMA pattern seems to be further optimized in the precision movement on the dominant hand (7). The above results suggest that with the mastery and proficiency of precision tasks, task-specific AMAs will also be formed simultaneously. Therefore, it is reasonable to believe that skilled activities of hand have developed their specific AMA patterns. In addition, the highly developed human motor cortex and the extensive representative areas of the hand further provide a structural basis for the specialization of the precision movements of the hand. An experiment on monkeys indicated that firing neurons in the motor cortex were significantly different during the execution of reach and grasp (10). Thus, the human motor cortex is very likely to show these task-specific neuron activations, which represent different motor commands, respectively. Increasing pieces of evidence revealed that AMAs and the recruitment of prime mover shared the same motor command (11, 12). This means that the AMA patterns of the precision reach and grasp activities in humans may be task-specific. However, most previous studies using fast-arm flexion, reaching or pointing as their test paradigm (3), rarely consider hand manipulations. Whether such task-specific AMA patterns exist in the forward-reaching tasks involving finger movements is still unknown. This exploration of task-specific AMAs may help the development of motor intention recognition for the arm-hand tasks and provide personalized neurofeedback rehabilitation training for patients with motor dysfunction of the upper limb.

For most stroke survivors, the recovery of arm-hand function is one of the longest and most challenging topics. On the one hand, damage to the central nervous system directly leads to the loss of control of hand movements. On the other hand, abnormal muscle synergy patterns (typically flexor synergy) (13) and spasticity (14) that appear in the upper limbs during the recovery process can also hinder normal arm-hand movements. In addition, even if the single joint movements of the wrist and fingers can be restored, a lot of effort is still needed to regain the dexterity of functional arm-hand movements, such as precision grasp (15). A large number of studies have confirmed that APA training helps to restore the trunk function and balance of patients with stroke (16, 17). Given the important role of AMAs in upper-limb activities, we have reason to believe that targeted

training based on AMAs may help the recovery of forearm and hand function in patients with stroke. However, before that, we need to learn more about the AMA patterns in the forearm-hand movement of patients with stroke.

In the stroke population, delayed or even abnormal AMAs occur commonly in global muscles (18) and manifest a systemic less response to the upcoming disturbances, with more severe impairment to the contralateral side (19). These abnormalities require more voluntary compensation from both trunk and limb muscles to counteract disturbances and even ensure the accuracy of movement (6). Unfortunately, these pathological movement patterns involving atypical feedforward AMAs along with abnormal neuromodulation pathways would be over-enhanced with the time past for the severely injured stroke population (20–22). Therefore, evaluating the AMAs early after the stroke onset may allow us to more clearly find the functional defects before the occurrence of overcompensation. And the targeted training of AMAs for the arm-hand movement may be more effective.

Nevertheless, unresponsive AMAs in the stroke population may be submerged in the abnormal background noise and hard to detect (23). Besides the improvement from an sEMG signal processing technology (24), the introduction of the StartReact Effect (SE) (25) may provide a novel approach to trigger AMAs. A loud acoustic stimulus approximately higher than 110 dB could lead to the early initiation of prepared movements, including AMAs (4, 26). This phenomenon is explained as a well-prepared program that can be triggered output in advance mainly through the cortical reticulospinal tract (25). Coincidentally, the functional neuroregulatory structures of APAs include supplementary motor area (27), primary motor cortex (28), and pontomedullary reticular formation (29), which have a high degree of overlap with cortical reticulospinal formation. In healthy subjects, the loud acoustic stimulus has been confirmed to increase the response frequency of AMAs during gait initiation (4). Moreover, some studies further revealed that the exposure to startling does not impact the upper-limb voluntary activities but enhances the actual reaching performance in stroke subjects (30, 31). However, not all movement initiation can be triggered by SE early, it is negative in some distal finger manipulation activities (32). Whether startle has similar effects on reaching tasks involving precision hand movements remains unclear.

In the present study, we have designed a series of goal-directed hand manipulation tasks based on the forward-reaching paradigm (33–35) at a sitting position with the torso fully involved. We hypothesize that there is likely to be specific AMAs in different hand manipulation tasks, and patients with stroke may retain or lose these specificities. Meanwhile, positive SE may exist in these tasks and has a significant impact on the AMAs of patients with stroke. The first aim of our study was to investigate the task specificities of AMAs among different hand activities and further probe into its preservation or atypical changes in the stroke population. Simultaneously, we explored the SE on the occurrence proportion, muscle onset latency, and amplitude of AMAs on trunk and limb muscles in both healthy and stroke participants. The results of this study provide a basis for a better understanding of the AMAs in 3-D upper-limb grasp activities and give suggestions to develop novel approaches to APA rehabilitation after stroke based on SE.

MATERIALS AND METHODS

Participants

Experiments were carried out in age-matched 20 male subjects, 10 healthy volunteers, and 10 patients with stroke. The inclusion criteria for stroke subjects were: (1) first onset of ischemic or hemorrhage of the unilateral cortex and sub-cortex at the subacute phase (7 days to 6 months) (36); (2) age between 18 and 65 years old; (3) able to perform at least 30-degree shoulder flexion with the paretic arm without support at the sitting position; (4) no hearing impairment and able to understand movement instructions; and (5) good tolerance for 114 dB sudden audio stimulation. Participants would be excluded if they suffer impairments from other diseases or states that severely affect the participant's upper-limb and trunk function, such as fracture, rheumatoid arthritis, amputation, and high fever. Finally, all participants need to sign the informed consent before participation. This study was approved by the institutional ethical committee of Tongji Hospital (No. TJ-IRB20210648) and has completed the online pre-registration for clinical research (No. ChiCTR2100048222).

However, we failed to collect the data from one male patient with stroke, due to the missing anterior deltoid (AD) muscle onset data caused by loosely attached electrodes to the sEMG unit. For stroke subjects #8 and #9, the data of bilateral lower trapezius (LT) and latissimus dorsi (LD) were missing due to the temporary malfunction of electrodes. Finally, data from 10 healthy subjects and 9 patients with stroke were used for the analyses of this study. The baseline characteristics were summarized in **Table 1**. The mean age of stroke and healthy groups was 42.42 ± 13.26 and 36.50 ± 6.95 years old, respectively. The mean time post-stroke onset for the 9 patients was 2.83 ± 2.11 months.

Clinical Assessments

In subjects with stroke, the Fugel-Meyer assessment for upper extremity (FMA-UE) (37) was used for the evaluation of the motor function of the upper limb. Moreover, the spasticity was assessed by the modified Ashworth scale on biceps (38) on the paretic side. All patients have impairments in the upper extremity with a mean score of FMA-UE at 33.78. And their median score (Grade 1) of modified Ashworth scale revealed normal or slightly increased spasticity. Age, body mass index, and dominant hands were all comparable in both groups (see **Table 1**).

Experimental Procedure

In a warm, dry, and quiet room, participants were ordered to sit with their hips and knees flexed $\sim 90^{\circ}$ on a height-adjustable seat 1.5 m in front of a blank blackboard. The subject's upper limbs were asked to place next to the trunk as a starting position and keep the whole body relaxed as much as possible. A pallet tripod with 80% shoulder height was placed on the subject's anterolateral side (45°) with a distance of 120% arm length from

TABLE 1 | Demographic characteristics of the participants.

Subjects	Age (yr.)	BMI (kg/m^2)	Time from onset (mos.)	Dominant hand	Paretic side	Stroke type	Lesion location	FMA-UE (/60)	MAS (/4)
#1	48	19.16	5.5	R	R	I	Sub- & Cortical	11	0
#2	60	25.09	0.5	R	L	I	Subcortical	65	0
#3	53	20.52	0.5	R	L	I	Cortical	8	0
#4	41	23.72	5	R	R	H	Sub- & Cortical	13	1$^+$
#5	42	23.59	1	R	L	I	Sub- & Cortical	10	0
#6	40	18.01	4	R	L	H	Cortical	32	1$^+$
#7	53	26.73	1	R	R	I	Cortical	40	1
#8	18	25.39	3	R	R	H	Sub- & Cortical	61	1
#9	27	18.34	5	R	L	H	Cortical	64	1
#**Stroke group (*n* = 9)**	42.44 (13.26)	22.28 (3.31)	2.83 (2.11)	all R	4R/5L	4H/5I	Cortical: 2 Subcortical: 1 Sub- & Cortical: 4	33.78 (24.63)	1 (Mid.)
Healthy group (*n* = 10)	36.50 (6.95)	21.86 (2.55)	N/A	all R	N/A	N/A	N/A	N/A	N/A

BMI, body mass index; FMA-UE, Fugel-Meyer assessment for upper extremity; MAS, modified Ashworth scale.
#Represents the stroke participations. The yr. is same as years old. The mos. represent months. Sub- means sub-cortical lesion of the subject. The I and H represent ischemia and hemorrhagic stroke, respectively. The median score of the 9 stroke subjects was provided as grade 1 (Mid.). N/A means not applicable.

the acromion to the pallet center. Participants were asked to perform the required task correctly according to the auditory information from a stereophonic headphone (Sennheiser HD25-I; Wedemark, Germany). These tasks include reaching the center of the pallet, reach to grasp a tennis ball (about 58 g), or an inverted coffee takeaway cup with palm inward (7 cm base and 15 cm high) at the same weight. An illustration of the details in the task "reach to grasp a cup" in our study is provided in **Figure 1**.

The 3 tasks with 10 repetitions of each were randomly assigned into 30 trials within a test. Subjects would take an 1-min break after completing 10 consecutive trials. On each trial, within 5 s after the start of the experimental program, the subjects were verbally informed of the target action, such as "reaching to grasp the cup," and then hear a warning cue with continuous "beep" (82 dB, 1,000 Hz) for 0.5 s to prompt for "Get ready." In the next 2.5 to 3 s, the second auditory cue "Go" represents the initiation of the aiming task. Intervals between the two cues were separated randomly to prevent anticipation. In control trials, the "Go" cue was a 40-ms "beep" sound as same as the warning cue, whereas it was replaced with a broadband white noise (114 dB, 40 ms) for "Go" in the startle trials. Although some research suggests that 124-dB acoustic stimulus may be more efficient (39) because of patient acceptability, we chose a relatively mild startle stimulation used in similar researches (40, 41). There is a 15-s interval between every two trials to ensure that the subjects are fully relaxed and provide sufficient time for the replacement of the ball or cup on the tripod. About 30 trials were required for the test on each side for all participants, and half of those trials would use startle white noise as a "Go" cue. The orders of 15 control or 15 startling "Go" cues were also randomized in the test. At the beginning of these trials, 5–10 practices were implemented to ensure the smooth completion of the task. Healthy subjects were tested on the right hand first, and stroke participants completed it on the non-paretic side before using the paretic arm. Regardless of the performance, the test operators encouraged all subjects to complete the corresponding task as quickly and accurately as possible throughout the test. Additional encouragement for stroke subjects with obvious muscle paralysis would also be provided. The Psychtoolbox-3 toolkit based on MATLAB (2017b, MathWorks, Natick, MA, USA) was used for the design and execution of all tests.

Surface Electromyography and Data Preprocessing

The Ag/AgCl surface electrodes connecting to wireless sEMG units were placed bilaterally on the subject's right and left sternocleidomastoid muscles (SCM), the bilateral (LT), bilateral (LD), and tibialis anterior (TA). AD, flexor carpi radialis (FCR), and extensor carpi radialis (ECR) of the motion side were also placed with electrodes for sEMG recording. All operations in our experiment followed the SENIAM recommendations, and the signals were visually verified by voluntary contraction. The sEMG signals were collected by the Ultimu EMG system (Noraxon USA Inc., Scottsdale, AZ, USA) at a sampling rate of 2,000 Hz.

The raw data of sEMG were output and processed *via* the MATLAB software (2017b, MathWorks, Natick, MA, USA). The raw data directly output pre-processed first, including data segmentation and data filtering process by using a 30–300 Hz bandpass filter and a 50-Hz notch filter. The Teager–Kaiser energy operation was used to process the filtered data, which was based on the simultaneous sEMG amplitude and instantaneous frequency as a reference basis and has achieved higher reliability than normal methods (24). After data rectification and normalization,

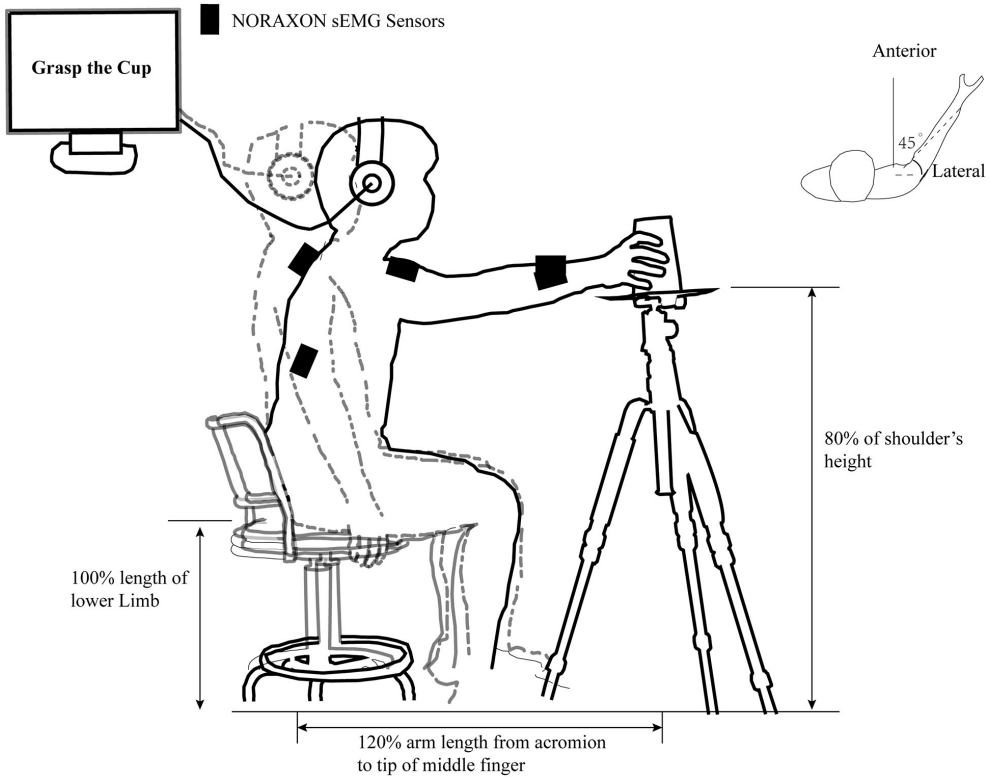

FIGURE 1 | An illustration of the task "reach to grasp a cup" in our study. The outline of the human body in the gray dashed line and the black solid line represent the position of the subject in the pre-motor preparation and motor execution phases in the "reach to grasp a cup" task, respectively. The black rectangle represents the position where the infinite surface EMG sensors is placed. The individually adjusted seat height, the relative position of the cup, and the acromion of movement side are clearly marked. The computer-generated "Warning" and "Go" cues were communicated to the subject through a headset.

the threshold detection method was used to determine the onset time of muscle activation. The threshold T can be set as:

$$T = \mu + h\sigma$$

where μ and σ are the mean and SD of baseline amplitudes of the time window 2,500–500 ms before each "Go" cue, and h is a preset variable ($h = 3$ in this study). Finally, the morphological operation (42) was used to eliminate false-positive activation points.

According to the video recording, trials with obvious task errors (such as movement initiation before the "Go" cue or performing the wrong task) were eliminated first. The left and right side data of healthy subjects were converted to the same model, and the data of patients with stroke were converted to the non-paretic side and the paretic side data. The muscle activation onset time of AD was considered as time zero (T_0) for all tasks. Moreover, the premotor reaction time was calculated for the interval between the rise of the "Go" signal to T_0. Trials were also excluded from the data analysis if the reaction time of AD is within 30 ms after the "Go" cue or exceeds 400 ms for muscle response. The remaining trials were considered valid. Furthermore, the reaction time of SCM was also calculated. If the reaction time of either SCM was in the time window of 30 to 130 ms after the "Go" cue, the trial will be marked as a positive SCM^+ trial. SCM^+ has been suggested as a sign of a complete SE in the upper-limb movements (25). The onset latency of the other muscles each was calculated as the difference between muscle activation onset to T_0. The integrals of sEMG of the muscle activation amplitude were calculated at the APAs window (−100 to +50 ms) (6, 43) to T_0. A detailed description of the definition and calculation process of the parameters and outcome variables were provided in **Table 2**.

Statistical Analyses

Demographic data and proportion variables (e.g., number of valid trials and incidence of SCM^+) were first checked for their normality of distribution. And independent Student's t-tests were used for demographic data comparisons between healthy and stroke subjects. Differences in proportion variables between the two sides of stroke subjects were tested by paired t-tests. A general linear model using 3 move sides (healthy vs. non-paretic side vs. paretic side), 2 conditions (startle or normal), and 3 move tasks (reach, reach to grasp a ball or cup) as fixed factors were performed to test the differences. The original model included the main effects of the above 3 fixed factors, interaction effects of each two fixed factors, and a random intercept for subjects.

TABLE 2 | The definition and calculation process of the parameters and outcome variables.

Parameters/outcomes	Definition	Calculation methods
T_0	The muscle activation onset time point of anterior deltoid in each trial	Over 10 consecutive samples of the smoothed signal exceeding the threshold (the mean with 3 SD of baseline amplitudes of for anterior deltoid in the time window 2,500 to 500 ms before each "Go" cue).
Premotor reaction time	The response time of motor initiation (shoulder flexion)	The interval between the rise of "Go" signal to T_0 at each trial.
Valid trials numbers	Valid trials numbers in the total 60 trials for each subject	Trials were excluded if the premotor reaction time is within 30 ms after the "Go" cue or exceeds 400 ms for muscle response.
Incidence of SCM$^+$	The percentage of valid startle trials with positive activation of muscle sternocleidomastoid (positive startle react effect) in total valid trails for each subject	"Number of valid startling trials with muscle activation time of either side of bilateral SCMs was in the time window of 30 to 130 ms after 'Go' cue"/total valid trails including normal and white noise signals.
AMA onset	Anticipatory muscle activation onset of the testing muscles	The onset time point calculation through the threshold method ($T = \mu + h\sigma$). In valid trials, the number of muscle activation onset at the APAs window: -100 to $+$ 50 ms to T_0 for each muscle except AD and SCMs.
Proportion (incidence) of AMAs in valid trials	The percentage of AMA onset trial numbers in total valid trial numbers for each muscle of each subject	"AMA onset trial numbers for each muscle of each subjects" / "total valid trial numbers for each muscle of each subject"
Muscle onset latency	The interval of muscle onset time to T_0 in each trial with positive AMA onset	Use the actual activation time of the target muscle minus the time point of T_0
AMA amplitude	The muscle activation amplitude of each muscle at the APA window in each valid trial with AMA onset	The integral of the amplitude of sEMG signal after the preprocessing step in the time window -100 to $+$ 50 ms to T_0.

SCM$^+$ represents a positive response of sternocleidomastoid muscle. AMA represents anticipatory muscle activation.

Since no significant effect of interaction terms was found in all tests, they were excluded from the model analysis. Factors without significant main effects were also excluded from the final model for the analyses of corresponding variable. For the final positive models, *post-hoc* comparisons with Bonferroni corrections were used for those fixed factors with significant main effects. Moreover, for the healthy subjects, we made a model involving 2 conditions and 3 move tasks as fixed factors and a random intercept for subjects to do the analysis. Another general linear model using 2 move sides (non-paretic side vs. paretic side), 2 conditions (startle or normal), and 3 move tasks (reach, reach to grasp a ball, or reach to grasp a cup) as fixed factors and including random intercept for subjects was also performed to test the differences in stroke subjects. In the final positive models, *post-hoc* comparisons with Bonferroni corrections were used. The software IBM SPSS 22.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses, and $p < 0.05$ was set as the significant level.

RESULTS

The Proportion of Valid Trials and Trials With Valid AMA Onset

Those proportion variables were compared between healthy participants and stroke subjects. A total of 1,027 trials were successfully screened out from the tests of 19 participants (1,140 trials). The healthy group had significantly higher numbers of valid trials than the stroke group (55.90 $\pm$ 3.28 vs. 52.00 $\pm$ 2.60, $F = 1.02$, $p = 0.01$). However, no difference was detected in the numbers of valid trials between the non-paretic and paretic sides ($p > 0.05$) in stroke subjects.

The numbers of valid AMA onset trials of each muscle in the 8 testing muscles range from 418 to 666, and the top two incidences of AMAs were in FCR and ECR as 64.86% and 62.90%, respectively. The contralateral LD (cLT) achieved the lowest at 40.70%. Moreover, the percentage of valid AMA trials in ECR, FCR, and both TAs all indicated lower AMA incidence in the stroke group ($p < 0.01$). No significant differences were detected between the two groups in the proportions of valid AMA trials of bilateral LT and LD ($p < 0.01$). It was worth mentioning that the four patients with lower FMA scores can still detect obvious AMAs in ECR and FCR (see **Table 3**).

Muscle Onset Latency

In the analyses on the effects of the 3 above fixed factors (move sides, conditions, and tasks) on muscle onset latency, no main effect of conditions was observed ($p > 0.05$). The factor move sides have significant main effects on the activation onset latency of muscle ECR, FCR, bilateral LT, and bilateral TA ($p < 0.05$). No main effects were observed of the 3 fixed factors for the muscle onset latency of bilateral LD ($p > 0.05$). The *post-hoc* comparisons were made on onset latency of the above muscles except LD in the different sides (healthy, non-paretic, and paretic sides). Significant activation delays on muscle ECR, FCR, bilateral LT, and ipsilateral TA (iTA) were observed in the healthy side when compared with the paretic side ($p < 0.01$). Differences of muscle onset latency between the healthy and non-paretic sides were also found in ECR (-5.85 ± 44.23 vs. -17.85 ± 52.80 ms, $p = 0.04$) and contralateral TA (cTA; -20.05 ± 51.76 vs. -41.59 ± 54.11 ms, $p < 0.01$). The muscle onsets of FCR and bilateral LT in the movement of the paretic side were also earlier than the non-paretic side ($p \leq 0.02$).

TABLE 3 | Proportion of startle responses and anticipatory muscle activations (AMAs) of subjects.

Subjects	Valid trial numbers	Incidence of SCM^+ (%)	Proportion of AMAs in valid trials (%)							
			ECR	FCR	iLT	cLT	iLD	cLD	iTA	cTA
#1	53	15.09	56.60	52.83	62.26	60.378	58.49	52.83	56.60	32.08
#2	56	23.21	67.86	78.57	82.14	66.07	46.43	41.07	66.07	58.93
#3	52	21.15	61.54	53.85	92.31	65.38	75.00	61.54	50.00	51.92
#4	48	12.50	35.42	35.42	41.67	37.50	33.33	27.08	50.00	37.50
#5	54	7.41	37.04	44.44	59.26	57.41	44.44	55.56	18.52	22.22
#6	54	18.52	51.85	46.30	48.15	40.74	33.33	38.89	48.15	27.78
#7	52	19.23	59.62	71.15	78.85	69.23	38.46	55.77	38.46	40.38
#8	50	20.00	50.00	58.00	N/A	N/A	N/A	N/A	18.00	40.00
#9	49	12.24	34.69	34.69	N/A	N/A	N/A	N/A	24.49	28.57
#Stroke group, mean (SD)	52.00 (2.60)	16.60 (5.11)	50.51 (12.27)	52.81 (14.88)	66.38 (18.65)	56.67 (12.63)	47.07 (15.11)	47.53 (12.19)	41.14 (17.31)	37.71 (11.82)
Healthy group, mean (SD)	55.90 (3.28)	25.85 (7.25)	72.69 (9.06)	74.37 (13.51)	69.48 (15.10)	48.18 (7.39)	60.55 (15.66)	48.00 (14.60)	64.36 (20.59)	55.47 (19.50)
***F*-value**	1.02	0.39	1.48	0.01	0.78	2.75	0.17	0.02	0.06	2.70
***p*-value**	0.01*	< 0.01**	< 0.01**	< 0.01**	0.718	0.114	0.105	0.946	< 0.01**	< 0.01**

*Incidence of SCM^+ represents the percentage of numbers of valid trials with position earlier onset of sternocleidomastoid muscle in total valid trial number of subjects. ECR, FCR, i/cLT, i/cLD and i/cTA represents muscle extensor carpi radialis, flexor carpi radialis, ipsilateral/contralateral lower trapezius, ipsilateral/contralateral latissimus dorsi, and ipsilateral/contralateral tibialis anterior. *p-value < 0.05, **p-value < 0.01. # represents the stroke participations.*

The factor move tasks only have significant main effects on the muscle onset latency of ECR ($F = 3.56$, $p = 0.03$, $\eta^2_p = 0.011$) and ipsilateral LT (iLT) ($F = 3.92$, $p = 0.02$, $\eta^2_p = 0.013$). And *post-hoc* comparisons revealed significant differences between the move task reach (ECR, -5.37 ± 45.91; iLT, -8.66 ± 50.03 ms) and cup (ECR, -17.42 ± 50.05; iLT, -22.01 ± 53.69 ms) ($p < 0.03$), indicating an obvious earlier muscle onset of ECR and iLT in the move task cup. However, no differences were detected in onset latency of the above two muscles between task reach and ball ($p > 0.05$).

A further separate general linear model analysis involving fixed factors of conditions and tasks was made for the muscle onset latency of ECR and iLT in healthy subjects. No obvious main effects of conditions were observed for the two variables ($p > 0.05$). And the model was negative for the exploration of the main effect on the conditions, move tasks for muscle onset latency of iLT ($p > 0.05$). Only move tasks have significant main effects on the muscle onset latency of ECR ($F = 4.98$, $p < 0.01$, $\eta^2_p = 0.024$). Moreover, the *post-hoc* comparisons of the above model on different move tasks revealed significant earlier AMA onset of ECR in move task cup when compared to task reach ($p < 0.01$). However, no difference of AMA onset of ECR was detected between task reach and ball or ball and cup ($p > 0.05$). **Figure 2** provides mean with SEM of AMA onset latency on each muscle across the 3 move tasks and different move sides.

The general linear model analyses involving factors of move sides, conditions, and tasks for the muscle onset latency of ECR, FCR, bilateral LTs, bilateral LDs, and bilateral TAs of both sides were made in stroke subjects. The results indicated that no main effect of conditions and tasks was observed in the model on the muscle onset latency of all muscles ($p > 0.05$). It also revealed the only significant main effect of move sides for onset latency of FCR ($F = 5.54$, $p = 0.02$, $\eta^2_p = 0.022$), iLT ($F = 18.86$, $p < 0.01$, $\eta^2_p = 0.072$), and cLT ($F = 12.74$, $p < 0.01$, $\eta^2_p = 0.058$). The results revealed a significantly earlier muscle onset of FCR, iLT, and cLT when using the paretic side to complete reaching and grasp move tasks.

AMA Amplitude of Muscles

In the general linear model analyses, no main effects of conditions on AMA amplitude of these muscles were found ($p > 0.05$). However, significant main effects of factor move sides were observed in the AMA amplitude of ECR ($F = 8.82$, $p < 0.001$, $\eta^2_p = 0.026$), FCR ($F = 18.09$, $p < 0.001$, $\eta^2_p = 0.052$), iLT ($F = 12.99$, $p < 0.001$, $\eta^2_p = 0.042$), cLT ($F = 7.35$, $p = 0.001$, $\eta^2_p = 0.027$), ipsilateral LD (iLD) ($F = 6.01$, $p = 0.003$, $\eta^2_p = 0.023$), and cLD ($F = 24.33$, $p < 0.001$, $\eta^2_p = 0.099$). And the *post-hoc* comparison on move sides revealed the significant smaller AMA amplitude of ECR, FCR, and cLD in both non-paretic and paretic sides of the stroke subjects ($p < 0.01$). The AMA amplitude of cLT on the paretic side was also smaller than healthy side ($p < 0.01$). Nevertheless, significant larger AMA amplitude of iLT and iLD of the paretic side was observed when compared to the non-paretic side ($p < 0.05$). The AMA amplitude of iLT on paretic side also performed larger than healthy side (38.47 ± 35.55 vs. 26.37 ± 27.41 times, $p < 0.01$). The AMA amplitude of iLD on paretic side was equivalent

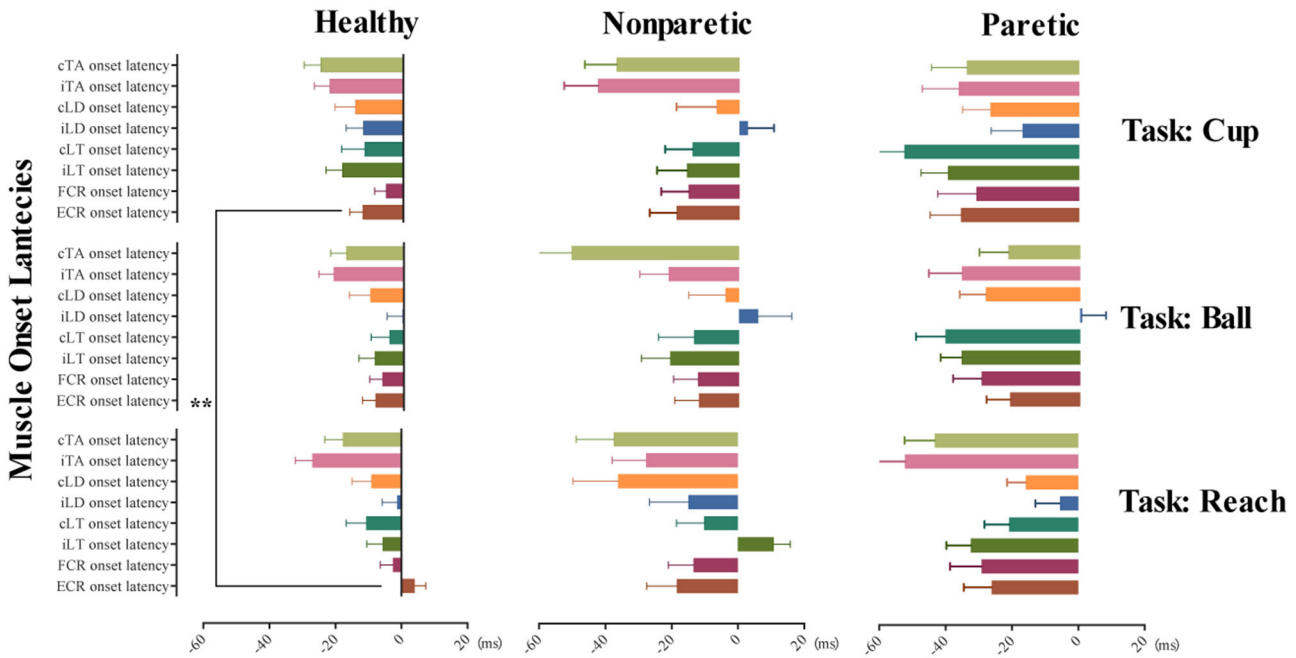

FIGURE 2 | Tunes of AMA onset in the three move tasks of the healthy, non-paretic, and paretic side. This illustrates the tunes of AMA onset in task reach, grasp a ball, and grasp a cup with different move sides, including healthy subjects, non-paretic side, and paretic side of stroke subjects, respectively. Horizontally arranged from left to right are the mean with SEM of AMA onset latency in healthy, non-paretic, and paretic sides; vertically arranged from top to bottom are the different AMA onset latency (mean with SEM) in tasks cup, ball, and reach. $^{**}p$-value < 0.01.

to the healthy side (43.62 ± 35.14 vs. 41.35 ± 36.43 times, $p > 0.05$).

For the fixed factor of move tasks, only a significant main effect on the AMA amplitude of iLT was observed ($F = 3.81$, $p = 0.02$, $\eta^2_p = 0.013$). And the *post-hoc* analyses on move tasks revealed a larger AMA amplitude of iLT in task reach (32.50 ± 31.66 times) compared with task ball (24.97 ± 26.39 times) ($p = 0.02$). But no difference was detected between reach and cup (26.40 ± 27.96 times) ($p > 0.05$). For AMA amplitude of bilateral TAs, no significant main effects of the three fixed factors (move sides, conditions, and tasks) were detected ($p > 0.05$). The muscle onset latency and AMA amplitude of ECR and iLT are shown as examples in **Figures 3B–E**. **Supplementary Material 1** provides the detailed results of positive general linear models and the *post-hoc* comparisons for these variables.

Premotor Reaction Time

In the general linear model analyses on all subjects, significant main effects of stimuli conditions ($F = 60.68$, $p < 0.001$, $\eta^2_p = 0.056$) and move sides ($F = 7.87$, $p < 0.001$, $\eta^2_p = 0.015$) were found in the premotor reaction time. However, no main effect of move tasks on premotor reaction time was observed ($p > 0.05$). It was significantly faster in the startle condition (146.47 ± 66.02 ms) than normal condition (183.65 ± 84.56 ms) ($p < 0.001$). And the *post-hoc* comparisons revealed significant differences between the healthy and paretic sides (160.47 ± 68.71 *vs.* 181.51 ± 93.25 ms, $p = 0.005$) and between the non-paretic and paretic sides (159.80 ± 79.03 *vs.* 181.51 ± 93.25 ms, $p = 0.001$). No differences were detected between the healthy and non-paretic sides ($p > 0.05$). The comparisons of AD reaction time of different move sides in startle and normal conditions are shown in **Figure 3A**.

Incidence of SCM$^+$

In the 525 valid trials with startling "Go" cue, 183 trials were marked as positive SE with SCM$^+$ (34.86%). Incidence of SCM$^+$ in stroke subjects was significantly lower than healthy participants ($F = 0.39$, $p < 0.01$).

Considering that SE on AMAs is systemic (44), and the percentage of valid AMA trial numbers over 50% would provide better reliability (45), we selected the ECR AMA onset to further explore the SE on the incidence of AMAs. Both the healthy and stroke groups showed a higher incidence of ECR AMA onset in startle than normal condition ($p < 0.05$).

The difference in the incidence of ECR AMA onset in stroke subjects at different conditions of the two sides was further compared. Higher incidence of ECR AMA onset was observed in startle condition on both non-paretic and paretic sides when compared to the normal condition ($t = -3.21$, $p = 0.01$; $t = -2.83$, $p = 0.02$). No difference was detected in the incidence of ECR AMA onset in the startle condition between the two sides of stroke subjects ($p > 0.05$; see **Table 3**).

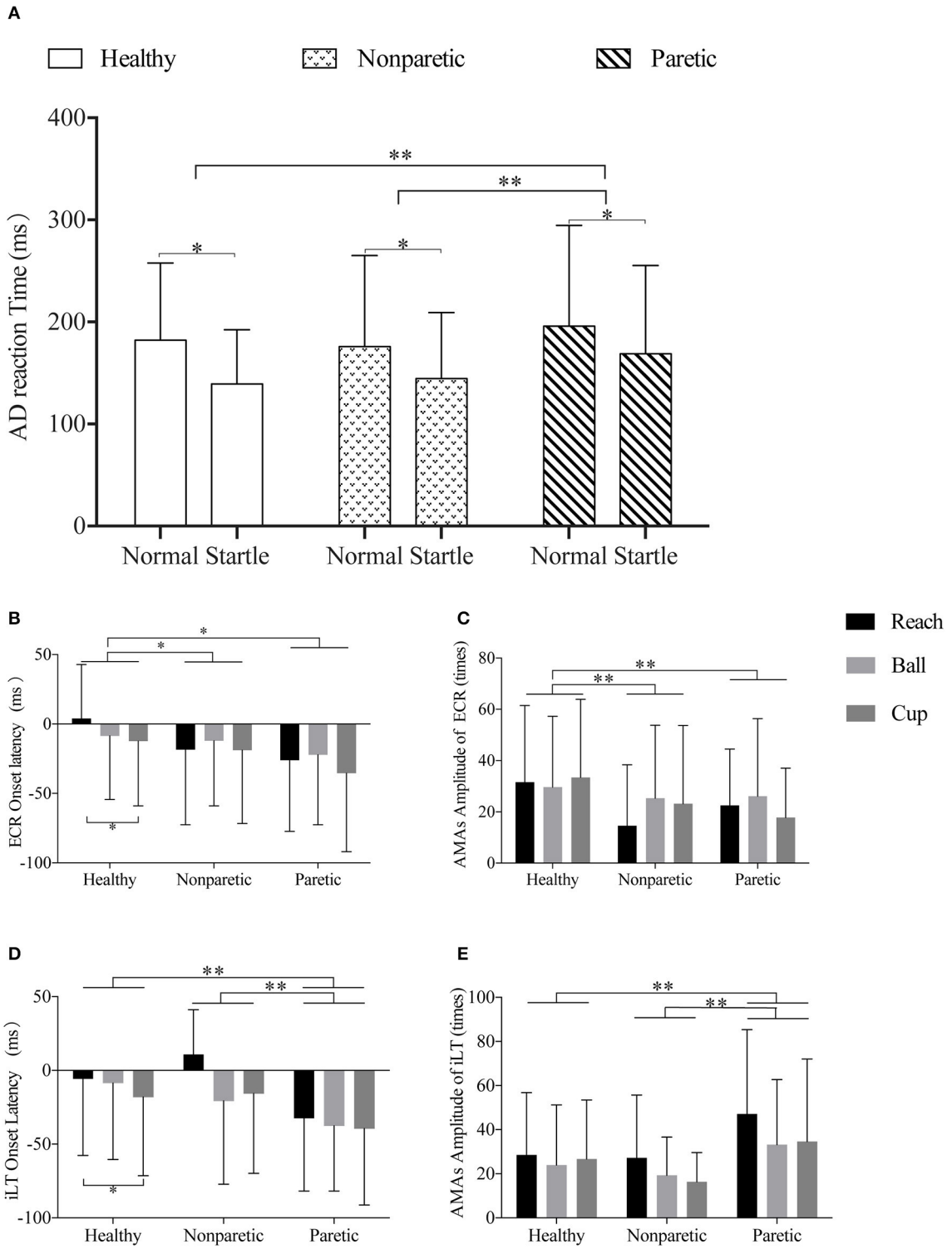

FIGURE 3 | Illustrations of the comparisons across different sides and move tasks in premotor reaction time, muscle onset latency, and amplitude of ECR and iLT. **(A)** Representation of the different AD reaction times of normal or startle conditions of healthy, non-paretic, and paretic sides. **(B,C)** Representation of the different ECR onset latency and ECR AMA amplitude of the "reach," "ball," and "cup" tasks in healthy, non-paretic, and paretic sides, respectively. **(D,E)** Representation of the different iLT onset latency and iLT AMA amplitude of the "reach," "ball," and "cup" tasks in healthy, non-paretic, and paretic sides, respectively. All data were presented by mean and SD. *p-value < 0.05; **p-value < 0.01.

DISCUSSION

In the present study, we first confirmed the existence of task-specific AMA patterns of precision reach and grasp activities at the forearm in the healthy population. At the same time, the AMAs of the proximal joints, trunk, and lower limbs did not show specific adjustments to these hand manipulation tasks. In our test paradigm, a significantly earlier AMA initiation of muscle ECR was observed in tasks with cylinder-shaped grasping movement. However, these task-specific AMAs of ECR disappeared in stroke subjects. Moreover, we found widespread decreased AMA incidence and amplitude on bilateral muscles caused by stroke, which was more pronounced in the limbs on the paretic side. Fortunately, these survivors with severe upper-limb motor impairment still preserved the activation of AMAs in the forearm muscles. Meanwhile, although the patients with stroke performed lower SE incidence, the startle can induce significantly shorter premotor reaction time for all participants in our test paradigm (**Figure 3**). Startle can also help to increase the incidence of AMAs, but not affect the latency and amplitude of AMAs. In other words, SE leads to the early initiation of AMAs, but it did not affect the corresponding inherent AMA tunes of forward-reaching tasks.

Consistent with previous researches (18, 19), we found systemic AMA dysfunctions in subjects with subacute stroke. And a significant decline of AMA incidence of bilateral muscles in stroke subjects was observed. However, most of the previous studies ignored the fluctuations of AMA response at the individual levels, and the incidence of AMA onset was rarely reported (3, 46, 47). As shown by recent studies, the incidence of AMAs (45, 48, 49) and proportion of SCM^{+} trials (25, 44, 50) were important parameters for the evaluation of APAs or the state of startle-related pathways. It has been suggested in a previous study that stroke-induced atypical APAs *via* an unbalanced excitability/inhibitory control of the central nervous system (51), and typically the system was inhibited (44). Therefore, the proportion variables are important references to the state of this control system. In addition, increasing pieces of evidence suggested the impaired motor programing, and APA deficits were caused by the imbalance or atypical controls of the bilateral cortical reticulospinal tract (44, 51, 52). One pilot study has confirmed the potential benefits in reaching movement performance (31). This improvement in functional performance may have a certain relationship with the response incidence of AMAs. Given the special contribution of the startle to activation of this pathway, some rehabilitation approaches developed based on startle may be helpful for increasing the APA incidence and even improve the arm-hand motor performance.

Compared with the experimental results of Yang et al. (44), the muscles on the non-paretic side did not show large-scale AMA onset abnormalities in our study, which may be due to the choice of different motor test paradigms and participants. Yang uses the reaching task in the standing position as the test paradigm, and does not involve precision hand manipulation. This type of AMAs that do not involve finger movements may be different from precision tasks of the hand. Moreover, our study recruited subjects with subacute stroke, whereas Yang et al. (44) and Pereira et al. (46) recruited participants at the chronic phase from 1 to 20 years after stroke onset. Due to the high adaptability and neuroplasticity of the central nervous system, increasing compensation could be adaptive, which may develop new movements or behavioral patterns based on the remaining neural substrate (36). These changes may strengthen certain abnormal AMA responses (20, 53). It is possible that the non-paretic side of stroke survivors still retains the normal AMA control at the early phase, but this control is replaced by a more compensational one over time. Therefore, a timely understanding of the characteristics of AMA deficit in the subacute phase after stroke may be more helpful to the APA rehabilitation strategies at this stage.

In our research, the ECR AMAs in the cup task showed obvious earlier onset than in the reach task. It is worth mentioning that this task-specific ECR AMA onset was only manifested in normal subjects, and stroke participants did not have this feature. This end-adjustment strategy for different hand activities in ECR AMA onset reflects that our central nervous system tends to adopt remote AMAs to adapt to the execution of various dexterity tasks. This kind of regulation of distal-specific muscles that can improve the task performance has also been found on muscle TA of the anterior leg in fencing athletes (54). Compared with the reaching task, the columnar grasping (task: cup) performs additional wrist flexion and rotations of the forearm, which requires higher control of the forearm. The participation of wrist and finger movements would cause greater disturbance to the arm, which leads to the earlier onset of ECR AMAs for combating the disturbance and improving the task performance. As the onset of several muscles had been used as the predictor of forthcoming movements (3), the task-specific AMA onset latency of ECR might be a useful predictor of the forthcoming wrist and finger movements. The reason why we failed to observe similar changes on muscle FCR may be related to our test paradigms. All tasks were performed in palm-down and palm-inward postures, and the difference in forearm posture may lead to changed AMA onset of both ECR and FCR (9).

However, this task-specific performance in ECR disappeared in stroke subjects even at the non-paretic side (see **Figures 3B,D**). This phenomenon has been suggested as the obvious deficit of feedforward motor preparation in stroke subjects (55). In previous imaging studies, abnormal hyperexcitability of the bilateral premotor cortex was revealed in stroke survivors, and it had a negative correlation with the recovery of motor function (56–58). As we have learned, the premotor cortex is mainly responsible for motor planning and preparation, and the excessive excitability of these areas would induce reinforced inhibition to the cortical reticulospinal tract (44) and consequently affect the modulation of task-specific AMAs. This was supported by the lower incidence of ECR AMAs and positive SE response, which may reflex the impaired cortical reticulospinal tract after stroke (22, 44). Therefore, rehabilitation interventions for the impaired cortical reticulospinal tract may

be helpful for the recovery of AMAs after stroke. For the arm-hand movements, novel treatments could be developed based on the task-specific AMA onset of ECR, such as neurofeedback training for humancomputer interaction and rehabilitation robotics (59).

On the contrary to most previous researches (46), we observed comprehensive earlier AMA onset in ECR, FCR, and bilateral LTs and TAs in stroke subjects. This could not be fully explained by the change of AMAs accompanied by the alignment of the scapula and thorax (60) as mentioned by Pereira et al. (46) in a similar study. One possible explanation is that sufficient time for preparation results in the delayed activation of AMAs in proficient movements. A similar research of Akbaş et al. (54) revealed that the onset of TAs in professional fencers at a well-prepared state was significantly delayed than that of normal people. The time of about 2.5 s, we set, is enough for the subjects to make adequate preparations (61). Another reasonable explanation is that the AMA onset latency of subacute stroke survivors is polarized, with premature or delayed activation onset, and the delayed part has been filtered out by the time window we set and considered as negative AMA response. And a state of full preparation before the motor execution improved the stability of AMA performance in healthy subjects (61) but has limited effects for stroke survivors.

Our research also has some limitations. First of all, we did not use SCM^+ as the marker to screen valid SE trials for group comparisons. Instead, we included all valid trials that used the startle "Go" cue into the final analysis. In our tests, the positive incidence of SCM^+ for stroke and normal participants was 16.6 and 25.9%, respectively. The result of healthy subjects in our study has comparable SCM^+ proportions with the result from a previous study (40) at the same stimuli intensity (114 dB). Such occurrence proportions of SCM^+ may lead us to underestimate the influence of SE on motor initiation and AMA onset latency or amplitude. Early muscle onset can also be found without premature activation of SCM in trials with startling "Go" cues (62). Simply emphasizing the use of data from positive SCM^+ trials may lose valuable information from SCM^- trials. In the case that the participant is acceptable, a 124-dB cue (39) might be better. The second limitation of our study was that our experiment did not strictly limit the severity of motor impairment of participants. The large difference in FMA score may indicate different dominant neural pathways they rely on (22), which may lead to unstable results. Stroke survivors within different motor function levels may use different motor synergies of flexors and extensors (22) and perform different AMA responses. Stratified analysis should be necessary according to the subject's motor function states in further researches with a higher sample size. At last, our research focused on the initiation of AMAs and did not include classic APA evaluation indicators, such as onset or velocity of displacement of body center of mass on the trunk (3, 5) in this study. SE may affect the movement amplitude and velocity of the trunk and limbs of stroke survivors (30, 31). The integration of a wearable inertial measurement unit with sEMG may better optimize our conclusions. In addition, future research design around upper-limb functional rehabilitation may need to consider more direct and effective evaluation methods, such as grip strength.

CONCLUSIONS

The present research revealed task-specific AMAs of muscle ECR in forward-reaching movements involving precision hand manipulations. This research also indicated the impaired APAs with lower incidence of SE and AMA response, changed AMA onset latency, and smaller AMA amplitude in patients with stroke. And startle can improve the incidence of AMAs in both healthy and stroke populations, but it does not affect the tunes and amplitude of AMA onset. And the deficit of such task-specific AMAs in ECR indicates the impairment of APA programming for arm-hand precision movements on both hands in the stroke population. Finally, these findings may provide support to develop novel methods for APA rehabilitation after stroke.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding authors.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institutional Ethical Committee of Tongji Hospital. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

XH, JX, and NX: designed the research. NX, CH, YL, MG, ZC, and XW: participated in the subject recruitment, research implementation, and data collection. NX and CH: performed the data analysis. NX: wrote the draft. All authors had full access to the data. All authors have reviewed the research and approved the submitted version.

FUNDING

The study was supported by the National Natural Science Foundation of China (Grant Nos. U 1913601 and 91648203).

ACKNOWLEDGMENTS

We thank all volunteers who participated in this study for their support.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2021.789176/full#supplementary-material

Supplementary Material 1 | Results of liner model and *post-hoc* comparison of variables. The positive liner model based on data from all subjects and significant main effects of the 3 fixed factors (3 move sides, 2 stimuli conditions, and 3 move tasks) in different variables were provided. The *post-hoc* comparisons with Bonferroni corrections under each fixed factor with significant main effects in its model were provided after each liner model. H, N, and P represent healthy, non-paretic, and paretic sides, respectively. R, B, and C represent the move task reach, reach to grasp a ball, and reach to grasp a cup, respectively. N/A means not applicable.

REFERENCES

1. Bouisset S, Do MC. Posture, dynamic stability, and voluntary movement. *Neurophysiol Clin.* (2008) 38:345–62. doi: 10.1016/j.neucli.2008.10.001
2. Cavallari P, Bolzoni F, Bruttini C, Esposti R. The organization and control of intra-limb anticipatory postural adjustments and their role in movement performance. *Front Hum Neurosci.* (2016) 10:525. doi: 10.3389/fnhum.2016.00525
3. Chikh S, Watelain E, Faupin A, Pinti A, Jarraya M, Garnier C. Adaptability and prediction of anticipatory muscular activity parameters to different movements in the sitting position. *Percept Mot Skills.* (2016) 123:190–231. doi: 10.1177/0031512516656817
4. Delval A, Dujardin K, Tard C, Devanne H, Willart S, Bourriez JL, et al. Anticipatory postural adjustments during step initiation: elicitation by auditory stimulation of differing intensities. *Neuroscience.* (2012) 219:166–74. doi: 10.1016/j.neuroscience.2012.05.032
5. Kennefick M, Wright AD, Smirl JD, van Donkelaar P. Anticipatory postural adjustments as a function of response complexity in simple reaction time tasks. *Neurosci Lett.* (2018) 684:1–5. doi: 10.1016/j.neulet.2018.06.058
6. Santos MJ, Kanekar N, Aruin AS. The role of anticipatory postural adjustments in compensatory control of posture: 1. Electromyographic analysis. *J Electromyogr Kinesiol.* (2010) 20:388–97. doi: 10.1016/j.jelekin.2009.06.006
7. Bruttini C, Esposti R, Bolzoni F, Cavallari P. Higher precision in pointing movements of the preferred vs. non-preferred hand is associated with an earlier occurrence of anticipatory postural adjustments. *Front Hum Neurosci.* (2016) 10:365. doi: 10.3389/fnhum.2016.00365
8. Wentink EC, Beijen SI, Hermens HJ, Rietman JS, Veltink PH. Intention detection of gait initiation using EMG and kinematic data. *Gait Posture.* (2013) 37:223–8. doi: 10.1016/j.gaitpost.2012.07.013
9. Caronni A, Cavallari P. Anticipatory postural adjustments stabilise the whole upper-limb prior to a gentle index finger tap. *Exp Brain Res.* (2009) 194:59–66. doi: 10.1007/s00221-008-1668-2
10. Suresh AK, Goodman JM, Okorokova EV, Kaufman M, Hatsopoulos NG, Bensmaia SJ. Neural population dynamics in motor cortex are different for reach and grasp. *Elife.* (2020) 9:e58848. doi: 10.7554/eLife.58848
11. Petersen TH, Rosenberg K, Petersen NC, Nielsen JB. Cortical involvement in anticipatory postural reactions in man. *Exp Brain Res.* (2009) 193:161–71. doi: 10.1007/s00221-008-1603-6
12. Caronni A, Cavallari P. Supra-spinal circuits shape inhibitory postural adjustments anticipating voluntary index-finger flexion. *Exp Brain Res.* (2009) 198:19–28. doi: 10.1007/s00221-009-1931-1
13. Brunnstrom S. Motor testing procedures in hemiplegia: based on sequential recovery stages. *Phys Ther.* (1966) 46:357–75. doi: 10.1093/ptj/46.4.357
14. Kuo C-L, Hu G-C. Post-stroke spasticity: a review of epidemiology, pathophysiology, and treatments. *Int J Gerontol.* (2018) 12:280–4. doi: 10.1016/j.ijge.2018.05.005
15. Kong KH, Chua KS, Lee J. Recovery of upper limb dexterity in patients more than 1 year after stroke: frequency, clinical correlates and predictors. *NeuroRehabilitation.* (2011) 28:105–11. doi: 10.3233/NRE-2011-0639
16. Aruin AS. Enhancing anticipatory postural adjustments: a novel approach to balance rehabilitation. *J Nov Physiother.* (2016) 6:e144. doi: 10.4172/2165-7025.1000e144
17. Lee NG, You JSH, Yi CH, Jeon HS, Choi BS, Lee DR, et al. Best core stabilization for anticipatory postural adjustment and falls in hemiparetic stroke. *Arch Phys Med Rehabil.* (2018) 99:2168–74. doi: 10.1016/j.apmr.2018.01.027
18. Dickstein R, Shefi S, Marcovitz E, Villa Y. Anticipatory postural adjustment in selected trunk muscles in post stroke hemiparetic patients. *Arch Phys Med Rehabil.* (2004) 85:261–7. doi: 10.1016/j.apmr.2003.05.011
19. Slijper H, Latash ML, Rao N, Aruin AS. Task-specific modulation of anticipatory postural adjustments in individuals with hemiparesis. *Clin Neurophysiol.* (2002) 113:642–55. doi: 10.1016/S1388-2457(02)00041-X
20. Li S, Chen YT, Francisco GE, Zhou P, Rymer WZ, A. Unifying pathophysiological account for post-stroke spasticity and disordered motor control. *Front Neurol.* (2019) 10:468. doi: 10.3389/fneur.2019.00468
21. Choudhury S, Shobhana A, Singh R, Sen D, Anand SS, Shubham S, et al. The relationship between enhanced reticulospinal outflow and upper limb function in chronic stroke patients. *Neurorehabil Neural Repair.* (2019) 33:375–83. doi: 10.1177/1545968319836233
22. Senesh MR, Barragan K, Reinkensmeyer DJ. Rudimentary dexterity corresponds with reduced ability to move in synergy after stroke: evidence of competition between corticoreticulospinal and corticospinal tracts? *Neurorehabil Neural Repair.* (2020) 34:904–14. doi: 10.1177/1545968320943582
23. Canning CG Ada L, O'Dwyer NJ. Abnormal muscle activation characteristics associated with loss of dexterity after stroke. *J Neurol Sci.* (2000) 176:45–56. doi: 10.1016/S0022-510X(00)00305-1
24. Solnik S, Rider P, Steinweg K, DeVita P, Hortobagyi T. Teager-Kaiser energy operator signal conditioning improves EMG onset detection. *Eur J Appl Physiol.* (2010) 110:489–98. doi: 10.1007/s00421-010-1521-8
25. Carlsen AN, Maslovat D. Startle and the StartReact Effect: Physiological mechanisms. *J Clin Neurophysiol.* (2019) 36:452–9. doi: 10.1097/WNP.0000000000000582
26. Coppens MJM, Roelofs JMB, Donkers NAJ, Nonnekes J, Geurts ACH, Weerdesteyn V, et al. startling acoustic stimulus facilitates voluntary lower extremity movements and automatic postural responses in people with chronic stroke. *J Neurol.* (2018) 265:1625–35. doi: 10.1007/s00415-018-8889-5
27. Bolzoni F, Bruttini C, Esposti R, Castellani C, Cavallari P. Transcranial direct current stimulation of SMA modulates anticipatory postural adjustments without affecting the primary movement. *Behav Brain Res.* (2015) 291:407–13. doi: 10.1016/j.bbr.2015.05.044
28. Palmer E, Cafarelli E, Ashby P. The processing of human ballistic movements explored by stimulation over the cortex. *J Physiol.* (1994) 481:509–20. doi: 10.1113/jphysiol.1994.sp020459
29. Schepens B, Stapley P, Drew T. Neurons in the pontomedullary reticular formation signal posture and movement both as an integrated behavior and independently. *J Neurophysiol.* (2008) 100:2235–53. doi: 10.1152/jn.01381.2007
30. Rahimi M, Swann Z, Honeycutt CF. Does exposure to startle impact voluntary reaching movements in individuals with severe-to-moderate stroke? *Exp Brain Res.* (2021) 239:745–53. doi: 10.1007/s00221-020-06005-4
31. Rahimi M, Honeycutt CF. StartReact increases the probability of muscle activity and distance in severe/moderate stroke survivors during two-dimensional reaching task. *Exp Brain Res.* (2020) 238:1219–27. doi: 10.1007/s00221-020-05797-9
32. Kirkpatrick NJ, Ravichandran VJ, Perreault EJ, Schaefer SY, Honeycutt CF. Evidence for startle as a measurable behavioral indicator of motor learning. *PLoS ONE.* (2018) 13:e0195689. doi: 10.1371/journal.pone.0195689
33. Ma HI, Lin KC, Hsieh FH, Chen CL, Tang SF, Wu CY. Kinematic manifestation of arm-trunk performance during symmetric bilateral reaching after stroke: within vs. beyond arm's length. *Am J Phys Med Rehabil.* (2017) 96:146–51. doi: 10.1097/PHM.0000000000000554

34. Tsai WC, Lien HY, Liu WY, Guo SL, Lin YH, Yang TF. Early and anticipatory postural adjustments in healthy subjects under stable and unstable sitting conditions. *J Electromyogr Kinesiol.* (2018) 43:21–7. doi: 10.1016/j.jelekin.2018.08.005
35. Collins KC, Kennedy NC, Clark A, Pomeroy VM. Kinematic components of the reach-to-target movement after stroke for focused rehabilitation interventions: systematic review and meta-analysis. *Front Neurol.* (2018) 9:472. doi: 10.3389/fneur.2018.00472
36. Stinear CM, Lang CE, Zeiler S, Byblow WD. Advances and challenges in stroke rehabilitation. *Lancet Neurol.* (2020) 19:348–60. doi: 10.1016/S1474-4422(19)30415-6
37. Gladstone DJ, Danells CJ, Black SE. The fugl-meyer assessment of motor recovery after stroke: a critical review of its measurement properties. *Neurorehabil Neural Repair.* (2002) 16:232–40. doi: 10.1177/154596802401105171
38. Chen CL, Chen CY, Chen HC, Wu CY, Lin KC, Hsieh YW, et al. Responsiveness and minimal clinically important difference of Modified Ashworth Scale in patients with stroke. *Eur J Phys Rehabil Med.* (2019) 55:754–60. doi: 10.23736/S1973-9087.19.05545-X
39. Carlsen AN. A broadband acoustic stimulus is more likely than a pure tone to elicit a startle reflex and prepared movements. *Physiol Rep.* (2015) 3:e12509. doi: 10.14814/phy2.12509
40. Maslovat D, Franks IM, Leguerrier A, Carlsen AN. Responses to startling acoustic stimuli indicate that movement-related activation is constant prior to action: a replication with an alternate interpretation. *Physiol Rep.* (2015) 3:e12300. doi: 10.14814/phy2.12300
41. Leow LA, Uchida A, Egberts JL, Riek S, Lipp OV, Tresilian J, et al. Triggering mechanisms for motor actions: the effects of expectation on reaction times to intense acoustic stimuli. *Neuroscience.* (2018) 393:226–35. doi: 10.1016/j.neuroscience.2018.10.008
42. Yang D, Zhang H, Gu Y, Liu H. Accurate EMG onset detection in pathological, weak and noisy myoelectric signals. *Biomed Signal Process Control.* (2017) 33:306–15. doi: 10.1016/j.bspc.2016.12.014
43. Mehta R, Cannella M, Henry SM, Smith S, Giszter S, Silfies SP. Trunk postural muscle timing is not compromised in low back pain patients clinically diagnosed with movement coordination impairments. *Motor Control.* (2017) 21:133–57. doi: 10.1123/mc.2015-0049
44. Yang CL, Creath RA, Magder L, Rogers MW, McCombe Waller S. Impaired posture, movement preparation, and execution during both paretic and nonparetic reaching following stroke. *J Neurophysiol.* (2019) 121:1465–77. doi: 10.1152/jn.00694.2018
45. Smith JA, Ignasiak NK, Jacobs JV. Task-invariance and reliability of anticipatory postural adjustments in healthy young adults. *Gait Posture.* (2020) 76:396–402. doi: 10.1016/j.gaitpost.2020.01.003
46. Pereira S, Silva CC, Ferreira S, Silva C, Oliveira N, Santos R, et al. Anticipatory postural adjustments during sitting reach movement in post-stroke subjects. *J Electromyogr Kinesiol.* (2014) 24:165–71. doi: 10.1016/j.jelekin.2013.10.001
47. Curuk E, Lee Y, Aruin AS. Individuals with stroke improve anticipatory postural adjustments after a single session of targeted exercises. *Hum Mov Sci.* (2020) 69:102559. doi: 10.1016/j.humov.2019.102559
48. Rajachandrakumar R, Fraser JE, Schinkel-Ivy A, Inness EL, Biasin L, Brunton K, et al. Atypical anticipatory postural adjustments during gait initiation among individuals with sub-acute stroke. *Gait Posture.* (2017) 52:325–31. doi: 10.1016/j.gaitpost.2016.12.020
49. Delafontaine A, Vialleron T, Hussein T, Yiou E, Honeine JL, Colnaghi S. Anticipatory postural adjustments during gait initiation in stroke patients. *Front Neurol.* (2019) 10:352. doi: 10.3389/fneur.2019.00352
50. Carlsen AN, Chua R, Inglis JT, Sanderson DJ, Franks IM. Startle response is dishabituated during a reaction time task. *Exp Brain Res.* (2003) 152:510–8. doi: 10.1007/s00221-003-1575-5
51. Cohen O, Sherman E, Zinger N, Perlmutter S, Prut Y. Getting ready to move: transmitted information in the corticospinal pathway during preparation for movement. *Curr Opin Neurobiol.* (2010) 20:696–703. doi: 10.1016/j.conb.2010.09.001
52. Yang CL, Gad A, Creath RA, Magder L, Rogers MW, Waller SM. Effects of transcranial direct current stimulation (tDCS) on posture, movement planning, and execution during standing voluntary reach following stroke. *J Neuroeng Rehabil.* (2021) 18:5. doi: 10.1186/s12984-020-00799-8
53. Jang SH, Lee SJ. Corticoreticular Tract in the human brain: a mini review. *Front Neurol.* (2019) 10:1188. doi: 10.3389/fneur.2019.01188
54. Akbaş A, Marszałek W, Bacik B, Juras G. Two aspects of feedforward control during a fencing lunge: early and anticipatory postural adjustments. *Front Human Neurosci.* (2021) 15:638675. doi: 10.3389/fnhum.2021.638675
55. Garland SJ, Gray VL, Knorr S. Muscle activation patterns and postural control following stroke. *Motor Control.* (2009) 13:387–411. doi: 10.1123/mcj.13.4.387
56. Brihmat N, Tarri M, Gasq D, Marque P, Castel-Lacanal E, Loubinoux I. Cross-modal functional connectivity of the premotor cortex reflects residual motor output after stroke. *Brain Connect.* (2020) 10:236–49. doi: 10.1089/brain.2020.0750
57. Ward NS, Brown MM, Thompson AJ, Frackowiak RS. Neural correlates of motor recovery after stroke: a longitudinal fMRI study. *Brain.* (2003) 126:2476–96. doi: 10.1093/brain/awg245
58. Ward NS, Brown MM, Thompson AJ, Frackowiak RS. Neural correlates of outcome after stroke: a cross-sectional fMRI study. *Brain.* (2003) 126:1430–48. doi: 10.1093/brain/awg145
59. Frolov AA, Mokienko O, Lyukmanov R, Biryukova E, Kotov S, Turbina L, et al. Post-stroke rehabilitation training with a motor-imagery-based brain-computer interface (BCI)-controlled hand exoskeleton: a randomized controlled multicenter trial. *Front Neurosci.* (2017) 11:400. doi: 10.3389/fnins.2017.00400
60. Seitz AL, Uhl TL. Reliability and minimal detectable change in scapulothoracic neuromuscular activity. *J Electromyogr Kinesiol.* (2012) 22:968–74. doi: 10.1016/j.jelekin.2012.05.003
61. Cuisinier R, Olivier I, Nougier V. Effects of foreperiod duration on anticipatory postural adjustments: determination of an optimal preparation in standing and sitting for a raising arm movement. *Brain Res Bull.* (2005) 66:163–70. doi: 10.1016/j.brainresbull.2005.04.010
62. McInnes AN, Castellote JM, Kofler M, Honeycutt CF, Lipp OV, Riek S, et al. Cumulative distribution functions: an alternative approach to examine the triggering of prepared motor actions in the StartReact effect. *Eur J Neurosci.* (2021) 53:1545–68. doi: 10.1111/ejn.14973

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

frontiers in Neurology

ORIGINAL RESEARCH
published: 02 February 2022
doi: 10.3389/fneur.2022.833908

Impaired Lower Limb Proprioception in Spinocerebellar Ataxia Type 3 and Its Affected Factors

Xia-Hua Liu[1], Zhi-Yong Wang[1], Ying Li[2], Hao-Ling Xu[3], Arif Sikandar[3], Jun Ni[1] and Shi-Rui Gan[3]*

[1] Department of Rehabilitation Medicine, The First Affiliated Hospital, Fujian Medical University, Fuzhou, China, [2] The Third Clinical Medical College, Fujian Medical University, Fuzhou, China, [3] Department of Neurology, Institute of Neurology, The First Affiliated Hospital, Fujian Medical University, Fuzhou, China

Background: Spinocerebellar ataxia type 3 (SCA3) is one of the most common hereditary neurodegenerative diseases. Postural control dysfunction is the main symptom of SCA3, and the proprioceptive system is a critical sensory component of postural control. Accordingly, proprioception quantification assessment is necessary in monitoring the progression of SCA3.

Objective: We aimed to quantitatively assess lower limb proprioception and investigate the relationship between proprioception and clinical characteristics in patients with SCA3.

Methods: A total of 80 patients with SCA3 and 62 health controls were recruited, and their lower limb proprioception was measured using the Pro-kin system. Clinical characteristics of the SCA3 patients were collected. Multivariable linear regression was used to investigate potential affected factors for lower limb proprioception.

Results: We found that the patients with SCA3 experience poorer lower limb proprioception characterized by significant impairment in the average trace error (ATE) and time to carry out the test time execution (TTE) compared to controls ($P < 0.05$). Moreover, there were significant differences in TTE between the right and left lower limbs ($P < 0.05$) of the patients. Regression analyses revealed that increasing age at onset (AAO) predicts poorer lower limb proprioception for both ATE ($\beta = 2.006$, $P = 0.027$) and TTE ($\beta = 1.712$, $P = 0.043$) and increasing disease duration predicts poorer lower limb proprioception for ATE ($\beta = 0.874$, $P = 0.044$). AAO ($\beta = 0.328$, $P = 0.019$) along with the expanded alleles ($\beta = 0.565$, $P = 0.000$) could affect the severity of ataxia. By contrast, ATE ($\beta = 0.036$, $P = 0.800$) and TTE ($\beta = -0.025$, $P = 0.862$) showed no significant predictors.

Conclusions: Lower limb proprioception in patients with SCA3 is significantly impaired when compared to healthy controls. Increasing AAO and disease duration are related to impaired lower limb proprioception.

Keywords: spinocerebellar ataxia type 3, lower limb proprioception, Pro-kin system, postural control, disease progression

OPEN ACCESS

Edited by:
Paolo Cavallari, University of Milan, Italy

Reviewed by:
Angelo Amico, Policlinico, Italy
Roberto Rodríguez-Labrada, Cuban Neuroscience Center, Cuba

***Correspondence:**
Zhi-Yong Wang
fjykdxwzy@163.com

Specialty section:
This article was submitted to Neurorehabilitation, a section of the journal Frontiers in Neurology

Received: *12 December 2021*
Accepted: *11 January 2022*
Published: *02 February 2022*

Citation:
Liu X-H, Wang Z-Y, Li Y, Xu H-L, Sikandar A, Ni J and Gan S-R (2022) Impaired Lower Limb Proprioception in Spinocerebellar Ataxia Type 3 and Its Affected Factors. Front. Neurol. 13:833908. doi: 10.3389/fneur.2022.833908

INTRODUCTION

Spinocerebellar ataxia type 3 (SCA3), also known as Machado-Joseph disease (MJD), is the most common inherited spinocerebellar ataxias and one of autosomal dominant neurodegenerative disorders with high clinical heterogeneity (1). SCA3 is caused by the expansion of cytosine-adenine-guanine (CAG) triplet repetitions in the coding region of the ATXN3 gene (14q32.1), which results in an expanded polyglutamine repeat in the encoded ataxin-3 protein, causing severe atrophy of the cerebellar Purkinje cell layer, brain stem, cortex and spinal cord (2, 3). The clinical characteristics of patients with SCA3 have various manifestations, including postural control dysfunction, gait ataxia, oculomotor abnormalities, dysarthria and peripheral neuropathy (4).

Postural control dysfunction, one of the main factors of SCA3 directly affecting gait, is associated with an increased incidence of falls in this population (5–7). Postural control is a complex process requiring the central integration of numerous sensory-motor processes (8). The influence of motor control and vision aspects on postural control has been reported in SCAs (9, 10). The proprioceptive system is a critical sensory component of postural control (11). It has been suggested that cerebellar damage may cause varied impairments to proprioceptive sense (12). Therefore, pathological processing of proprioceptive information may be a key pathological mechanism of postural control dysfunction in SCA3. Several studies about other neurological disorders, such as stroke, multiple sclerosis, Parkinson's disease, and Huntington's disease, have suggested that disturbances in proprioception are important for the postural control of patients (13–15). However, little attention has been directed toward proprioceptive deficits in the progression of SCA3, which is the most common subtype of SCAs (16).

Pro-kin system [Prokin 254 (Pro-Kin Software Stability), TecnoBody S. r. l., Dalmine, 24044 Bergamo, Italy] is an advanced evaluation technology with a computerized proprioceptive kinematic footboard. It can analyze and integrate the on-screen tracks of patients to generate targeted assessment and rehabilitation paths of proprioceptive deficits (15). The validity of Pro-kin to assess postural instability in patients with SCA3 has been demonstrated (17), and the system has been used to test lower limb proprioception function in patients with hemiparetic stroke, multiple sclerosis, total knee prosthesis and knee osteoarthritis (15, 18, 19). Our previous research used the Pro-kin system to evaluate the postural control stability of SCA3 patients and showed that postural instability may be correlated with disease severity (17). Using the Pro-kin system to assess the postural control dysfunction of advancing neurodegenerative diseases, including SCA3, can become a potential longitudinal biomarker. However, as one component of postural control, proprioception in SCA3 is barely studied, and the relationship between proprioception and the clinical characteristics of patients with SCA3 remains unclear.

In this study, we intend to use the Pro-kin system to quantitatively identify lower limb proprioception in SCA3 and explore the correlation between lower limb proprioception and the clinical characteristics of patients with SCA3 in order to formulate a rehabilitation treatment plan for SCA3 for reference.

METHODS

Participants

Employing a cross-sectional design, this study included both individuals with a diagnosis of molecular-confirmed SCA3 (20) and healthy controls (HCs) as participants. Between October 2018 and December 2019, we recruited 80 patients with SCA3 and 62 HC participants at The First Affiliated Hospital of Fujian Medical University in Fuzhou. The protocol was approved by the Ethics Committee of The First Affiliated Hospital, Fujian Medical University [Approval No: MRCTA, ECFAH of FMU(2018)201]. The design and procedures of the study were performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from the participants prior to their participation.

The inclusion criteria for participants with SCA3 were (1) a definite genetic diagnosis of SCA3; (2) 20–80 years of age; (3) Mini-Mental State Examination score > 27; (4) ability to stand independently in the upright position for 30 s; (5) no evidence of other neurological, musculoskeletal or cardiovascular disorders; and (6) a willingness to participate. The exclusion criteria were (1) unstable vital signs and uncontrolled hypertension; (2) history of vestibular symptoms or vestibular disease; (3) presence of cognitive impairment, visual or hearing pathologies; (4) inability to stand independently for 30 s with eyes closed; (5) lack of sensitivity in the lower limbs; (6) musculoskeletal, cardiovascular or respiratory system impairments or other accompanying ailments; (7) engagement in another rehabilitative study protocol; (8) peripheral neuropathy; or (9) on medication affecting the musculoskeletal system or proprioception and postural stability (e.g., anti–depressants, dopaminergic agents, hypnotics).

The control group, which included mostly spouses and caregivers of patients with SCA3/MJD, was matched for age, gender and environmental characteristics. Relatives at risk were excluded from the HC group. The control group comprised 62 individuals without neurological, musculoskeletal or cardiorespiratory impairments.

Genotype and Phenotype Analysis

Genomic DNA was extracted from peripheral blood samples provided by each patient using QIAamp DNA Blood Mini kit (Qiagen, Hilden, Germany). The numbers of CAG repeats of the patients were determined by polymerase chain reaction amplification combined with Sanger sequencing, as previously reported (20).

Ataxia specialists interviewed each patient to obtain all information needed for the present study. Age at onset (AAO) was defined as the age when ataxia symptoms related to SCA3 first appeared, which was estimated according to the reports of patients, close relatives, or care providers. Disease duration was the time span between AAO and the age at first visit. The severity of ataxia was assessed with the Scale for the Assessment and Rating of Ataxia (SARA), which comprised of eight cerebellar

FIGURE 1 | Participant used the Pro-kin system to test the lower limb proprioception.

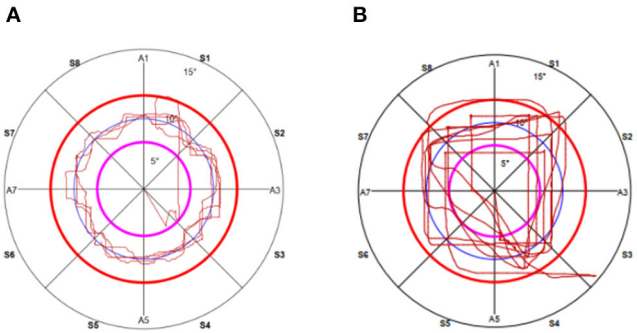

FIGURE 2 | The actual recording of the path of circular during proprioceptive multiaxial assessment in the right lower limb in **(A)** a health control subject and **(B)** a SCA3 patient.

function tests with a total score ranging from 0 (absence of ataxia) to 40 (most severe ataxia) (21).

Pro-kin System Assessment

We conducted an observational study between SCA3 patients and HC participants at the same time of the day. Pro-kin system was used to measure the proprioception on a multiaxial balance evaluator for lower limbs. A rehabilitation therapist blinded to the groups conducted the assessments. All participants received the assessments in a quiet and naturally and brightly lit room. Participants are evaluated as shown in **Figure 1**.

To measure lower limb proprioception, the footboard of the system was set to allow angular movements in the sagittal and frontal planes. Participants placed their right limb on the footboard and then their left limb on a fixed support platform equal in height to the footboard (15). They were then asked to draw circular route lines on the screen by moving their lower limb (on the footboard). Their motor task was to try to keep the circular route lines drawn by the movements of their lower limb (on the footboard) superimposed as much as possible on those already drawn by the system (**Figure 2**). The test stopped automatically at the end of five turns. The right lower limb was measured first and then the left lower limb. Average trace error (ATE) and time to carry out the test time execution (TTE) [s] were evaluated (15, 18, 19). Large ATE values mean large errors in path control, which indicate poor lower limb proprioception. TTE was the time from the start to the end of the trial.

Each test was repeated three times and the mean scores were recorded. The assessment lasted approximately 20 minutes. The participants were oriented to the test in the evaluation mode before performing the actual test. To reduce the risk of falls and minimize interference from external support, a trainer stayed close alongside or behind the participants.

Statistical Analyses

For analyses of the basic demographics between SCA3 patients and HC subjects, Chi-square tests were used to compare the gender distribution. Two independent samples T-tests and Mann-Whitney U tests test were used, respectively, for normal and non-normal distributed variables, the result of which were confirmed by Kolmogorov-Smirnov testing. Following the results of these tests, variables with normal distribution and non-normal distribution were expressed as mean ± SD and median (range), respectively.

We used multivariable linear regression to examine the relationship between proprioception and phenotype variability in patients with SCA3. First, we assessed the predictors of proprioception measures: ATE and TTE. These measures were predicted by the following independent variables: gender (binary), AAO, disease duration, SARA score and length of normal and expanded CAG repeats. Next, we analyzed the predictors of the severity of ataxia as measured with the SARA score by using the following independent variables: ATE, TTE, gender (binary), AAO and length in normal and expanded CAG repeats.

All the statistical analyses were performed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). The results were considered statistically significant at $P < 0.05$.

RESULTS

Table 1 shows the demographic characteristics of 80 patients with SCA3 (male: 43, female: 37) and 62 healthy control participants (male: 31, female: 31). There were no statistically significant sociodemographic (i.e., age and gender) differences between patients with SCA3 and the HC group. In the patients, the mean

TABLE 1 | Demographic characteristics of study subjects.

	SCA3 group	HC group	*P*-value
Sample size, *N*	80	62	NA
Age, years	39.14 ± 9.58	42 (18–65)	0.594[a]
Gender (male/female)	43/37	31/31	0.657[b]
Dominant side (right/left)	Right	Right	NA
Disease duration, years	7.10 ± 3.56	NA	NA
Age at onset, years	32.34 ± 8.63	NA	NA
Normal alleles, *N*	19 (13–44)	NA	NA
Expanded alleles, *N*	75 (69–81)	NA	NA
SARA score	9.23 ± 2.86	NA	NA

SARA, The Scale for the Assessment and Rating of Ataxia; N, number; NA, not applicable. Variables with normal distribution were represented as mean ± standard deviation; variables in non-normal distribution were expressed as median (range).
[a]*Mann-Whitney U-test.*
[b]*Chi-square test.*

TABLE 2 | Lower limb proprioception measures in SCA3 and health controls.

Indices	Lower limb	SCA3 group	HC group	*P*-value
ATE	R	33 (8.66–124.33)	26 (3.67–101.33)	0.066[a]
	L	53.66 ± 29.43	29.67 (3.00–124.00)	**0.035**[a]
	P-value	0.142[a]	0.192[a]	
TTE	R	100 (73.67–202)	76(0–152.67)	**0**[a]
	L	100.66(0–205.33)	79.67(61.67–154.00)	**0**[a]
	P-value	**0.042**[a]	0.327[a]	

ATE, Average Tace Error; TTE, Test Time Execution; R, Right; L, Left.
Variables with normal distribution were represented as mean ± standard deviation; variables in non-normal distribution were expressed as median (range). Bold value showed significance.
[a]*Mann-Whitney U-test.*

TABLE 3 | The affected factors on lower limb proprioception.

	Coefficient estimate	Standard error	*P*-value
ATE			
Gender[a]	0.081	6.368	0.547
AAO	2.006	2.409	**0.027**
Disease duration	0.874	2.864	**0.044**
SARA	0.122	2.498	0.685
Normal alleles	−0.039	0.445	0.771
Expanded alleles	−0.200	1.616	0.301
TTE			
Gender[a]	0.074	7.007	0.557
AAO	1.712	2.651	**0.043**
disease duration	0.707	3.151	0.08
SARA	0.030	2.748	0.915
Normal alleles	0.081	0.489	0.514
Expanded alleles	−0.159	1.778	0.376

ATE, Average Tace Error; TTE, Test Time Execution; AAO, Age At Onset; SARA, The Scale for the Assessment and Rating of Ataxia.
Bold value showed significance.
[a]*Male vs. female.*

TABLE 4 | The influences of lower limb proprioception on disease severity.

	Coefficient estimate	Standard error	*P*-value
SARA			
Gender[a]	−0.189	0.62	0.094
AAO	0.328	0.044	**0.019**
Normal alleles	0.099	0.044	0.374
Expanded alleles	0.565	0.137	**0.000**
ATE	0.036	0.016	0.800
TTE	−0.025	0.014	0.862

ATE, Average Tace Error; TTE, Test Time Execution; AAO, Age At Onset; SARA, The Scale for the Assessment and Rating of Ataxia.
Bold value showed significance.
[a]*Male vs. female.*

AAO was 32.34 ± 8.63 years, average disease duration was 7.10 ± 3.56 years, median length of expanded alleles was 75 (69–81), median length of CAG repeats in normal alleles was 19 (13–44) and average SARA score was 9.23 ± 2.86.

There are two groups of lower limb proprioception outcome variables presented in **Table 2**. We first compared all outcome variables separately for the right and left limbs between the patient and control groups. We found that ATE on the left limb and TTE on both lower limbs were significantly worse for patients compared to controls ($P < 0.05$). Second, we compared all outcome variables separately for the patient and control groups between the right and left limbs. We found that though both groups have bigger outcomes in ATE and TTE in the left limb compared to the right limb, while there was only a significant difference in TTE between their right and left limbs in SCA3 patients ($P < 0.05$).

Multivariable linear regression was used to examine the relationship between lower limb proprioception measures and clinical characteristics in patients. First, we investigated the predictors of lower limb proprioception (**Table 3**) using regression models predicting ATE and TTE. The results indicated that increasing AAO predicts poorer lower limb proprioception for both ATE ($\beta = 2.006$, $P = 0.027$) and TTE ($\beta = 1.712$, $P = 0.043$) and increasing disease duration predicts poorer lower limb proprioception for ATE ($\beta = 0.874$, $P = 0.044$). On the contrary, higher lengths of CAG repeats in expanded alleles do not predict poorer lower limb proprioception for both ATE ($\beta = -0.200$, $P = 0.301$) and TTE ($\beta = -0.159$, $P = 0.376$). Next, we also performed multivariable linear regression to examine whether lower limb proprioception could affect the severity of ataxia (**Table 4**). We found that AAO ($\beta = 0.328$, $P = 0.019$) along with the expanded alleles ($\beta = 0.565$, $P = 0.000$) could affect the severity of ataxia. By contrast, ATE ($\beta = 0.036$, $P = 0.800$) and TTE ($\beta = -0.025$, $P = 0.862$) showed no significant predictors.

DISCUSSION

To date, rehabilitation for SCA3 is a research hotspot, but there are few studies focusing on lower limb proprioception.

Impaired lower limb proprioception can affect postural control and increase the risk of falling, which further aggravates the disease process of SCA3. Therefore, exploring the relevant influencing factors of proprioception and effectively formulating a corresponding rehabilitation plan are of great significance for the treatment of SCA3. The present study was the first to use the Pro-kin system to investigate lower limb proprioception in patients with SCA3 and explore the relationship between proprioception and clinical characteristics in patients.

Compared to the HC group, the patients with SCA3 exhibited significant impairments in lower limb proprioception. Our finding confirmed that cerebellar damage results in deficits of proprioception (12). Both groups have poor proprioception outcomes in their left limb compared with their right. This phenomenon may be explained that subjects of both groups are right-limb dominance, which was associate with better activation characteristics in the left primary sensorimotor cortex and the basal ganglia (22). Within the patient group, our regression analyses revealed that AAO and lengths of expanded CAG repeats predicted the severity of SCA3. Increasing AAO and disease duration predicted poorer lower limb proprioception. The correlations between disease duration and disease severity in SCAs and between greater functional loss and longer duration of the disease have been described (17, 23). Our findings are consistent with these research results. However, multivariable linear regression of SARA related to ATE and TTE showed no significant, so we failed to indicate that lower limb proprioception can predict the severity of ataxia in SCA3 patients.

In this work, we performed the lower limb proprioceptive function test instead of weakening somatosensory feedback by asking participants to stand on foam with both feet to analyze the interactions between postural stability and proprioceptive function (24). To the best of our knowledge, this study is the first to analyze the proprioception of the left and right feet separately in patients with SCA3. Our finding of significant impairments in lower limb proprioception represented by ATE and TTE measures using the Pro-kin system was supported by other studies on neurological disorders. For example, Sergio Bagnato found a significant increment of the ATE and TTE on the unaffected side leg in stroke patients as measured by the Pro-kin system (18). Patients with multiple sclerosis have also been reported to have worse assessment outcomes of ATE and TTE before proprioceptive training with the Pro-kin system (15).

Although the mechanism of how lower limb proprioception affects postural control in SCA3 is still poorly understood, there are several possibilities. First, patients present muscular rigidity and a locking of knees and ankles when undergoing testing for lower limb proprioception, causing abnormal joint movements related to postural control. The decline of knee and ankle joint position sense affects the implementation of knee and ankle strategies that are associated with postural control (25–28), which may be the cause of poor postural control function in SCA3 patients. Second, the pathological involvement of spinocerebellar proprioceptive input and the loss of integrity of the medial somatosensory descending system may explain the abnormal postural control (24, 29). Third, the cortical motor areas receive abnormalities in the peripheral afferent input or the brain response to sensory input may interfere with motor program processing in the cortical motor areas (18, 28).

This study is not without limitations. First, the force platform was limited to SCA3 patients who could safely perform the test (i.e. those able to stand unassisted for a certain duration). Second, as the study had a cross-sectional observational design and its evaluation of disease progression was retrospective, we did not provide information on changes in lower limb proprioception over time in our patients. Third, we did not use neurophysiological methods such as functional magnetic resonance imaging and somatosensory evoked potential. These methods are more specific to study the function of somatosensory descending system and cortical motor reaction, which could help indicate how lower limb proprioception affects postural control. Fourth, determining how to formulate targeted training of proprioception for SCA3 is worthy of further in-depth thinking.

CONCLUSION

In this cross-sectional study, we showed that lower limb proprioception in patients with SCA3 was significantly impaired. Increasing AAO and disease duration were found to be related to impaired lower limb proprioception. However, lower limb proprioception could not predict the severity of ataxia in patients. These findings are important as they can help characterize the disease and thus assist in the development of new therapies and rehabilitation programs.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of The First Affiliated Hospital, Fujian Medical University. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

X-HL: study concept and design, statistical analysis and interpretation, writing of the manuscript, and critical revision of the manuscript for important intellectual content. YL, H-LX, and AS: acquisition of data. JN and S-RG: study concept and design and acquisition of data. Z-YW: study concept and design, acquisition of data, analysis and interpretation, and critical revision of the manuscript for important intellectual content. All authors contributed to the article and approved the submitted version.

FUNDING

This work was supported by the Startup Fund for Scientific Research, Fujian Medical University (Grant Number: 2019QH1095) to X-HL.

ACKNOWLEDGMENTS

The authors sincerely thank the participants for their help and willingness to participate in this study. We also thank the reviewers for their helpful comments.

REFERENCES

1. Schöls L, Bauer P, Schmidt T, Schulte T, Riess O. Autosomal dominant cerebellar ataxias: clinical features, genetics, and pathogenesis. *Lancet Neurol.* (2004) 3:291–304. doi: 10.1016/S1474-4422(04)00737-9
2. Kawaguchi Y, Okamoto T, Taniwaki M, Aizawa M, Inoue M, Katayama S, et al. CAG expansions in a novel gene for Machado-Joseph disease at chromosome 14q32.1. *Nature Genet*. (1994) 8:221–8. doi: 10.1038/ng1194-221
3. McLoughlin HS, Moore LR, Paulson HL. Pathogenesis of SCA3 and implications for other polyglutamine diseases. *Neurobiol Dis.* (2020) 134:104635. doi: 10.1016/j.nbd.2019.104635
4. Klockgether T, Mariotti C, Paulson HL. Spinocerebellar ataxia. *Nat Rev Dis Primers.* (2019) 5:24. doi: 10.1038/s41572-019-0074-3
5. Fonteyn EM, Schmitz-Hübsch T, Verstappen CC, Baliko L, Bloem BR, Boesch S, et al. Falls in spinocerebellar ataxias: results of the EuroSCA fall study. *Cerebellum.* (2010) 9:232–9. doi: 10.1007/s12311-010-0155-z
6. Luo L, Wang J, Lo RY, Figueroa KP, Pulst SM, Kuo PH, et al. The initial symptom and motor progression in spinocerebellar ataxias. *Cerebellum.* (2017) 16:615–22. doi: 10.1007/s12311-016-0836-3
7. Yuan X, Ou R, Hou Y, Chen X, Cao B, Hu X, et al. Extra-cerebellar signs and non-motor features in chinese patients with spinocerebellar ataxia type 3. *Front Neurol.* (2019) 10:110. doi: 10.3389/fneur.2019.00110
8. Paillard T, Noé F. Techniques and methods for testing the postural function in healthy and pathological subjects. *Biomed Res Int.* (2015) 2015:891390. doi: 10.1155/2015/891390
9. Van de Warrenburg BP, Bakker M, Kremer BP, Bloem BR, Allum JH. Trunk sway in patients with spinocerebellar ataxia. *Mov Disord.* (2005) 20:1006–13. doi: 10.1002/mds.20486
10. Nanetti L, Alpini D, Mattei V, Castaldo A, Mongelli A, Brenna G, et al. Stance instability in preclinical SCA1 mutation carriers: a 4-year prospective posturography study. *Gait Post.* (2017) 57:11–4. doi: 10.1016/j.gaitpost.2017.05.007
11. Onursal Kilinç Ö, Ayvat E, Ayvat F, Sütçü G, Kilinç M, Aksoy S, et al. The relationship between trunk position sense and postural control in ataxic individuals. *Gait Post*. (2019) 68:258–63. doi: 10.1016/j.gaitpost.2018.12.007
12. Bhanpuri NH, Okamura AM, Bastian AJ. Predictive modeling by the cerebellum improves proprioception. *J Neurosci.* (2013) 33:14301–6. doi: 10.1523/JNEUROSCI.0784-13.2013
13. Seiss E, Praamstra P, Hesse CW, Rickards H. Proprioceptive sensory function in Parkinson's disease and Huntington's disease: evidence from proprioception-related EEG potentials. *Exp Brain Res.* (2003) 148:308–19. doi: 10.1007/s00221-002-1291-6
14. Ryerson S, Byl NN, Brown DA, Wong RA, Hidler JM. Altered trunk position sense and its relation to balance functions in people post-stroke. *J Neurol Phys Ther.* (2008) 32:14–20. doi: 10.1097/NPT.0b013e3181660f0c
15. Amico AP, Nisi M, Covelli I, Polito AM, Damiani S. Efficacy of proprioceptive training with prokin system in balance disorders from multiple sclerosis. *J Mult Scler.* (2014) 1:110. doi: 10.4172/jmso.1000110
16. Li T, Martins S, Peng Y, Wang P, Hou X, Chen Z, et al. Is the high frequency of machado-joseph disease in china due to new mutational origins? *Front Genet*. (2019) 9:740. doi: 10.3389/fgene.2018.00740
17. Liu XH, Li Y, Xu HL, Sikandar A, Lin WH, Li GH, et al. Quantitative assessment of postural instability in spinocerebellar ataxia type 3 patients. *Ann Clin Transl Neurol.* (2020) 7:1360–70. doi: 10.1002/acn3.51124
18. Bagnato S, Boccagni C, Boniforti F, Trinchera A, Guercio G, Letizia G, et al. Motor dysfunction of the "non-affected" lower limb: a kinematic comparative study between hemiparetic stroke and total knee prosthesized patients. *Neurol Sci.* (2009) 30:107–13. doi: 10.1007/s10072-009-0031-0
19. Ye J, Simpson MW, Liu Y, Lin W, Zhong W, Cai S, et al. The effects of baduanjin qigong on postural stability, proprioception, and symptoms of patients with knee osteoarthritis: a randomized controlled trial. *Front Med.* (2020) 6:307. doi: 10.3389/fmed.2019.00307
20. Gan SR, Shi SS, Wu JJ, Wang N, Zhao GX, Weng ST, et al. High frequency of Machado-Joseph disease identified in southeastern Chinese kindreds with spinocerebellar ataxia. *BMC Med Genet.* (2010) 11:47. doi: 10.1186/1471-2350-11-47
21. Schmitz-Hübsch T, du Montcel ST, Baliko L, Berciano J, Boesch S, Depondt C, et al. Scale for the assessment and rating of ataxia: development of a new clinical scale. *Neurology.* (2006) 66:1717–20. doi: 10.1212/01.wnl.0000219042.60538.92
22. Kapreli E, Athanasopoulos S, Papathanasiou M, Van Hecke P, Strimpakos N, Gouliamos A, et al. Lateralization of brain activity during lower limb joints movement. An fMRI study. *NeuroImage.* (2006) 32:1709–21. doi: 10.1016/j.neuroimage.2006.05.043
23. Konno KM, Zonta MB, Guimarães A, Camargo C, Munhoz RP, Raskin S, et al. Balance and physical functioning in Spinocerebellar ataxias 3 and 10. *Acta Neurol Scand.* (2021) 143:458–63. doi: 10.1111/ane.13384
24. Helmchen C, Kirchhoff JB, Göttlich M, Sprenger A. Postural ataxia in cerebellar downbeat nystagmus: its relation to visual, proprioceptive and vestibular signals and cerebellar atrophy. *PLoS ONE.* (2017) 12:e0168808. doi: 10.1371/journal.pone.0168808
25. Pearson KG. Proprioceptive regulation of locomotion. *Curr Opin Neurobiol.* (1995) 5:786–91. doi: 10.1016/0959-4388(95)80107-3
26. Devanne H, Maton B. Role of proprioceptive information in the temporal coordination between joints. *Exp Brain Res.* (1998) 119:58–64. doi: 10.1007/s002210050319
27. Miall RC, Christensen LO, Cain O, Stanley J. Disruption of state estimation in the human lateral cerebellum. *PLoS Biol.* (2007) 5:e316. doi: 10.1371/journal.pbio.0050316
28. Weeks HM, Therrien AS, Bastian AJ. Proprioceptive localization deficits in people with cerebellar damage. *Cerebellum.* (2017) 16:427–37. doi: 10.1007/s12311-016-0819-4
29. Hasan Z. Role of proprioceptors in neural control. *Curr Opin Neurobiol.* (1992) 2:824–9. doi: 10.1016/0959-4388(92)90140-g

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

frontiers in Human Neuroscience

ORIGINAL RESEARCH
published: 02 March 2022
doi: 10.3389/fnhum.2022.762380

Visual Perturbation Suggests Increased Effort to Maintain Balance in Early Stages of Parkinson's to be an Effect of Age Rather Than Disease

Justus Student[1,2]*, *David Engel*[1,3], *Lars Timmermann*[2,3], *Frank Bremmer*[1,3†] *and Josefine Waldthaler*[2,3†]

[1]Department of Neurophysics, University of Marburg, Marburg, Germany, [2]Department of Neurology, University Hospital of Marburg, Marburg, Germany, [3]Center for Mind, Brain and Behavior (CMBB), University of Marburg and Justus-Liebig-University of Gießen, Marburg, Germany

OPEN ACCESS

Edited by:
Eric Yiou,
Université Paris-Saclay, France

Reviewed by:
Marica Giardini,
Scientific Clinical Institute Maugeri (ICS Maugeri), Italy
Chiara Palmisano,
Julius Maximilian University of Würzburg, Germany

***Correspondence:**
Justus Student
justus.student@physik.uni-marburg.de

†These authors have contributed equally to this work and share senior authorship

Specialty section:
This article was submitted to Motor Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *21 August 2021*
Accepted: *02 February 2022*
Published: *02 March 2022*

Citation:
Student J, Engel D, Timmermann L, Bremmer F and Waldthaler J (2022) Visual Perturbation Suggests Increased Effort to Maintain Balance in Early Stages of Parkinson's to be an Effect of Age Rather Than Disease. Front. Hum. Neurosci. 16:762380. doi: 10.3389/fnhum.2022.762380

Postural instability marks a prevalent symptom of Parkinson's disease (PD). It often manifests in increased body sway, which is commonly assessed by tracking the Center of Pressure (CoP). Yet, in terms of postural control, the body's Center of Mass (CoM), and not CoP is what is regulated in a gravitational field. The aim of this study was to explore the effect of early- to mid-stage PD on these measures of postural control in response to unpredictable visual perturbations. We investigated three cohorts: (i) 18 patients with early to mid-stage PD [Hoehn & Yahr stage (1–3); 1.94 ± 0.70]; (ii) a group of 15 age-matched controls (ECT); and (iii) a group of 12 young healthy adults (YCT). Participants stood on a force plate to track their CoP, while the movement of their entire body was recorded with a video-based motion tracking system to monitor their CoM. A moving room paradigm was applied through a head-mounted virtual reality headset. The stimulus consisted of a virtual tunnel that stretched in the anterior-posterior direction which either remained static or moved back and forth in an unpredictable fashion. We found differences in mean sway amplitude (MSA) and mean velocities of CoP and CoM between the groups under both conditions, with higher MSA of CoP and CoM for PD and higher mean velocities of both variables for PD and ECT when compared with YCT. Visual perturbation increased mean CoP velocity in all groups but did not have effects on mean CoM velocity or MSA. While being significantly lower for the young adults, the net effect of visual perturbation on mean CoP velocity was similar between patients with PD and age-matched controls. There was no effect of the visual perturbation on mean CoM velocity for any of the groups. Our simultaneous assessment of CoP and CoM revealed that postural control is reflected differently in CoM and CoP. As the motion of CoM remained mostly unaffected, all groups successfully counteracted the perturbation and maintained their balance. Higher CoP velocity for PD and ECT revealed increased corrective motion needed to achieve this, which however was similar in both groups. Thus, our results suggest increased effort, expressed in CoP velocity, to be an effect of age rather than disease in earlier stages of PD.

Keywords: Parkinson's disease, body sway, virtual reality, center of mass (CoM), center of pressure (CoP)

INTRODUCTION

Due to the ongoing demographic transition and subsequent over-aging of modern societies in many industrialized countries, neurodegenerative diseases are gaining in prevalence, with Parkinson's disease (PD) being the second most common after Alzheimer's disease (Lange and Erbguth, 2017; Tysnes and Storstein, 2017). In addition to the cardinal symptoms of rigidity, hypokinesia and resting tremor, as the disease progresses, most patients also develop postural instability (Jankovic, 2008). The onset of postural instability, as determined by clinical tests, can vary widely between individuals and ranges from months to decades after initial diagnosis. Postural instability comprises the inability to maintain equilibrium under dynamic and static conditions such as preparation of movements, perturbations, and quiet stance (Appeadu and Gupta, 2021) and leads to an increased risk of falls. Reportedly, postural instability is associated with a reduction in quality of life and even diminished life expectancy of those affected (Koller et al., 1989; Fasano et al., 2017; Bäckström et al., 2018). However, since only some patients exhibit a progressive form with severe instability, it is crucial to identify those who are prone to falls. A common indicator to predict the individual risk of future falls is whether the patient had experienced more than two falls in the preceding year (Pickering et al., 2007). This implies, however, that patients already had a history of falls and thus hampers the usefulness as a predictor to take preventive measures. Thus, identifying reliable biomechanical indicators of postural instability is crucial to monitor the development of this symptom and allow early intervention.

Maintaining equilibrium, i.e., a stable upright body position in space, involves complex, intertwined processing of various sensory inputs. Out of these inputs, visual information is claimed to be one of the most important contributors (Berthoz et al., 1975; Bronstein, 1986; Laurens et al., 2010). Sense of balance can easily be manipulated by external visual stimuli, which in turn has the potential to give insight into the underlying neural processing (van Asten et al., 1988; Alghadir et al., 2019). Regarding such visual manipulations, previous research has shown that unpredictable perturbations of the visual scene generate a strong dynamic destabilization of a quiet upright stance (Winter et al., 1990; Guerraz et al., 2001; Musolino et al., 2006; Barela et al., 2009). In particular, patients with PD show an increased reliance on the visual system to maintain an upright stance as compared to healthy individuals (Bronstein et al., 1990; Weil et al., 2016). Moreover, the stimulus used in this study was found to successfully produce different responses in patients with PD and age-matched controls (Engel et al., 2021b). Based on these previous results, a visual disturbance was added in this study with the aim to increase potential differences between PD and ECT.

A sensitive measurable indicator of this destabilization constitutes an increased sway of the body (Horak and Mancini, 2013; Pantall et al., 2018). The body's Center of Mass (CoM) is claimed to be the main variable controlled by the central nervous system to maintain equilibrium (Horak and Macpherson, 1996; Peterka, 2002). However, considering the heterogenic mass distribution of the human body, assessment of CoM requires tracking and subsequent mathematical processing of several body segments. Therefore, tracking of the Center of Pressure (CoP), which reflects the total of forces enacted on the ground, is widely used in body sway research, as its motion can directly be assessed through simple force platforms (Vsetecková and Drey, 2013). Existing models to describe the relationship between CoP and CoM during human bipedal upright stance include that of an inverted pendulum (Winter et al., 1997; Gage et al., 2004; Laurens et al., 2010). In this context, CoM typically is considered to be the controlled variable, while CoP is the controlling variable. Accordingly, CoP controls CoM and keeps its position above the base of support (Winter et al., 1996; Takeda et al., 2017; Morasso, 2020). Displacements of CoM which exceed this area lead to falls if the current velocity is directed away from the center (Horak et al., 1989; Hof et al., 2005; Roman-Liu, 2018).

The velocity of these body sway parameters has proven to be a suitable measure to compare body sway between particular groups with balance impairments and healthy controls (Takeda et al., 2017), while the sole displacement of their trajectories is suggested to be less suitable to identify potential differences (Masani et al., 2014). For instance, Palmieri and colleagues showed that an increase in CoP velocity signifies increased postural instability while slower CoP velocity indicates more effective balance control in an upright stance (Palmieri et al., 2002). Moreover, Nantel and colleagues showed that higher CoP velocities seem to be an indicator of the severity of postural instability in PD. Their study revealed that age-matched controls are able to maintain their posture more effectively, signalized by a lower CoP velocity (Nantel et al., 2012). Thus, CoP velocity might serve as a potential biomarker for deterioration of postural stability (Maurer et al., 2003; da Conceição et al., 2019) and might predict fallers in PD (Beretta et al., 2018). However, there is evidence that increased CoP velocities also occur in the healthy elderly (Roman-Liu, 2018). Since most people affected by PD are of advanced age (Rijk et al., 1995), it is unclear whether this deterioration of postural control is due to the disease alone.

Due to the hitherto cumbersome assessment of CoM, the majority of existing studies only investigated the motion of CoP. CoM is claimed to be the main controlled variable by the central nervous system, as it represents the interaction of the body with the gravitational field. Even though recent technologies allow for easier tracking of the whole body, research on CoM motion, especially in response to visual perturbations, remains sparse. Moreover, in this way, tracking of CoM provides insight into actual 3-D motion of the body, as opposed to COP, which only describes a 2-D projection on the ground Thus, investigation of CoM motion bears the potential to investigate additional alterations that might be related to PD as well as age.

Recently, affordable, and user-friendly equipment, which was originally designed for the gaming industry, has been validated for research purposes. This includes the Microsoft Kinect v2 (Microsoft, Redmond, WA, USA), which allows for video-based full-body motion tracking, as well as the Nintendo Wii Balance Board (Nintendo, Kyoto, Japan) to

replace a research-grade force platform (Chang et al., 2013; Dehbandi et al., 2017; Clark et al., 2018). In addition, a convenient means to perform visual manipulations that has recently been established is the use of commercially available virtual reality headsets to apply a moving room paradigm (Engel et al., 2020, 2021a). Accordingly, a combination of these experimental tools and approaches enables a straightforward simultaneous assessment of CoP and CoM under visual perturbations, through which empirical conclusions can be drawn about the relationship between both parameters.

Thus, the aim of this study was to simultaneously assess CoP and CoM dynamics to investigate differences in mean sway amplitude (MSA) and mean velocity of both parameters between patients with early-to-mid stage PD (PD), a control group (ECT) of age-matched healthy adults and a third group of young (YCT) healthy adults. To assess potential differences which occur before the onset of recurrent falls due to postural instability, we purposely recruited patients in early to mid-stages of the disease. This study may hence provide a proof-of-concept to demonstrate the feasibility of postural assessment using a low-cost set-up in patients with PD. By this means, we aim to lay a foundation for the long-term goal of our research which is to establish nuanced and sensitive measures to detect PD patients at risk of falls before the onset of clinically apparent postural instability.

Postural behavior was evaluated under two conditions: (i) during quiet standing, while participants' visual field remained stable; and (ii) while they underwent unpredictable perturbations of their visual surroundings in the anterior-posterior (AP) direction. By testing three different groups, our goal was to differentiate between potential disease-specific and age-related alterations in body sway during quiet stance as well as under visual perturbation, which might be expressed differently in CoP and CoM. We hypothesized: (1) that patients with PD show the largest MSA and highest velocity of both parameters under both conditions, followed by the elderly healthy adults, while both parameters will be smallest for the young group. Moreover, we expected to find (2) that MSA and mean velocity of both parameters increase under visual perturbation in all groups. Lastly, we hypothesized (3) that these increases will again be strongest for the group of patients and weakest for the group of young healthy adults.

MATERIALS AND METHODS

Participants

Eighteen patients with PD [age: range: (42–76); mean ± standard deviation: 58.10 ± 8.66] diagnosed based on the Movement Disorder Society diagnostic criteria (Postuma et al., 2015) in early to moderate disease stages {Hoehn and Yahr: [(1–3); 1.94 ± 0.70; Hoehn and Yahr, 1967] with a mean disease duration of 4.8 years [(0–15); 4.79 ± 4.71]} participated in the study. A prerequisite for the inclusion of patients was that they were able to walk without any assistance and did not report more than one fall in the previous year. Only one patient reported a previous fall event. Also, none of the patients had experienced *Freezing of Gait* before or during the experiment. All of the patients were assessed "on" their regular dose of dopaminergic medication [Levodopa Equivalent Daily Dose (LEDD): (105–1980); 651.63 ± 529.97]. The two control groups consisted of 15 age-matched healthy individuals [age: (49–70); 59.80 ± 6.45] as well as 12 young healthy participants [age: (22–28); 23.92 ± 1.50].

Exclusion criteria were any neurological disorder other than PD (e.g., neuropathies, epilepsy, multiple sclerosis, schizophrenia, severe, depression, dementia, etc.) or orthopedic (e.g., at the hip, spine, knee, etc.) disorders which could affect their balance and upright stance as well as cognitive impairment based on the Montreal Cognitive Assessment as a screening tool for general cognitive abilities with a cut-off score of 24 points (Ciesielska et al., 2016). All subjects had normal or corrected to normal visual acuity.

All participants gave written informed consent prior to the experiment, including with regard to the storage and processing of their data. Experimental procedures involving healthy individuals were approved by the Ethics Committee of the Psychology Department, University of Marburg. Research including patients with PD was approved by the Ethics Committee of the Faculty of Medicine, University of Marburg (Case 77/19). All research was conducted in accordance with the Declaration of Helsinki.

Technical Setup

Participants stood on a Wii Balance board (Nintendo, Kyoto, Japan) to track their CoP (**Figure 1**). Wearing no shoes, they were instructed to position their feet about shoulder-width apart, about parallel on the ground. During trials, their arms were to hang at their sides without effort. They were instructed to remain their gaze straight ahead. To perform tracking of their body motion, we used a Kinect v2 video-based motion tracking system (Microsoft, Redmond, WA, USA) which recorded the 3-D positions of 25 different "body joints" as determined by an internal algorithm. The camera was located 210 cm in front of the participants and fixed at a height of 140 cm. Visual stimuli were presented through a head-mounted virtual reality headset (HTC Vive, HTC, New Taipei City, 206 Taiwan). The frame rate was 90 Hz. The field of view extended over 110° in the vertical as well as horizontal directions.

In the virtual world, participants stood inside a tunnel that was world-fixed and stretched in the AP direction. The visual stimulus was custom made, based on the open-source Python pyopenvr framework[1]. The demarcation of the tunnel was made up of black spheres, whose position was randomly generated for every trial. The length of the tunnel was set to 50 m and the radius was adjusted to the eye level of every subject so that their gaze was directed at the radial center of the tunnel, 25 m in front of them. Just before the end of the tunnel, at a distance of 24 m, we implemented a fixation dot at the radial center.

To prevent participants from falling, they were secured by a harness which was attached to the ceiling. We ensured that the harness guaranteed subjects' safety but was not providing

[1]https://github.com/cmbruns/pyopenvr

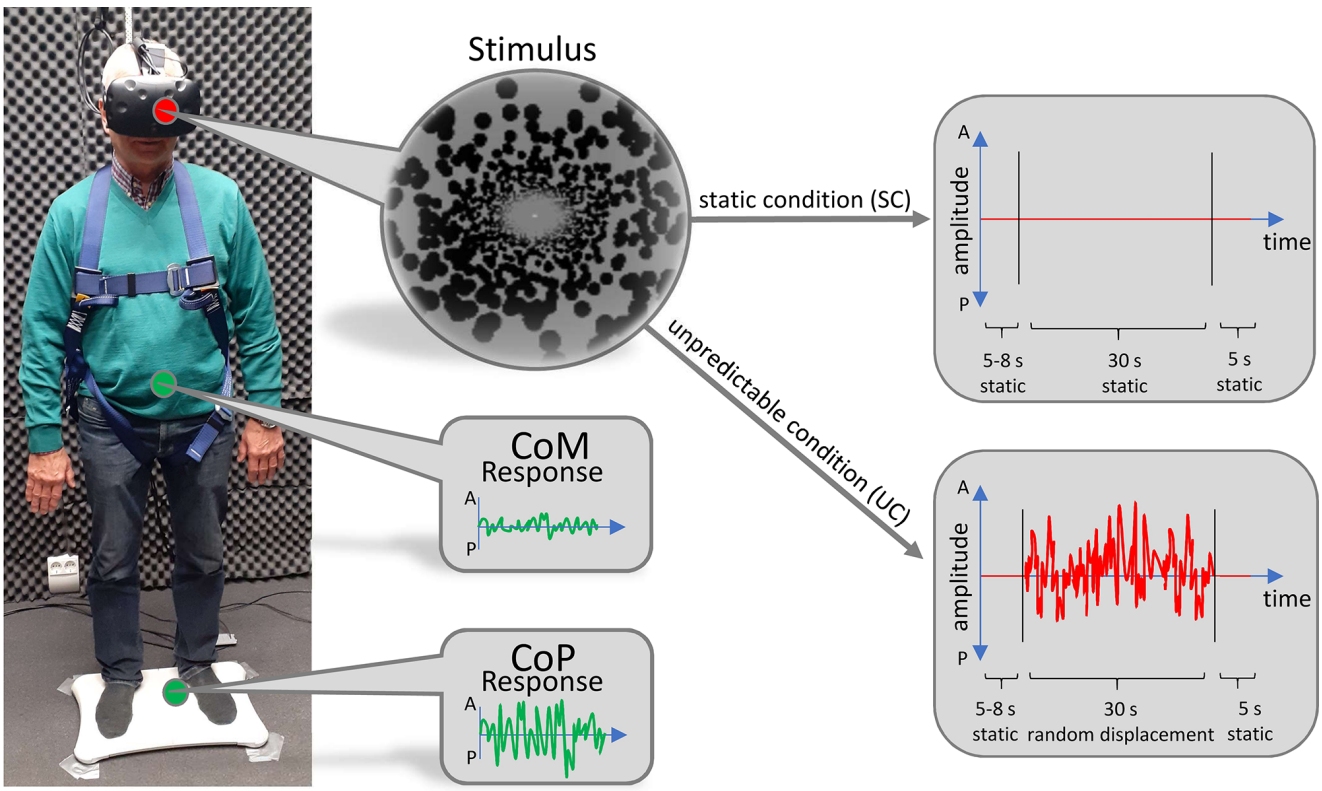

FIGURE 1 | Technical setup. Subjects stood on a Wii Balance Board to track their CoP. Their body movement was tracked by a video-based motion tracking system positioned in front of them (not displayed). Visual stimuli were presented through a head-mounted virtual reality headset. Stimuli consisted of a virtual tunnel in anterior-posterior (AP)-direction, which either remained static (upper right panel) or moved back and forth unpredictably (lower right panel).

lift during trials. The setup has successfully been established and described in more detail in previous work (Engel et al., 2021a,b).

Experimental Paradigm

Each subject performed 10 trials of the static condition (SC) where the tunnel remained motionless and 20 trials of the unpredictable condition (UC), during which the tunnel was moving back and forth in an unpredictable fashion. In this way, every subject performed a total of 30 trials. The order of trials was pseudorandomly shuffled. The unpredictable motion of the tunnel was made up of a series of random tunnel displacements along the AP axis which were based on a flattened random frequency spectrum (random white noise). This was to ensure that all frequencies were equally present in the sequence, which improved comparability between trials and avoided biases towards specific frequencies that might have interfered with the body sway of individual subjects. The maximum step size was set to 80 cm. At the beginning of each trial, the tunnel remained motionless and—in the UC—started moving after a randomized onset time between 5 and 8 s. The motion lasted for 30 s, after which the tunnel remained static for another 5 s to provide the subjects with relaxation time. In this way, the duration of each trial was 40–43 s.

As soon as the subjects indicated by a verbal command that they were ready, the experimenter started the next trial. To signal its beginning, the fixation dot changed its color from red to white. During the 30 s motion phase (or static phase), the fixation dot occasionally shifted its color to black in a transient fashion. This event occurred randomly between zero and 10 times over the course of each trial. Participants' task was to pay attention to these shifts and keep track of their numbers to ensure that they kept fixating. After the end of each trial, subjects had to report the number of changes they noticed. If the reported number was off by more than two, the respective trial was discarded. After each trial, subjects had time to relax and adjust their posture as long as they needed. Across all trials, every subject had a minimum of two larger breaks to prevent fatigue. During these breaks, participants were able to leave the setup and sit down or walk around. The entire experiment took about 2 h to complete.

Data Analysis

A custom-made Python script was used for recording and storing raw data. Further analyses were conducted in MATLAB (The MathWorks, Inc., Natick, USA). For all following analyses, we extracted the time-courses of CoP and the 3-D body segments which corresponded to the AP-directions. Time courses of the CoP, which more precisely reflect the displacement, and the

3-D body segments from individual trials were aligned to the respective stimulus onset.

To determine the position of CoM, we calculated the 3-D center positions of 16 body segments and summed them with individual weighting factors taken from Winter (2009, p. 86). Before determining our final variables, in each trial, we subtracted a first-order polynomial from the raw data of CoP and CoM using the detrend function in MATLAB. This was to eliminate potential continuous motion artifacts which might have occurred during trials (Cruz et al., 2021). To determine the MSA, we calculated the standard deviation of the detrended time courses. Afterward, we computed the mean velocity by taking the first derivative of the detrended time courses and calculated the average of the absolute values of the derivation across time. In order to investigate additional temporal dynamics of the obtained MSA and mean velocities, we also distributed the detrended signals into small bins of 0.5 s, of which we calculated MSA and mean velocity individually.

Lastly, to gain insight into the net effect of the unpredictable condition on the motion of CoP and CoM we subtracted MSA values obtained during the static condition from the MSA values obtained during visual perturbation for each parameter, respectively. In the same way, we calculated the net effect of the visual perturbation on the mean velocities of both parameters.

Statistics

We used non-parametric testing on ranked data due to our unequal group size, the relatively small number of participants, and subsequent non-comparable variance. Kruskal-Wallis tests with follow-up pairwise comparisons using Dunn's test with Bonferroni correction were used to evaluate group differences (PD, ECT, YCT). Differences between groups according to *post hoc* pairwise comparisons are reported as effect sizes based on correlation coefficients (r) using z-standardized test statistics. To test the influence of the unpredictable movement of the tunnel on MSA and the mean velocities of CoP and CoM within each group, we performed a Wilcoxon signed-rank test. We considered 95% confidence intervals ($p < 0.05$) to reject the null hypothesis. Statistical analyses were performed in SPSS (IBM, Armonk, NY, USA).

RESULTS

In a first step, we analyzed baseline data, i.e., MSA and velocity of CoP and CoM while the tunnel remained static (SC). There was a significant effect of group on the mean CoP sway amplitude ($H_{(2)} = 20.21, p < 0.001$) and on mean CoP velocity ($H_{(2)} = 14.91$, $p = 0.001$). As displayed in **Figure 2A**, there was a visible trend across groups, with patients with PD showing the highest mean CoP sway amplitude, followed by the ECT group, which in turn exhibited a slightly higher mean CoP sway amplitude than the YCT group. In *post hoc* pairwise comparisons, there were significant differences between PD and ECT ($p = 0.009$, $r = 0.51$) and between PD and YCT ($p < 0.001$, $r = 0.79$). However, there was no difference between ECT and YCT ($p = 0.41$, $r = 0.29$). A similar trend became apparent in mean CoP velocities, displayed in **Figure 3A**. However, there were neither significant differences between PD and ECT ($p = 0.255$, $r = 0.35$) nor between ECT and YCT ($p = 0.376$, $r = 0.36$). Only the higher mean CoP velocity of PD deviated significantly from the mean CoP velocity of the YCT group ($p = 0.001$, $r = 0.70$).

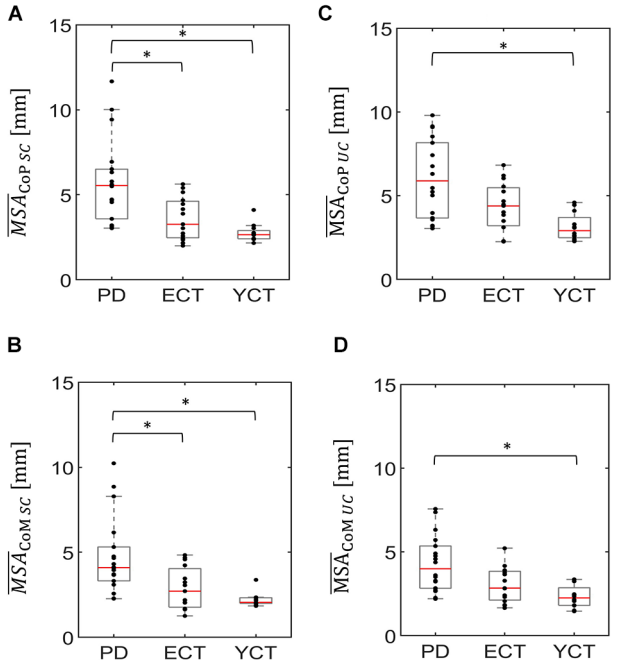

FIGURE 2 | Box plots representing the mean sway amplitude of CoP (panel **A**) and CoM (panel **B**) of all groups under the static condition (SC) and the mean sway amplitude of CoP (panel **C**) and CoM (panel **D**) of all groups under the unpredictable condition (UC), when the tunnel moved unpredictably in the AP direction. In each plot, red lines indicate the respective group medians. Gray boxes indicate the 25th (lower edge) and 75th (upper edge) percentiles of each group, respectively. Black dots indicate data of single subjects within each group. The asterisks indicate that there is a significant difference between the groups. CoP, Center of Pressure; CoM, Center of Mass. *$p < 0.5$.

Regarding mean CoM sway amplitude (**Figure 2B**), there was also a significant effect of group ($H_{(2)} = 17.157$ $p < 0.001$). Here, a similar trend emerged as in the CoP data. *Post hoc* comparisons revealed significant differences between PD and ECT ($p = 0.013$ $r = 0.50$) and between PD and YCT ($p < 0.001$ $r = 0.72$). There was no statistically significant difference between the YCT and ECT ($p = 0.68$ $r = 0.23$). Further, the effect of group was also significant for mean CoM velocities ($H_{(2)} = 14.288$, $p = 0.001$), accompanied by a similar trend as for CoP (**Figure 3**). Here, there was also no significant difference between PD and ECT groups ($p = 0.351$, $r = 0.27$), while CoM of YCT moved significantly slower in comparison to PD ($p < 0.001$, $r = 0.69$). It also moved considerably slower than CoM of the elderly healthy adults, albeit not reaching statistical significance ($p = 0.079$ $r = 0.43$).

In a second step, we compared responses to the unpredictable visual movement of the tunnel between the groups in terms of MSA (CoP: $H_{(2)} = 14.42$, $p = 0.001$; CoM: $H_{(2)} = 13.63$, $p = 0.001$) and mean velocities (CoP: $H_{(2)} = 14.76$, $p = 0.001$; CoM: $H_{(2)} = 13.25$, $p = 0.001$). The results are displayed in panels C and D of **Figures 2**, **3**. Here, a similar trend across groups

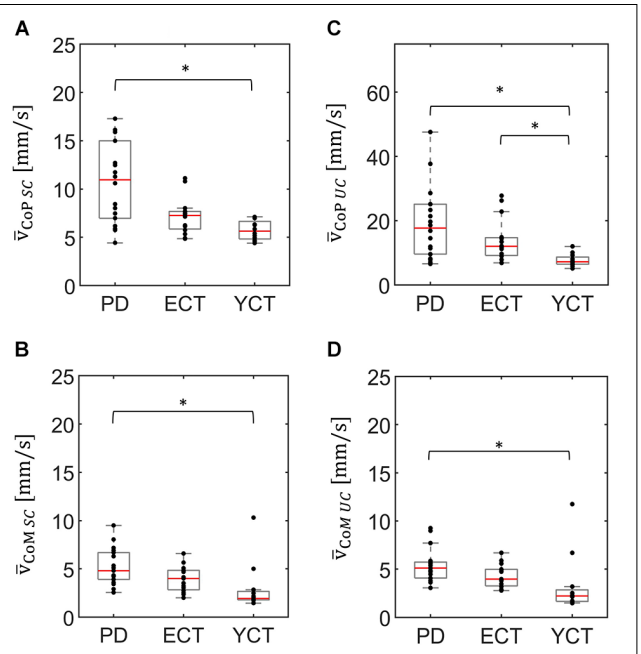

FIGURE 3 | Box plots representing the mean velocity of CoP (panel **A**) and CoM (panel **B**) of all groups under the static condition (SC) and the mean velocity of CoP (panel **C**) and CoM (panel **D**) of all groups under the unpredictable condition (UC), when the tunnel moved unpredictably in the AP direction. In each plot, red lines indicate the respective group medians. Gray boxes indicate the 25th (lower edge) and 75th (upper edge) percentiles of each group, respectively. Black dots indicate data of single subjects within each group. Note the different scaling of panel **(C)** as compared to panels **(A,B,D)**. $^*p < 0.5$.

like in the static condition (SC) became apparent. The PD group showed the highest mean CoP sway amplitude, followed by ECT. Mean CoP sway amplitude of the YCT was the lowest. In contrast to the SC, we were only able to detect statistically significant differences between PD and YCT ($p < 0.001$, $r = 0.69$), but neither between PD and ECT ($p = 0.21$, $r = 0.32$) nor between ECT and YCT ($p = 0.13$, $r = 0.39$). Furthermore, like in the SC, we did not observe statistical difference in mean CoP velocity between PD and ECT ($p > 0.999$, $r = 0.17$). However, there were significant differences between a higher mean CoP velocity of PD as compared to YCT ($p = 0.001$, $r = 0.69$) as well as between higher values of ECT as compared to YCT ($p = 0.034$, $r = 0.53$). Investigation of mean CoM sway amplitudes during the unpredictable condition showed the same trend. There was a significant difference between PD and YCT ($p = 0.001$, $r = 0.67$). However, neither PD and ECT ($p = 0.138$, $r = 0.347$) nor ECT and YCT ($p = 0.256$, $r = 0.33$) exhibited significant differences in their CoM MSA. The same applied to the mean CoM velocities. Here, there was also only a significant difference between the PD and YCT groups ($p = 0.001$, $r = 0.66$).

In addition to the differences between groups in both the SC and the UC, we also investigated the effect that the visual influence had on each group. For the mean CoP sway amplitude under visual perturbation, we were able to find an increase for both the ECT ($p = 0.004$, $r = 0.75$) and the YCT ($p = 0.023$, $r = 0.66$) groups when compared with the SC. On the other hand, we could not find any difference between the different conditions within the PD group ($p = 0.616$, $r = 0.12$). Mean CoM sway amplitudes were not influenced by the visual perturbation.

Unpredictable motion of the tunnel significantly increased mean CoP velocity in all groups when compared with the static condition (PD: $p = 0.001$, $r = 0.81$; ECT: $p = 0.001$, $r = 0.88$; YCT: $p = 0.002$, $r = 0.88$). This was also observed in the mean velocity of CoM, albeit to a much smaller extent. Here, statistical tests only yielded significant effects for ECT ($p = 0.001$, $r = 0.84$) and YCT ($p = 0.041$, $r = 0.59$).

As the motion of the tunnel led to an increase in mean velocity in each respective group and of MSA of CoP in ECT and YCT, we also investigated the net effect of visual perturbation (UC) on MSA and mean velocity of both parameters. To this end, for each group, we subtracted the average MSA during the static condition from the average MSA during perturbation. The same was done for the mean velocities. Even though in the case of CoM the increase in both parameters was rather small, for comparison, we also calculated the net effect of visual perturbation on CoM MSA and velocity. The results for the MSA data are displayed in panel A of **Figure 4** (CoP) and **Figure 5** (CoM), respectively, and the result for the mean velocities are shown in panel A of **Figure 6** (CoP) and **Figure 7** (CoM). Despite the apparent trend, we could not find an effect of the group on MSA, neither for CoP nor for the CoM data (CoP: $H_{(2)} = 5.41$, $p = 0.067$ and CoM: $H_{(2)} = 6.06$, $p = 0.048$). Even when Kruskal-Wallis testing of CoM data yielded $p < 0.05$, this could not be confirmed in the subsequent pairwise comparisons with corrected p-values.

Nevertheless, the net difference revealed that visual perturbation led to a strong increase of mean CoP velocity in both PD and ECT, while it had only a slight effect on YCT. This was backed by statistical testing, which yielded unpredictable visual perturbation to have a significantly different net effect on mean CoP velocity between PD and YCT ($p = 0.013$, $r = 0.52$) as well as between ECT and YCT ($p = 0.006$, $r = 0.59$). There was no significant difference between PD and ECT ($p > 0.999$, $r = 0.06$). To gain additional insight into the temporal dynamics of this effect, we sorted the mean CoP and CoM velocities of each group in temporal bins, as described in our methods. The resulting binned time series for mean CoP velocity can be seen in **Figure 6B**. Shortly after stimulus onset, mean CoP velocity increased drastically in both elderly groups (PD and ECT), but only minimally for the young. Remarkably, the rise in CoP velocity occurred with the same latency for PD and ECT, i.e., roughly 300 ms. The latency in the YCT was lower at around 100 ms. During the stimulus, each group maintained a considerably stable mean CoP velocity. When the motion of the tunnel stopped, again with similar latency (2.5 s), the mean CoP velocity of PD and ECT dropped to the prestimulus level.

This did not apply to the difference in mean velocities of CoM between the two conditions, as there was barely a visible net effect in any of the groups. This was also reflected in statistical testing between groups which revealed no significant effects. The net effects on mean CoM and their respective binned distribution over time are displayed in **Figure 4**.

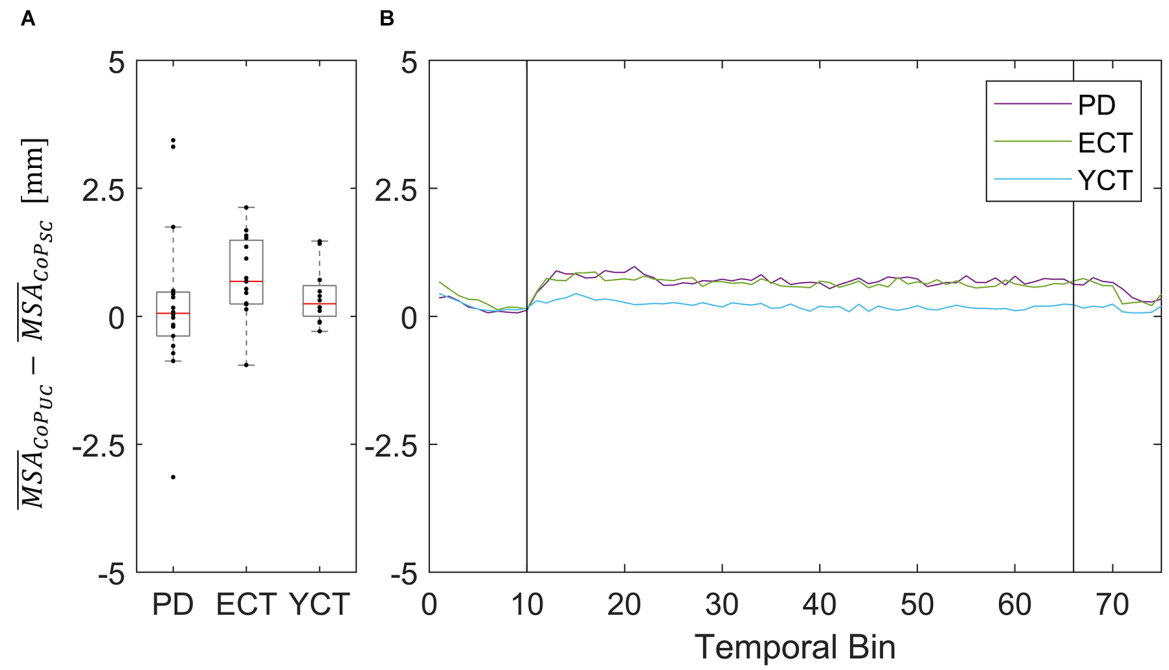

FIGURE 4 | (A) Box plots showing the net effect of the unpredictable tunnel motion on mean CoP sway amplitude as compared to the static condition for each group. Red lines indicate the respective group medians. Gray boxes indicate the 25th (lower edge) and 75th (upper edge) percentiles of each group, respectively. Black dots indicate data of single subjects within each group. **(B)** Net-effect "time courses" of resulting binned mean CoP sway amplitude across time. Black vertical lines indicate stimulus onset (left) and offset (right).

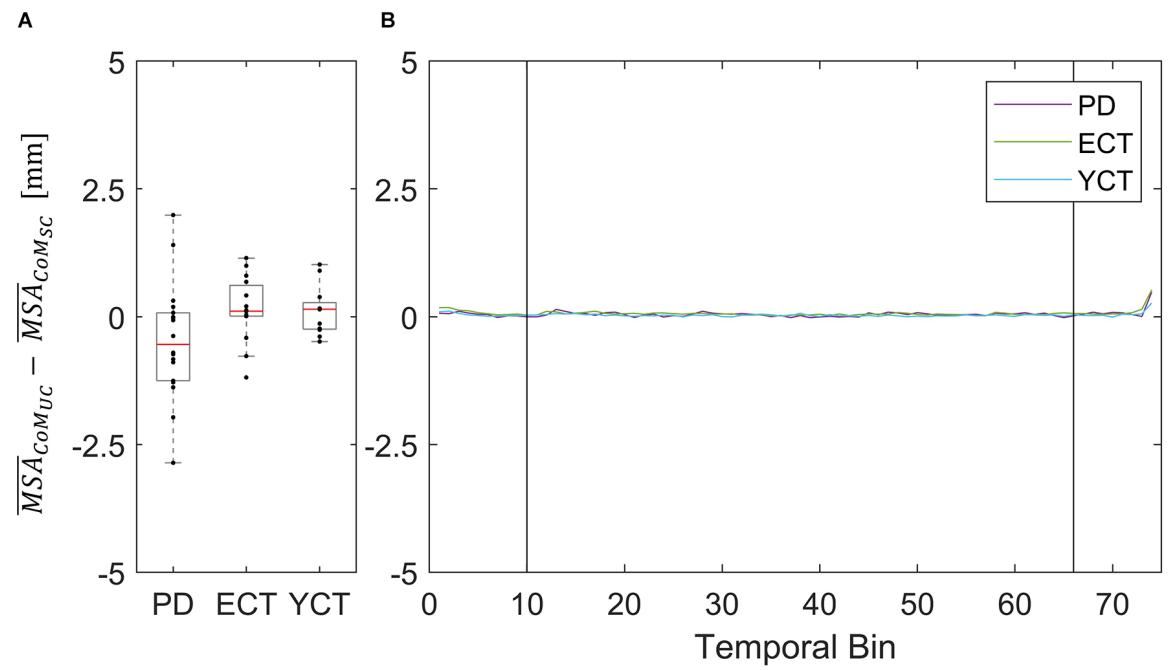

FIGURE 5 | (A) Box plots showing the net effect of the unpredictable tunnel motion on mean CoM sway amplitude as compared to the static condition for each group. Red lines indicate the respective group medians. Gray boxes indicate the 25th (lower edge) and 75th (upper edge) percentiles of each group, respectively. Black dots indicate data of single subjects within each group. **(B)** Net-effect "time courses" of resulting binned mean CoM sway amplitude across time. Black vertical lines indicate stimulus onset (left) and offset (right).

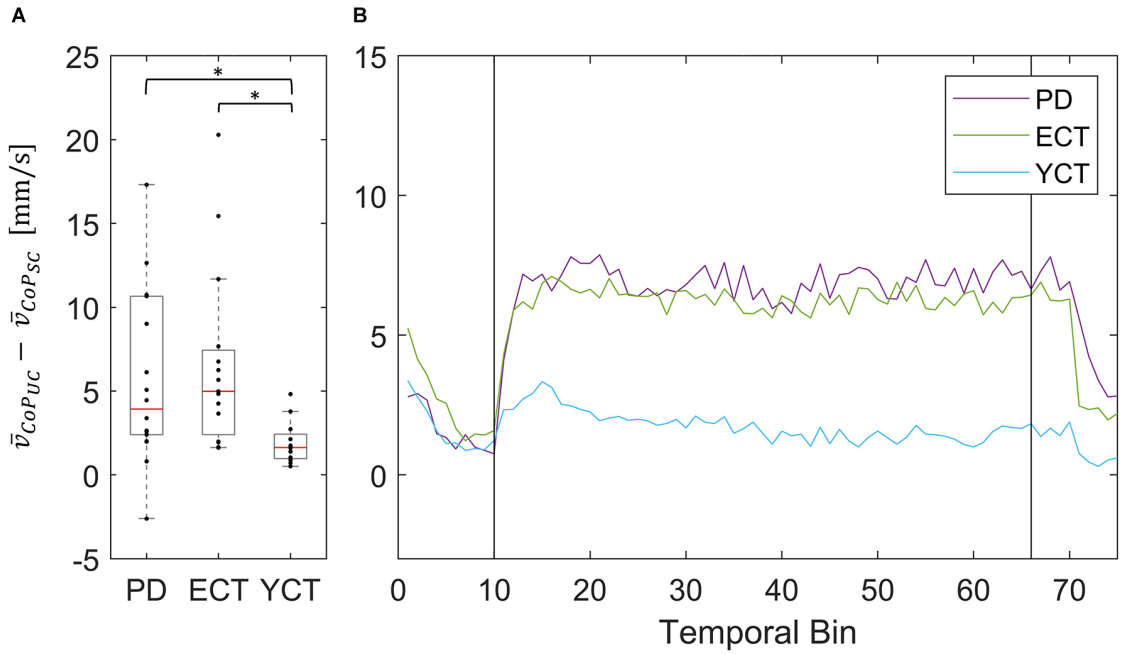

FIGURE 6 | (A) Box plots showing the net effect of the unpredictable tunnel motion on mean CoP velocities as compared to the static condition for each group. Red lines indicate the respective group medians. Gray boxes indicate the 25th (lower edge) and 75th (upper edge) percentiles of each group, respectively. Black dots indicate data of single subjects within each group. The asterisks indicate that there is a significant difference between the groups. **(B)** Net-effect "time courses" of resulting binned mean CoP velocities across time. Black vertical lines indicate stimulus onset (left) and offset (right).

DISCUSSION

In our study, we investigated potential disease- and age-specific changes in postural control during quiet stance in a static environment (static condition, SC) as well as in response to random visual perturbations (unpredictable condition, UC) by simultaneously assessing mean sway amplitude and mean velocity of CoP and CoM. For this purpose, we recruited three different cohorts: a group of patients with PD (PD), a group of age-matched healthy adults (ECT), and a group of young healthy adults (YCT).

Considering mean sway amplitude and mean velocity of both CoP and CoM, we hypothesized the highest amount of body sway for the group of patients with PD in both visual conditions, SC and UC, respectively. This was confirmed for MSA in both parameters which corroborates previous research (e.g., Bronstein et al., 1990; Cruz et al., 2018), whereas the observable trend in mean velocity data was not reaching statistical significance.

In terms of the effect of visual perturbation on body sway, we could only find increased mean CoP sway amplitudes for ECT and YCT but not for PD. There was no effect of the visual perturbation on mean CoM sway amplitudes in any of the groups. Based on our velocity data, we were able to partially confirm our second hypothesis, since all groups exhibited a higher mean velocity of their CoP when exposed to random displacements of the tunnel. However, this was again only true for CoP in the PD and ECT groups and did not hold for CoM in any of the groups. Thirdly, we expected that the net increase would again be strongest for the group of patients. Even though we found differences between groups, this hypothesis was not supported by our findings.

In general, CoP MSA was higher than CoM MSA in all groups, irrespective of the condition. These findings reflect the fact that displacement of CoP needs to exceed that of CoM in a given direction in order to properly counteract its movement (Winter, 2009; Zemková et al., 2016; Takeda et al., 2017). The same was true for the mean velocity of CoP, which was higher than the mean velocity of CoM in each group. This is in line with previous research, which revealed a higher dynamic range of CoP when compared to CoM (Winter, 1995; Winter et al., 1996; Horak et al., 2005).

In addition, across groups, there were the same trends regarding MSA and mean velocities of CoP and CoM under both conditions (**Figures 3**, **4**). Even though our data revealed a slight increase in CoP MSA for the ECT and YCT groups, MSA, in general, remained almost unaffected by the visual stimulation for both parameters. However, our data on mean CoP velocity revealed that it almost doubled for PD and ECT when exposed to the visual perturbation, and still increased slightly for the YCT group. Furthermore, the mean CoM velocity was barely affected by the visual perturbation in any of the groups. When compared to displacement (MSA) as a measure of postural sway, our findings suggest the mean velocity of CoP to better reflect postural destabilization due to the movement of the tunnel. Accordingly, as our stimulus and thus the perturbation quickly changed directions, it seems logical that CoP had to move more

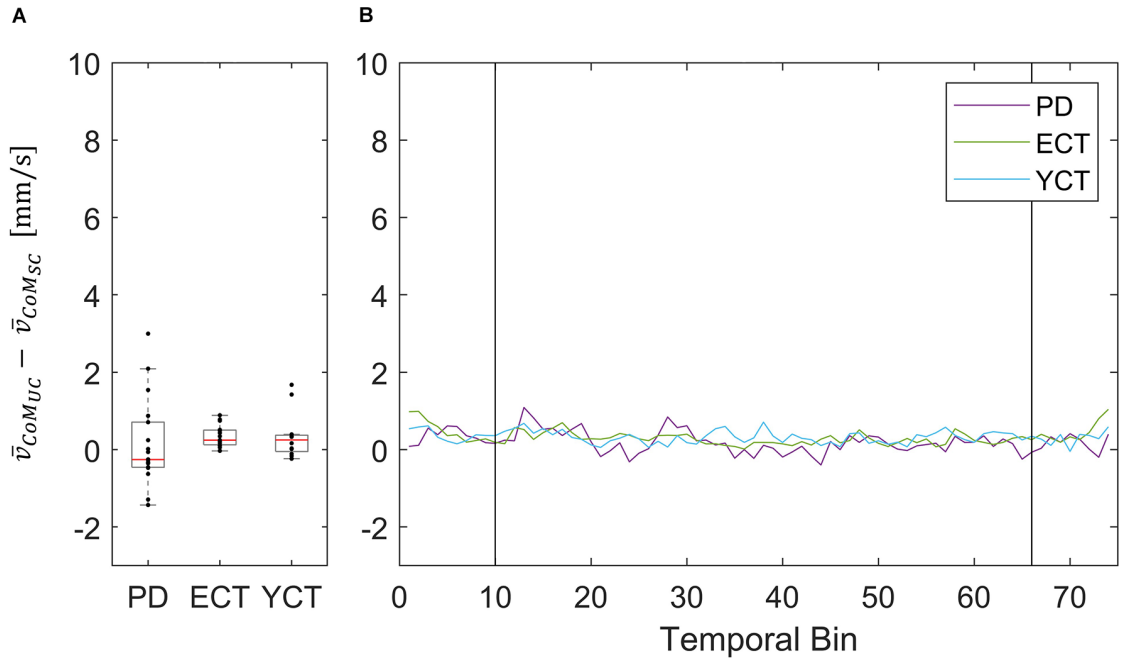

FIGURE 7 | (A) Box plots showing the net effect of the unpredictable tunnel motion on mean CoM velocities as compared to the static condition for each group. Red lines indicate the respective group medians. Gray boxes indicate the 25th (lower edge) and 75th (upper edge) percentiles of each group, respectively. Black dots indicate data of single subjects within each group. **(B)** Net-effect "time courses" of resulting binned mean CoM velocities across time. Black vertical lines indicate stimulus onset (left) and offset (right).

quickly, reflected in a higher velocity, to keep CoM stable. This is remarkable and supports the idea that CoP and CoM show different behavior in response to a destabilizing environment (Carpenter et al., 2010; Takeda et al., 2017).

The increased motion of CoP but unaffected motion of CoM could be explained by the two different functions these variables are claimed to represent in the context of balance control. As described in our introduction, CoM is suggested to be the variable controlled by the CNS to maintain equilibrium (Winter et al., 1990; Horak et al., 2005; Zemková et al., 2016). It, therefore, reflects the outcome of internal processes as a response to the sensory input and a slow overall velocity indicates general stability. As visual perturbation barely affected the motion of CoM, this can be interpreted that all the groups successfully maintained their balance. The motion of CoP, on the other hand, reflects the forces enacted on the ground to push the body (CoM) back towards its equilibrium position once it gets deflected. Hence, the increased motion of CoP, expressed in our study as mean velocity, might represent a certain kind of effort that was required to perform its task.

Although we could detect higher CoP MSA for PD when compared to ECT, to our surprise, we did not find significantly higher CoP or CoM velocities between patients with PD and age-matched controls. However, there was high variation within the group of patients, which might have masked possible effects. In order to find potential indicators for postural instability at the early and mid-stages of PD, we purposely selected a high proportion of patients who only had mild symptoms. Clinical postural instability, defined as H&Y 3, had only previously been diagnosed in a few patients included in our study (**Table 1**). Thus, our results might suggest that balance control as expressed in CoP and CoM velocity is not impaired in these early stages, which was in line with the clinical assessment of our patients. This result of our study indicates that these parameters may be unsuitable to identify early disease-related changes of postural instability.

TABLE 1 | Demographic information regarding age (in years), Montreal Cognitive Assessment (MoCA) score, Hoehn & Yahr stage (H & Y stage), levodopa equivalent dose (LEDD), and duration of the disease since initial diagnosis of each individual subject in the PD group.

Patient ID	Age (years)	MoCA	H & Y—Stage	LEDD (mg)	Disease duration (months)
1	55	27	2	900	79
2	51	30	1	105	29
3	70	26	2	282	9
4	52	29	2	250	5
5	51	29	1	242	15
6	62	26	3	821	86
7	53	29	2	935	176
8	70	28	3	210	40
9	50	29	3	774	62
10	55	28	1	150	21
11	53	28	2	786	43
12	68	26	3	1,880	188
13	53	29	2	1,980	133
14	76	24	2	465	32
15	65	28	1	515	61
16	57	29	2	780	32
17	42	29	1	121	2
18	63	28	2	532	33

On the other hand, mean CoP sway amplitude and velocity were lower for the group of young healthy adults. A similar effect could be seen in the CoM data. With CoM as an outcome of balance control mechanisms, both older groups exhibited greater instability compared to the younger adults. This indicates increased CoP and CoM velocity, both reflecting poorer balance control, to be an effect of age rather than disease (Masani et al., 2014; Roman-Liu, 2018). Since we used visual perturbation in our paradigm, this can possibly be explained by increased reliance on vision not only by the patients with PD, but by the elderly in general (Hay et al., 1996), but further experiments are required to settle this question.

In addition to our investigation of CoP and CoM displacements (MSA) and velocities between groups under both conditions separately, we also investigated the net effect of the visual perturbation on both parameters inside each group (**Figures 4–7**). There was no net effect on MSA, neither of CoP (**Figure 4A**) nor of CoM (**Figure 5A**). Regarding the net effect on CoP velocity (**Figure 6**), the differences between the groups as compared to the separate conditions became more pronounced. Here, the difference of data between both elderly groups and the young participants reached statistical significance, while there was again no significant difference between data from patients with PD and their age-matched peers. The net effect revealed a strongly visible gap between the elderly and the young (**Figure 6**), again speaking in favor of an age effect of increased CoP motion in response to the visual perturbation. By sorting the time-course data into bins and calculating MSA and mean velocity for each bin, we were able to probe the temporal dynamics of both parameters during stimulus presentation. Even though visual inspection of the mean of the binned data suggests an effect on CoP MSA in PD and ECT (**Figure 4B**), there was no statistical correlation. Accordingly, none of the groups exhibited an effect of the visual stimulation on the MSA of both parameters.

With regard to mean velocity, temporal dynamics did not only confirm the difference in behavior between both elderly groups and the young adults, but now also revealed that CoP velocity increased at a very short latency with respect to stimulus onset for all groups (**Figure 4B**). Moreover, it also decreased again with a similar delay for all groups. Hence, there seemed to be no measurable difference in response time between the groups, neither due to age nor due to disease. This is contrary to the evidence on prolonged latencies in response to motor tasks in PD (De Nunzio et al., 2007), but at the same time in line with other studies, which also did not detect differences in neural response latency (Rinalduzzi et al., 2015). A direct comparison of the net effects of the visual disturbance between MSA and mean COP velocity shows that only mean CoP velocity increases significantly due to the destabilizing effect of the unpredictably moving stimulus.

To our surprise, there was barely a noticeable net effect on CoM mean velocity, also considering temporal dynamics (**Figure 7**). None of the groups exhibited any destabilization in their CoM, as its velocity did not increase under visual perturbation. This means, as we stated before, that by increasing the motion of their CoP all groups were able to maintain their CoM at equilibrium and thus successfully counteracted the visual perturbation. In this regard, there was again neither an effect of age nor of disease on postural stability. The majority of patients (83%) in the PD group were in Hoehn & Yahr stages 1 or 2, i.e., exhibiting no postural instability in clinical examination. Only four of the patients were in H&Y stage 3. Hence, our results suggest that measuring CoM may accurately reflect the clinical state. In light of the differential results regarding CoM and CoP, the joint measurement of both variables adds significant value to exploring the equilibrium behavior. In addition, the inexpensive and easy-to-use alternative for measuring both CoP and CoM used in this study significantly simplified data collection compared with previous approaches for measuring CoM. Therefore, it would be intriguing to perform longitudinal studies with larger cohorts to also look into possible effects of disease progression on our measured parameters and to define a narrower time frame as to when balance deterioration starts to occur in PD.

The main limitations of our study include the relatively small and heterogenous groups. In a *post hoc* sample size calculation, the strong effect size regarding the influence of the mean CoP velocity by the stimulus compared to static condition translated into the minimum required sample sizes (PD: $n = 15$, ECT: $n = 13$, YCT: $n = 13$) that were satisfied by the number of participants in each group. Still, there is a risk that the study may have been underpowered for detecting meaningful differences in other measures between older healthy controls and participants with PD considering the trends in the data that did not reach statistical significance (for example, in mean CoP velocity). Furthermore, there was a rather large variety of disease duration, motor disease severity, and dosage of dopaminergic medication in the PD group. On the other hand, considering the large variability within PD itself regarding disease progression, this sample represents a typical cohort of PD patients in the early and mid-disease stages. Only three patients were diagnosed with postural instability, while the majority were in the early stages of the disease. However, despite postural impairment being claimed to only become present in advanced stages of the disease (Jankovic, 2008), we hoped to find impairments in balance control which were not yet manifested as apparent clinical symptoms. Moreover, all patients were treated with different doses of dopaminergic medication depending on their symptoms. Although the impact of dopaminergic medication on postural stability in general as well as on CoP velocity remains an area of debate as previous studies found conflicting results (Rocchi et al., 2002; Maurer et al., 2003; Nantel et al., 2012), we cannot exclude effects of medication on our results. Furthermore, no additional clinical scores (e.g., UPDRS-III) were recorded to more precisely capture motor symptom severity and balance impairment in relation to our findings.

The exact position and distance between the feet on the Wii Balance Board has not been specified which might have influenced CoP measurements between trials (Chiari et al., 2002; Palmisano et al., 2020). Lastly, although previous studies did not support a significant effect of a dual-task design on CoP

displacement in PD (Fernandes et al., 2015), maintaining balance under additional cognitive load caused by the counting task might have affected our findings.

CONCLUSION

In our study on visual perturbation of balance in PD and two healthy control groups, we found effects of visual perturbation on CoP dynamics, but only weak effects on CoM dynamics, which could be explained by the different natures of both parameters. These effects were much stronger for patients with PD and age-matched controls than they were for young healthy adults, which supports previous findings on the deterioration of balance with age. Against our expectations, we did not identify subclinical alterations of visuomotor balance control in patients with early- to mid-stage PD. Instead, we found similar behavior in both elderly groups when exposed to our unpredictable visual perturbations. Nonetheless, in light of their limitations, our findings suggest that the mean velocity of CoP may provide a useful quantitative measure to objectify clinical findings of balance control while experiencing a non-stationary visual scenery.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of the Psychology Department, University of Marburg and Ethics Committee of the Faculty of Medicine, University of Marburg (Case 77/19). The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

JS: conceptualization, formal analysis, investigation, data curation, writing—original draft, and visualization. DE: conceptualization, methodology, software, validation, formal analysis, writing—review and editing, visualization. LT: validation, writing—review and editing. FB: conceptualization, validation, resources, writing—review and editing, supervision, project administration, and funding acquisition. JW: conceptualization, validation, resources, writing—review and editing, supervision, and project administration. All authors contributed to the article and approved the submitted version.

FUNDING

Research was funded by Deutsche Forschungsgemeinschaft (DFG): IRTG-1901, CRC/TRR-135 (project number 222641018), EU: PLATYPUS, and HMWK—The Adaptive Mind.

REFERENCES

Alghadir, A. H., Alotaibi, A. Z., and Iqbal, Z. A. (2019). Postural stability in people with visual impairment. *Brain Behav.* 9:e01436. doi: 10.1002/brb3.1436

Appeadu, M., and Gupta, V. (2021). "Postural instability," in *StatPearls [Internet]*, (Treasure Island, FL: StatPearls Publishing).

Bäckström, D., Granåsen, G., Domellöf, M. E., Linder, J., Jakobson Mo, S., Riklund, K., et al. (2018). Early predictors of mortality in parkinsonism and parkinson disease: a population-based study. *Neurology* 91, e2045–e2056. doi: 10.1212/WNL.0000000000006576

Barela, A. M. F., Barela, J. A., Rinaldi, N. M., and Toledo de, D. R. (2009). Influence of imposed optic flow characteristics and intention on postural responses. *Motor Control* 13, 119–129. doi: 10.1123/mcj.13.2.119

Beretta, V. S., Barbieri, F. A., Orcioli-Silva, D., Dos Santos, P. C. R., Simieli, L., Vitório, R., et al. (2018). Can postural control asymmetry predict falls in people with Parkinson's disease? *Motor Control* 22, 449–461. doi: 10.1123/mc.2017-0033

Berthoz, A., Pavard, B., and Young, L. R. (1975). Perception of linear horizontal self-motion induced by peripheral vision (linearvection) basic characteristics and visual-vestibular interactions. *Exp. Brain Res.* 23, 471–489. doi: 10.1007/BF00234916

Bronstein, A. M. (1986). Suppression of visually evoked postural responses. *Exp. Brain Res.* 63, 655–658. doi: 10.1007/BF00237488

Bronstein, A. M., Hood, J. D., Gresty, M. A., and Panagi, C. (1990). Visual control of balance in cerebellar and parkinsonian syndromes. *Brain* 113, 767–779. doi: 10.1093/brain/113.3.767

Carpenter, M. G., Murnaghan, C. D., and Inglis, J. T. (2010). Shifting the balance: evidence of an exploratory role for postural sway. *Neuroscience* 171, 196–204. doi: 10.1016/j.neuroscience.2010.08.030

Ciesielska, N., Sokołowski, R., Mazur, E., Podhorecka, M., Polak-Szabela, A., and Kędziora-Kornatowska, K. (2016). Is the Montreal Cognitive Assessment (MoCA) test better suited than the Mini-Mental State Examination (MMSE) in mild cognitive impairment (MCI) detection among people aged over 60? Meta-analysis. [Czy test Montreal Cognitive Assessment (MoCA) może być skuteczniejszy od powszechnie stosowanego Mini-Mental State Examination (MMSE) w wykrywaniu łagodnych zaburzeń funkcji poznawczych u osób po 60. roku zycia? Metaanaliza]. *Psychiat. Pol.* 50, 1039–1052. doi: 10.12740/PP/45368

Chang, W. D., Chang, W. Y., Lee, C. L., and Feng, C. Y. (2013). Validity and reliability of wii fit balance board for the assessment of balance of healthy young adults and the elderly. *J. Phys. Ther. Sci.* 25, 1251–1253. doi: 10.1589/jpts.25.1251

Chiari, L., Rocchi, L., and Cappello, A. (2002). Stabilometric parameters are affected by anthropometry and foot placement. *Clin. Biomech. (Bristol, Avon)* 17, 666–677. doi: 10.1016/s0268-0033(02)00107-9

Clark, R. A., Mentiplay, B. F., Pua, Y. H., and Bower, K. J. (2018). Reliability and validity of the wii balance board for assessment of standing balance: a systematic review. *Gait Posture* 61, 40–54. doi: 10.1016/j.gaitpost.2017.12.022

Cruz, C. F., Barela, A. M. F., Doná, F., Genoves, G. G., Ferraz, H. B., Silva, S. M. C. d. A., et al. (2021). Parkinson's disease delays predictable visual cue processing without affecting complex and unpredictable visual cue processing in postural control. *Brain Res.* 1751:147209. doi: 10.1016/j.brainres.2020.147209

Cruz, C. F., Piemonte, M. E. P., Okai-Nobrega, L. A., Okamoto, E., Fortaleza, A. C. d. S., Mancini, M., et al. (2018). Parkinson's disease does not alter automatic visual-motor coupling in postural control. *Neurosci. Lett.* 686, 47–52. doi: 10.1016/j.neulet.2018.08.050

da Conceição, N. R., Nóbrega de Sousa, P., Pereira, M. P., Gobbi, L. T. B., and Vitório, R. (2019). Utility of center of pressure measures during obstacle

crossing in prediction of fall risk in people with Parkinson's disease. *Hum. Mov. Sci.* 66, 1–8. doi: 10.1016/j.humov.2019.03.010

De Nunzio, A. M., Nardone, A., and Schieppati, M. (2007). The control of equilibrium in parkinson's disease patients: delayed adaptation of balancing strategy to shifts in sensory set during a dynamic task. *Brain Res. Bull.* 74, 258–270. doi: 10.1016/j.brainresbull.2007.06.020

Dehbandi, B., Barachant, A., Harary, D., Long, J. D., Tsagaris, K. Z., Bumanlag, S. J., et al. (2017). Using data from the Microsoft kinect 2 to quantify upper limb behavior: a feasibility study. *IEEE J. Biomed. Health Inform.* 21, 1386–1392. doi: 10.1109/JBHI.2016.2606240

Engel, D., Schütz, A., Krala, M., Schwenk, J. C. B., Morris, A. P., and Bremmer, F. (2020). Inter-trial phase coherence of visually evoked postural responses in virtual reality. *Exp. Brain Res.* 238, 1177–1189. doi: 10.1007/s00221-020-05782-2

Engel, D., Schwenk, J. C. B., Schütz, A., Morris, A. P., and Bremmer, F. (2021a). Multi-segment phase coupling to oscillatory visual drive. *Gait Posture* 86, 132–138. doi: 10.1016/j.gaitpost.2021.03.010

Engel, D., Student, J., Schwenk, J., Morris, A. P., Waldthaler, J., Timmermann, L., et al. (2021b). Visual perturbation of balance suggests impaired motor control but intact visuomotor processing in Parkinson's disease. *J. Neurophysiol.* 126, 1076–1089. doi: 10.1152/jn.00183.2021

Fasano, A., Canning, C. G., Hausdorff, J. M., Lord, S., and Rochester, L. (2017). Falls in parkinson's disease: a complex and evolving picture. *Mov. Disord.* 32, 1524–1536. doi: 10.1002/mds.27195

Fernandes, Â., Sousa, A. S. P., Couras, J., Rocha, N., and Tavares, J. M. R. S. (2015). Influence of dual-task on sit-to-stand-to-sit postural control in Parkinson's disease. *Med. Eng. Phys.* 37, 1070–1075. doi: 10.1016/j.medengphy.2015.08.011

Gage, W. H., Winter, D. A., Frank, J. S., and Adkin, A. L. (2004). Kinematic and kinetic validity of the inverted pendulum model in quiet standing. *Gait Posture* 19, 124–132. doi: 10.1016/S0966-6362(03)00037-7

Guerraz, M., Thilo, K. V., Bronstein, A. M., and Gresty, M. A. (2001). Influence of action and expectation on visual control of posture. *Brain Res. Cogn. Brain Res.* 11, 259–266. doi: 10.1016/s0926-6410(00)00080-x

Hay, L., Bard, C., Fleury, M., and Teasdale, N. (1996). Availability of visual and proprioceptive afferent messages and postural control in elderly adults. *Exp. Brain Res.* 108, 129–139. doi: 10.1007/BF00242910

Hoehn, M. M., and Yahr, M. D. (1967). Parkinsonism onset, progression and mortality. *Neurology* 17, 427–442. doi: 10.1212/wnl.17.5.427

Hof, A. L., Gazendam, M. G. J., and Sinke, W. E. (2005). The condition for dynamic stability. *J. Biomech.* 38, 1–8. doi: 10.1016/j.jbiomech.2004.03.025

Horak, F. B., Dimitrova, D., and Nutt, J. G. (2005). Direction-specific postural instability in subjects with parkinson's disease. *Exp. Neurol.* 193, 504–521. doi: 10.1016/j.expneurol.2004.12.008

Horak, F., and Macpherson, J. (1996). "Postural orientation and equilibrium," in *Handbook Physiology*, eds L. B. Rowell and J. T. Sheperd (New York: Oxford University Press), 255–292.

Horak, F. B., and Mancini, M. (2013). Objective biomarkers of balance and gait for parkinson's disease using body-worn sensors. *Mov. Disord.* 28, 1544–1551. doi: 10.1002/mds.25684

Horak, F., Shupert, C., and Mirka, A. (1989). Components of postural dyscontrol in the elderly: a review. *Neurobiol. Aging* 10, 727–738. doi: 10.1016/0197-4580(89)90010-9

Jankovic, J. (2008). Parkinson's disease: clinical features and diagnosis. *J. Neurol. Neurosurg. Psychiatry* 79, 368–376. doi: 10.1136/jnnp.2007.131045

Koller, W. C., Glatt, S., Vetere-Overfield, B., and Hassanein, R. (1989). Falls and Parkinson's disease. *Clin. Neuropharmacol.* 12, 98–105. doi: 10.1097/00002826-198904000-00003

Lange, R., and Erbguth, F. (2017). Morbus Parkinson im alter [Parkinson's disease in the elderly]. *Z. Gerontol. Geriatr.* 50, 547–559. doi: 10.1007/s00391-017-1284-5

Laurens, J., Awai, L., Bockisch, C. J., Hegemann, S., van Hedel, H. J. A., Dietz, V., et al. (2010). Visual contribution to postural stability: interaction between target fixation or tracking and static or dynamic large-field stimulus. *Gait Posture* 31, 37–41. doi: 10.1016/j.gaitpost.2009.08.241

Masani, K., Vette, A. H., Abe, M. O., and Nakazawa, K. (2014). Center of pressure velocity reflects body acceleration rather than body velocity during quiet standing. *Gait Posture* 39, 946–952. doi: 10.1016/j.gaitpost.2013.12.008

Maurer, C., Mergner, T., Xie, J., Faist, M., Pollak, P., and Lücking, C. H. (2003). Effect of chronic bilateral subthalamic nucleus (stn) stimulation on postural control in Parkinson's disease. *Brain* 126, 1146–1163. doi: 10.1093/brain/awg100

Morasso, P. (2020). Centre of pressure versus centre of mass stabilization strategies: the tightrope balancing case. *R. Soc. Open Sci.* 7:200111. doi: 10.1098/rsos.200111

Musolino, M. C., Loughlin, P. J., Sparto, P. J., and Redfern, M. S. (2006). Spectrally similar periodic and non-periodic optic flows evoke different postural sway responses. *Gait Posture* 23, 180–188. doi: 10.1016/j.gaitpost.2005.02.008

Nantel, J., McDonald, J. C., and Bronte-Stewart, H. (2012). Effect of medication and stn-dbs on postural control in subjects with Parkinson's disease. *Parkinsonism Relat. Disord.* 18, 285–289. doi: 10.1016/j.parkreldis.2011.11.005

Palmieri, R. M., Ingersoll, C. D., Stone, M. B., and Krause, B. A. (2002). Center-of-pressure parameters used in the assessment of postural control. *J. Sport Rehabil.* 11, 51–66. doi: 10.1123/jsr.11.1.51

Palmisano, C., Brandt, G., Vissani, M., Pozzi, N. G., Canessa, A., Brumberg, J., et al. (2020). Gait initiation in Parkinson's disease: impact of dopamine depletion and initial stance condition. *Front. Bioeng. Biotech.* 8:137. doi: 10.3389/fbioe.2020.00137

Pantall, A., Suresparan, P., Kapa, L., Morris, R., Yarnall, A., Del Din, S., et al. (2018). Postural dynamics are associated with cognitive decline in parkinson's disease. *Front. Neurol.* 9:1044. doi: 10.3389/fneur.2018.01044

Peterka, R. J. (2002). Sensorimotor integration in human postural control. *J. Neurophysiol.* 88, 1097–1118. doi: 10.1152/jn.2002.88.3.1097

Pickering, R. M., Grimbergen, Y. A. M., Rigney, U., Ashburn, A., Mazibrada, G., Wood, B., et al. (2007). A meta-analysis of six prospective studies of falling in Parkinson's disease. *Mov. Disord.* 22, 1892–1900. doi: 10.1002/mds.21598

Postuma, R. B., Berg, D., Stern, M., Poewe, W., Olanow, C. W., Oertel, W., et al. (2015). Mds clinical diagnostic criteria for parkinson's disease. *Mov. Disord.* 30, 1591–1601. doi: 10.1002/mds.26424

Rijk, M. C. d., Breteler, M. M., Graveland, G. A., Ott, A., Grobbee, D. E., van der Meché, F. G., et al. (1995). Prevalence of parkinson's disease in the elderly: the rotterdam study. *Neurology* 45, 2143–2146. doi: 10.1212/wnl.45.12.2143

Rinalduzzi, S., Trompetto, C., Marinelli, L., Alibardi, A., Missori, P., Fattapposta, F., et al. (2015). Balance dysfunction in Parkinson's disease. *Biomed Res. Int.* 2015:434683. doi: 10.1155/2015/434683

Rocchi, L., Chiari, L., and Horak, F. B. (2002). Effects of deep brain stimulation and levodopa on postural sway in Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry* 73, 267–274. doi: 10.1136/jnnp.73.3.267

Roman-Liu, D. (2018). Age-related changes in the range and velocity of postural sway. *Arch. Gerontol. Geriatr.* 77, 68–80. doi: 10.1016/j.archger.2018.04.007

Takeda, K., Mani, H., Hasegawa, N., Sato, Y., Tanaka, S., Maejima, H., et al. (2017). Adaptation effects in static postural control by providing simultaneous visual feedback of center of pressure and center of gravity. *J. Physiol. Anthropol.* 36:31. doi: 10.1186/s40101-017-0147-5

Tysnes, O.-B., and Storstein, A. (2017). Epidemiology of Parkinson's disease. *J. Neural Transm. (Vienna)* 124, 901–905. doi: 10.1007/s00702-017-1686-y

van Asten, W. N., Gielen, C. C., and van der Denier Gon, J. J. (1988). Postural adjustments induced by simulated motion of differently structured environments. *Exp. Brain Res.* 73, 371–383. doi: 10.1007/BF00248230

Vsetecková, J. J., and Drey, N. (2013). What is the role body sway deviation and body sway velocity play in postural stability in older adults? *Acta Medica (Hradec Kralove)* 56, 117–123. doi: 10.14712/18059694.2014.19

Weil, R. S., Schrag, A. E., Warren, J. D., Crutch, S. J., Lees, A. J., and Morris, H. R. (2016). Visual dysfunction in Parkinson's disease. *Brain* 139, 2827–2843. doi: 10.1093/brain/aww175

Winter, D. A. (1995). Human balance and posture control during standing and walking. *Gait Posture* 3, 193–214. doi: 10.1016/0966-6362(96)82849-9

Winter, D. A. (2009). *Biomechanics and Motor Control of Human Movement (4th ed.)*. Hoboken, NJ: Wiley. Available online at: http://onlinelibrary.wiley.com/book/10.1002/9780470549148

Winter, D. A., Patla, A. E., and Frank, J. S. (1990). Assessment of balance control in humans. *Med. Prog. Technol.* 16, 31–51.

Winter, D. A., Patla, A., and Prince, F. (1997). Stiffness control of balance during quiet standing. *Gait Posture* 5, 154–155. doi: 10.1016/S0966-6362(97)83378-4

Winter, D. A., Prince, F., Frank, J. S., Powell, C., and Zabjek, K. F. (1996). Unified theory regarding a/p and m/l balance in quiet stance. *J. Neurophysiol.* 75, 2334–2343. doi: 10.1152/jn.1996.75.6.2334

Zemková, E., Kováčiková, Z., Jeleň, M., Neumannová, K., and Janura, M. (2016). Postural and trunk responses to unexpected perturbations depend on the velocity and direction of platform motion. *Physiol. Res.* 65, 769–776. doi: 10.33549/physiolres.933177

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers | Frontiers in Bioengineering and Biotechnology

ORIGINAL RESEARCH
published: 11 April 2022
doi: 10.3389/fbioe.2022.810560

Altered Muscle Contributions are Required to Support the Stance Limb During Voluntary Toe-Walking

Enrico De Pieri[1,2]*, *Jacqueline Romkes*[1,2], *Christian Wyss*[1,2], *Reinald Brunner*[1,2,3†] and *Elke Viehweger*[1,2,3†]

[1]Laboratory for Movement Analysis, University of Basel Children's Hospital, Basel, Switzerland, [2]Department of Biomedical Engineering, University of Basel, Basel, Switzerland, [3]Department of Paediatric Orthopaedics, University of Basel Children's Hospital, Basel, Switzerland

Toe-walking characterizes several neuromuscular conditions and is associated with a reduction in gait stability and efficiency, as well as in life quality. The optimal choice of treatment depends on a correct understanding of the underlying pathology and on the individual biomechanics of walking. The objective of this study was to describe gait deviations occurring in a cohort of healthy adult subjects when mimicking a unilateral toe-walking pattern compared to their normal heel-to-toe gait pattern. The focus was to characterize the functional adaptations of the major lower-limb muscles which are required in order to toe walk. Musculoskeletal modeling was used to estimate the required muscle contributions to the joint sagittal moments. The support moment, defined as the sum of the sagittal extensive moments at the ankle, knee, and hip joints, was used to evaluate the overall muscular effort necessary to maintain stance limb stability and prevent the collapse of the knee. Compared to a normal heel-to-toe gait pattern, toe-walking was characterized by significantly different lower-limb kinematics and kinetics. The altered kinetic demands at each joint translated into different necessary moment contributions from most muscles. In particular, an earlier and prolonged ankle plantarflexion contribution was required from the soleus and gastrocnemius during most of the stance phase. The hip extensors had to provide a higher extensive moment during loading response, while a significantly higher knee extension contribution from the vasti was necessary during mid-stance. Compensatory muscular activations are therefore functionally required at every joint level in order to toe walk. A higher support moment during toe-walking indicates an overall higher muscular effort necessary to maintain stance limb stability and prevent the collapse of the knee. Higher muscular demands during gait may lead to fatigue, pain, and reduced quality of life. Toe-walking is indeed associated with significantly larger muscle forces exerted by the quadriceps to the patella and prolonged force transmission through the Achilles tendon during stance phase. Optimal treatment options should therefore account for muscular demands and potential overloads associated with specific compensatory mechanisms.

Keywords: toe-walking, equinus gait, musculoskeletal modeling, muscle function, muscle contributions, joint moments, support moment

OPEN ACCESS

Edited by:
Teddy Caderby,
Université de la Réunion, France

Reviewed by:
Yaodong Gu,
Ningbo University, China
Shih-Wun Hong,
Tzu Chi University, Taiwan

***Correspondence:**
Enrico De Pieri
enrico.depieri@unibas.ch

†These authors have contributed equally to this work and share last authorship

Specialty section:
This article was submitted to Biomechanics, a section of the journal Frontiers in Bioengineering and Biotechnology

Received: *07 November 2021*
Accepted: *02 March 2022*
Published: *11 April 2022*

Citation:
De Pieri E, Romkes J, Wyss C, Brunner R and Viehweger E (2022) Altered Muscle Contributions are Required to Support the Stance Limb During Voluntary Toe-Walking. Front. Bioeng. Biotechnol. 10:810560. doi: 10.3389/fbioe.2022.810560

INTRODUCTION

Heel-striking is considered a vital feature of a normal gait pattern. The gait of most children reaches a fairly mature pattern approximately one year after the initiation of walking (Bertsch et al., 2004). During the first year of bipedal walking, typically developing children learn to heel-strike, allowing them to walk more efficiently and stabilize their motion (Hallemans et al., 2006; Zeininger et al., 2018). In some children, however, a heel-strike pattern is either not developed at all or lost during the maturation of gait. These children may remain on forefoot during all phases of the gait cycle, or the heel may touch the ground only at a later point later during the step. These forefoot or flatfoot patterns are referred to as toe-walking. Toe-walking is observed in children diagnosed with cerebral palsy (CP), autism, and various other neurologic and orthopedic pathologies (Schweizer et al., 2013). In the absence of neurological, orthopedic or psychiatric diseases, it is referred to as idiopathic toe-walking (ITW) (Engelbert et al., 2011). In patients affected by CP, alterations of the gait pattern persist until adulthood, often determining a decline in mobility (Morgan and McGinley, 2013). Toe-walking is also observed in adults who suffered a stroke (Balaban and Tok, 2014) or a traumatic brain injury (TBI) (Williams et al., 2009). Both stroke and TBI patients can present equinus foot deformities which are associated with altered joint kinematics, reduced walking speed, and difficulties in foot clearance (Kinsella and Moran, 2008; Fock et al., 2009; Boudarham et al., 2013; Schwachmeyer et al., 2013; Manca et al., 2014). Poor foot placement control can also lead to instability during gait and an increased risk of falling (Dean and Kautz, 2015). During toe-walking, stability is reduced because of the smaller contact area between the foot and the ground (Perry et al., 2003). Furthermore, several studies have reported complaints of fatigue and pain during walking tasks in toe-walkers (Balemans et al., 2015; Alriksson-Schmidt and Hägglund, 2016; Eken et al., 2019), which may lead to a reduced health-related quality of life (HR-QoL) (Williams and Haines, 2015). A better understanding of the energetic demands associated with abnormal gait patterns could help establish intervention strategies that prevent fatigue and the deterioration of gait (Opheim et al., 2009; Lundh et al., 2018).

Toe-walkers present alterations in gait kinematics and kinetics at various joints in the lower limb (Winters et al., 1987; Kelly et al., 1997; Schlough et al., 2020). These kinematic changes are associated with premature and prolonged electromyographic (EMG) activity of the ankle plantarflexors (Kalen et al., 1986; Perry et al., 2003). Similar lower-limb joint kinetics and EMG activities were also observed in able-bodied subjects during voluntary toe-walking (Davids et al., 1999; Kerrigan et al., 2000; Perry et al., 2003; Romkes and Brunner, 2007). Romkes and Brunner (Romkes and Brunner, 2007) observed similar gastrocnemius and tibialis anterior EMG activity between voluntary and obligatory unilateral toe-walking, suggesting that the altered activations of these muscles might be required to meet the altered kinetic demands at the ankle and could therefore be partially regarded as muscle activity which is necessary in order to toe-walk. Kerrigan et al. (Kerrigan et al., 2000) observed a reduction in peak joint moments at the ankle and the knee during toe-walking, suggesting that it might require less muscle strength compared to normal a heel-to-toe gait. Perry et al. (Perry et al., 2003), on the other hand, observed an increase in mean and peak EMG activity of the plantarflexors during voluntary toe-walking, despite a reduction in peak internal plantarflexion moment – and therefore in the expected plantarflexor muscle forces. The increase in muscle EMG intensity was thought to be a consequence of a reduction in the force-generation capacity of the calf muscles when the ankle was in a plantarflexed position, in line with previous studies (Herman and Bragin, 1967; Hoy et al., 1990). Computational approaches have also been used to characterize the different contributions of the lower-limb muscles to body weight support and propulsion, showing that not only the ankle plantarflexors but also knee extensors, knee flexors, and hip extensors present an altered function during toe-walking (Sasaki et al., 2008).

Gait analysis has evolved over recent years, notably through the use of musculoskeletal modeling in clinical settings (Smith et al., 2021). Musculoskeletal modeling represents a valuable non-invasive tool to estimate the internal body loads, which could not be directly measured otherwise (Vigotsky et al., 2019; Imani Nejad et al., 2020). Modeling estimates showed good agreement with experimentally measured quantities, such as joint loads from instrumented prostheses and muscle activations from EMGs (Lund et al., 2012; Marra et al., 2014; De Pieri et al., 2018, 2019; Lunn et al., 2020; Sun et al., 2020). Through conventional gait analysis and inverse dynamics, we are able to compute kinetic parameters such as net joint moments and joint powers, which provide us insight into the function of various muscle groups in healthy and pathological gait patterns (Sloot and van der Krogt, 2018). With current musculoskeletal modeling approaches, however, it is possible to additionally predict how the load is shared across individual muscles during a given motion (Erdemir et al., 2007; Andersen, 2021). This approach is particularly useful for the analysis of human locomotion (Sylvester et al., 2021) and reveals important information about the functional role of specific muscles, particularly of the biarticular ones (Thelen et al., 2011; Seth et al., 2018). Therefore, analyzing the muscular demands associated with toe-walking using musculoskeletal modeling could provide meaningful information for the clinical management of conditions characterized by this walking pattern.

Furthermore, a synthetic parameter that could provide an insight into the required muscular demands during gait is the support moment. This parameter was first introduced by D. Winter in 1980 and was defined as the sum of the sagittal extensive moments at the ankle, knee, and hip joints (Winter 1980). The support moment quantifies how much the limb is pushing away from the ground and can be used to estimate the muscular demands necessary to prevent a collapse of the stance limb during walking (Winter 2009). In 2000, A.L. Hof provided a mechanical interpretation for this concept, demonstrating that a slightly reformulated definition of the support moment was responsible for preventing the collapse of the knee due to external forces (Hof, 2000). The support moment seems

well-suited to investigate the required overall extensive muscular effort to maintain stance limb stability in pathological populations (Wyers et al., 2021).

The aim of this study was to understand and characterize, from a biomechanical perspective, gait deviations occurring during voluntary unilateral toe-walking, compared to normal gait, in a cohort of healthy volunteers. In particular, the focus was to describe the functional contributions of the major flexor and extensor muscles to the kinetics of gait. For this purpose, required muscle contributions to the joint sagittal moments were calculated using musculoskeletal modeling. The analysis of healthy individuals provides a unique insight on the muscular demands solely related to the specific gait pattern, independently of any underlying neuromuscular control disorder. As toe-walking alters the alignment of the stance limb relatively the ground reaction forces (GRF), functional adaptations for posture and movement control are expected in the lower-limb muscles to counteract these external forces. It was therefore hypothesized that toe-walking is associated with higher demands on the lower-limb muscles compared to normal walking. Additionally, the support moment is suggested as a synthetic indicator of the overall muscular demands during stance, and further clarifications about its physical meaning are provided.

MATERIALS AND METHODS

Participants and Gait Analysis

Nine healthy adult subjects (four males, five females; age 30.1 ± 3.7 years) without a history of neurologic or orthopedic disorders underwent kinematic (motion capture system: Vicon Motion Systems Ltd., Oxford, UK) and kinetic (force platforms: Kistler Group, Winterthur, CH) 3D gait analysis, as part of a previous study (Romkes and Brunner, 2007). Gait data were acquired barefoot at a self-selected speed using the Plug-in Gait lower-body marker-set (Kadaba et al., 1990). One of the ten healthy subjects originally included in Romkes and Brunner (2007) was excluded due to an incomplete set of markers. Subjects were first tested during normal walking and were then shown a sagittal plane video of a patient with unilateral CP. They were asked to mimic the unilateral toe walking pattern seen in the video. The subjects practiced until obtaining a reproducible pattern, while care was taken by the investigators to ensure that knee and ankle positions were correct. Four to six walking trials were measured for each walking modality per subject. Further details on the experimental data collection can be found in Romkes and Brunner (2007).

Musculoskeletal Modeling

Marker trajectories and ground reaction force (GRF) data were used as input for an inverse dynamics analysis in the AnyBody Modeling System (AnyBody Technology, Denmark) (Damsgaard et al., 2006). Individual models for each subject were created from a detailed musculoskeletal model of the lower limb (Carbone et al., 2015; De Pieri et al., 2018), which was scaled to match the overall anthropometrics and the marker data collected during a standing reference trial (Lund et al., 2015).

Each hip joint was modeled as a 3-degrees of freedom (DOF) ball-and-socket joint, while knee and talocrural joints were modeled as 1-DOF hinges. The position of the patella was defined as a function of the knee flexion angle, while the motion of the subtalar joint was restricted due to the reduced number of markers on the foot segment (one heel- and one toe-marker). Muscles were modeled as Hill-type actuators, with calibrated tendon slack-length (Heinen et al., 2016) and instantaneous muscle strength that followed force-length and force-velocity relationships (Hill, 1938; Zajac, 1989; Andersen, 2021).

Joint kinematics were first computed from the measured marker trajectories (Andersen et al., 2009) and were reported in anatomical coordinate systems according to the International Society for Biomechanics' (ISB) recommendations (Wu et al., 2002). An inverse dynamics analysis, based on a third-order-polynomial muscle recruitment criterion, was then performed to calculate the required muscle activations and forces, as well as the resulting joint moments (Andersen, 2021). At each joint level, the internal net sagittal moment was calculated in the proximal coordinate system according to ISB recommendations (Derrick et al., 2020). In each lower-limb joint, sagittal plane rotations were unconstrained, therefore the internal sagittal net joint moment is equal to the sum of the sagittal moments generated by all the muscles spanning the joint:

$$\boldsymbol{M}_{\boldsymbol{joint}}^{\boldsymbol{sagittal}} = \sum_{\boldsymbol{m_j=joint-spanning\ muscles}} \boldsymbol{M}_{\boldsymbol{m_j}}^{\boldsymbol{sagittal}}. \tag{1}$$

The contribution of each joint-spanning muscle to the joint net sagittal moment was computed as the product of the force exerted by the muscle times the distance of its instantaneous line of action from the center of rotation of the joint (De Pieri et al., 2018). For biarticular muscles, the contributions to the net sagittal moments around both joints were computed. Additionally, the force exerted by the quadriceps muscles on the patella and the force transmitted by the triceps surae to the Achilles tendon were calculated.

Support and Progression Moments

The support moment M_S was calculated as a weighted sum of the lower-limb joints sagittal extensive moments, according to the definition by A.L. Hof (Hof, 2000), in which the individual sagittal moments around the ankle (M_A), knee (M_K), and hip (M_H), were considered positive when extensive. This definition of the support moment is equal to the component of the GRF acting in the direction of the hip-ankle line (F_P) times knee eccentricity (q):

$$\boldsymbol{M_S} = \frac{\boldsymbol{1}}{\boldsymbol{2}}\boldsymbol{M_A} + \boldsymbol{M_K} + \frac{\boldsymbol{1}}{\boldsymbol{2}}\boldsymbol{M_H} = \boldsymbol{F_P}*\boldsymbol{q}. \tag{2}$$

As a corollary of this interpretation, it was suggested that the component of the GRF acting transversally to the direction of the hip-ankle line (F_T) is determined by the difference between hip and ankle sagittal moments divided by the distance between hip and ankle (p). We defined the difference between hip and ankle moments as progression moment M_P:

$$\boldsymbol{M_P} = \boldsymbol{M_{hip}} - \boldsymbol{M_{ankle}} = \boldsymbol{F_T}*\boldsymbol{p}. \tag{3}$$

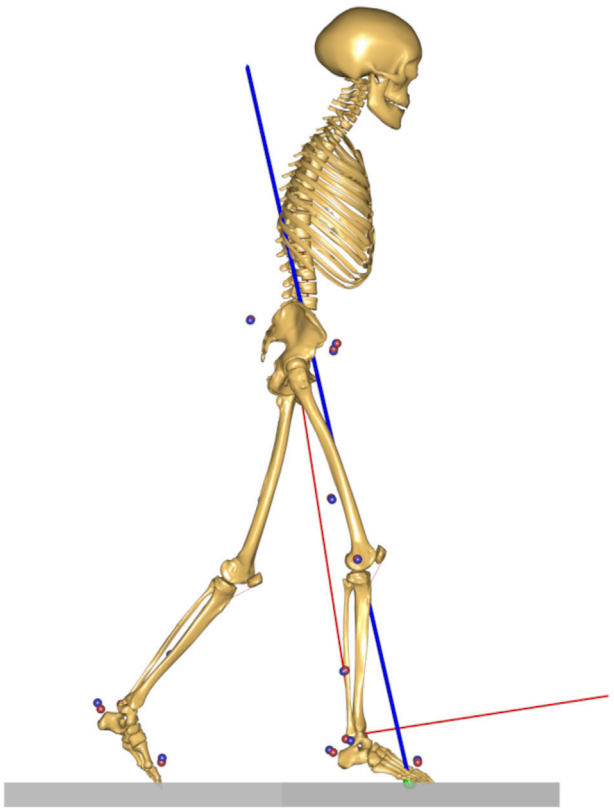

FIGURE 1 | Ground reaction force vector (in blue) and the newly defined reference frame (in red) with the vertical axis connecting the ankle and the hip joint centers, and the anterior-posterior axis transversal to the hip-ankle line.

p and q were calculated as a function of the knee flexion angle using trigonometric relationships, under the assumption that thigh and shank have equal lengths. The complete geometrical derivation of these relationships is reported in Hof (2000).

F_p and F_t were calculated by projecting the GRF vector into a newly defined reference frame, in which the vertical axis passes through the ankle and the hip joint centers. The mediolateral axis was parallel to the floor and perpendicular to the gait direction (defined by the floor-projection of the heel marker in two consecutive ipsilateral foot strikes), and the anteroposterior axis was defined as the cross-product of vertical and mediolateral ones (**Figure 1**).

The support and progression moments M_S and M_P, calculated as the sum or difference of the individual joint moments as described previously, were then compared to the physical quantities $F_P{*}q$ and $F_T{*}p$, respectively. Additionally, muscle contributions to the support and the progression moments were calculated by combining (**Eq. 1**) into (**Eqs 2, 3**), respectively:

$$M_S = \frac{1}{2}\sum_{m_A} M_{m_A} + \sum_{m_K} M_{m_K} + \frac{1}{2}\sum_{m_H} M_{m_H} = \left(\frac{1}{2}M_{Sol_A} + 0 + 0\right) + \left(\frac{1}{2}M_{Gas_A} + M_{Gas_K} + 0\right) + [\ldots], \quad (4)$$

$$M_P = \sum_{m_H} M_{m_H} - \sum_{m_A} M_{m_A} = -M_{Sol_A} - M_{Gas_A} - M_{TibAnt_A} + M_{GlutMax_H} + M_{Hams_H} + [\ldots]. \quad (5)$$

Data Analysis

Gait trials were processed and analyzed through the toolkit AnyPyTools (Lund et al., 2019) in the *Python* programming language (*Python* Software Foundation). The analysis of joint kinematics and joint kinetics, including muscle contributions, was focused on the sagittal plane as the plane of forward motion. Joint moments, muscle contributions to the joint moments, and support and progression moments were normalized by body mass. The muscle forces acting on the patella and the Achilles tendon were normalized by body weight (BW). Kinematic data (angles) were time-normalized during the gait cycle (GC) from foot strike (0%) to foot strike (100%), while kinetic data (moments and forces) were time-normalized for the duration of the loaded stance phase (ST), from foot strike (0%) to foot off (100%). Averages per subject were then calculated based on the four to six collected trials.

Statistical Parametric Mapping Analysis

Differences between normal walking and voluntary toe-walking were analyzed through statistical parametric mapping (SPM; www.spm1D.org, v0.43) (Friston et al., 1994; Pataky, 2012) for joint kinematics, joint moments, muscle contributions to the joint moments, muscle forces, and for support and progression moments. Due to the reduced number of tested subjects (n = 9), non-parametric (Pataky et al., 2015) two-tailed paired t-tests were used to identify statistically significant differences between the two walking modalities.

The comparison between support and progression moments and their respective physical equivalents, $F_P{*}q$ and $F_P{*}p$, was carried out through non-parametric, two-tailed, two-sample t-tests.

The output test statistic—SnPM{t}—was evaluated at each point of GC or ST. The significance level was set at $\alpha = 0.05$, and the corresponding critical thresholds—t^*—were calculated based on the temporal smoothness of the input data through random field theory. The probability that similar suprathreshold regions would have occurred from equally smooth random waveforms was then calculated. In the interest of clarity, only differences that were statistically significant for more than 2% of GC or ST are discussed.

RESULTS

Lower-Limb Kinematics

The subjects participating in this study were able to successfully reproduce a toe-walking pattern similar to the one they were shown in a video of a unilateral CP patient. In the sagittal plane, their voluntary toe-walking pattern was characterized by an initial toe-contact, and the foot-floor inclination angle significantly differed from their normal gait pattern throughout

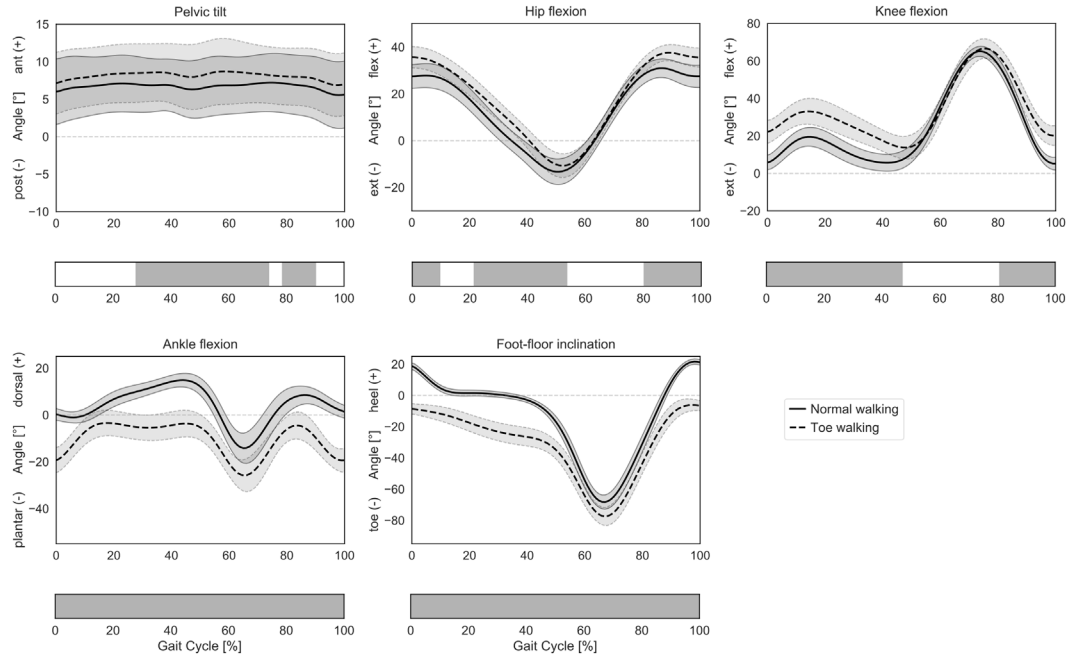

FIGURE 2 | Lower-limb sagittal plane kinematics during GC. Mean ± 1SD pelvic tilt, hip flexion, knee flexion, ankle flexion, and foot-floor inclination angles are reported as solid lines during normal walking and as dashed lines during voluntary toe-walking. Phases of GC for which a statistically significant difference in the SPM paired t-tests was found are indicated as grey bars below each subplot.

the GC, with the heel never touching the ground (**Figure 2**). During toe-walking, the ankle was significantly more plantarflexed during the whole GC, the knee was more flexed from mid-swing until terminal stance (81–47% GC), the hip was more flexed from mid-swing until loading response and during mid-stance (80–10% and 21–54% GC), and the pelvis was more anteriorly tilted from mid-stance until mid-swing (28–74% and 79–90% GC).

Joint Moments and Muscle Contributions

When walking on their toes, the subjects also presented statistically significant differences in the internal net sagittal joint moments compared to their normal gait pattern. These kinetic differences translated into altered required moment contributions in the sagittal plane from the muscles spanning each joint.

At the ankle (**Figure 3A**), toe-walking was associated with a significantly larger net extension (plantarflexion) moment during loading response and mid-stance (0–44% ST) and with a reduced extension moment during terminal-stance and push-off (52–90% ST). As a consequence of the altered kinetics, toe-walking required an earlier and larger extensive contribution during loading response and mid-stance from the gastrocnemius (0–38% ST) and the soleus (6–46% ST), while the gastrocnemius also provided a reduced contribution to the peak extension moment during terminal-stance and push-off (46–82% and 86–93% ST). The tibialis anterior did not provide any flexion (dorsiflexion) contribution during initial contact and loading response (0–16% ST) when toe-walking. Additional statistically significant differences in soleus (0–3% ST) and tibialis anterior (36–38% and 82–94% ST) were characterized by negligible magnitudes in both walking modalities.

At the knee (**Figure 3B**), the subjects presented a longer-lasting net flexion moment during loading response, decreased during 0–2% ST and increased during 6–13% ST when toe-walking. From mid- to terminal-stance (46–83% ST), the flexion moment was significantly reduced. No statistically significant differences were found during early mid-stance when the net sagittal moment was extensive for normal walking and toe-walking. In terms of muscles' contributions to the knee net sagittal moment, the gastrocnemius provided a larger flexion moment during the first half from loading response (1–36% ST) and a reduced flexion moment during mid-stance to push-off (42–93% ST) when toe-walking. A significantly larger extension moment was required from the vasti during mid-stance (41–58% ST) when walking on the toes, while their extensive contribution was almost null during this phase while normal walking. The peak extension moment from the vasti occurred for both walking modalities during loading response and was characterized by a larger mean value and a broader variability during toe-walking, albeit not significantly different (0.88 ± 0.44 Nm/kg at 23% ST during toe walking vs 0.65 ± 0.28 Nm/kg at 22% ST during normal walking). The hamstrings provided a reduced but longer-lasting flexion contribution during loading response (lower during 0–3% ST and increased during 8–18% ST). The rectus femoris provided a significantly larger extension contribution during initial contact (0–6% ST) but of negligible magnitude.

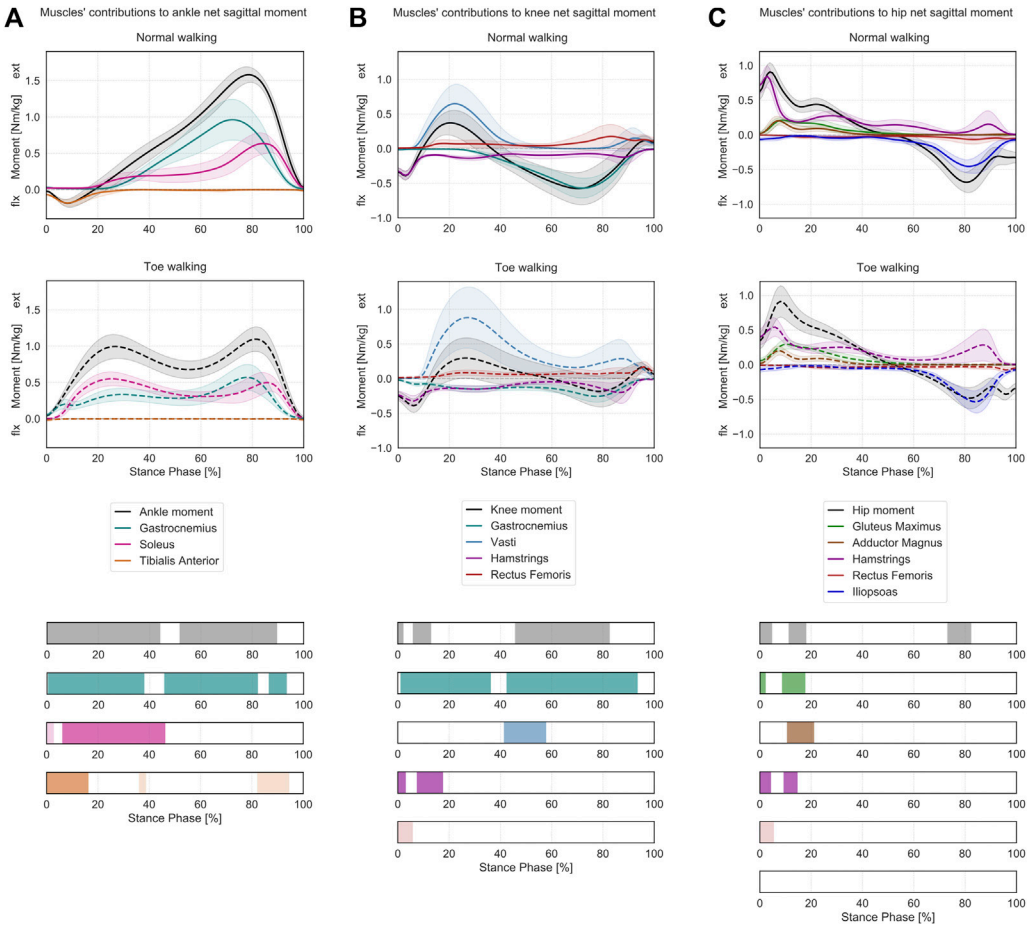

FIGURE 3 | Lower-limb sagittal plane kinetics during ST. Mean ± 1SD ankle **(A)**, knee **(B)** and hip **(C)** sagittal net internal moments (black/grey) and the sagittal moment contributions of the relative joint-spanning muscles (colored) are reported as solid lines during normal walking and as dashed lines during voluntary toe-walking. Phases of ST for which a statistically significant difference in the SPM paired *t*-tests was found are indicated as colored bars at the bottom. ST phases in which statistically significant differences were observed but the moment contributions were characterized by negligible magnitudes are reported in lighter colors.

At the hip (**Figure 3C**), toe-walking was characterized by a larger and delayed net extension moment during loading response (lower during 0–5% ST and increased during 11–18% ST) and by a reduced net flexion moment during terminal-stance (73–82% ST). When toe-walking, the gluteus maximus provided a larger contribution to the extension moment during initial stance (0–2% and 8–17% ST), similarly to the adductor magnus (11–21% ST), while the hamstrings provided a reduced extensive contribution during initial contact (0–4% ST) and a slightly increased one during loading response (11–21% ST). The significant flexing contribution of the rectus femoris (0–5% ST) was of negligible magnitude.

Support Moment

Toe-walking was associated with a significantly higher support moment during mid-stance (34–65% ST) (**Figure 4A**), as a consequence of the altered joint sagittal moments (**Figure 4B**).

The support moment calculated according to Hof's formulation showed a similar trend and comparable magnitude with the product of the GRF component acting in the direction of the hip-ankle line (F_P) times knee eccentricity (q) (**Figure 4C**). Statistically significant differences between M_S and $F_P{*}q$ were found during the initial transition phase and pre-swing (0–4% and 71–100% ST for normal walking, 0–6% and 72–100% ST for toe-walking). This confirms that a weighted sum of the three lower-limb joint moments is responsible for preventing the collapse of the knee during stance.

When looking at the contribution of the major lower-limb muscles to the support moment during normal walking (**Figure 6A**), it emerges that the hamstrings briefly provide extensive vertical support during initial heel-strike while the other major hip extensors – gluteus maximus and adductor magnus – immediately follow and provide some support throughout the initial phases of stance. The largest contributor during loading response is the vasti, with a synergistic contribution from the rectus femoris. Approximatively around

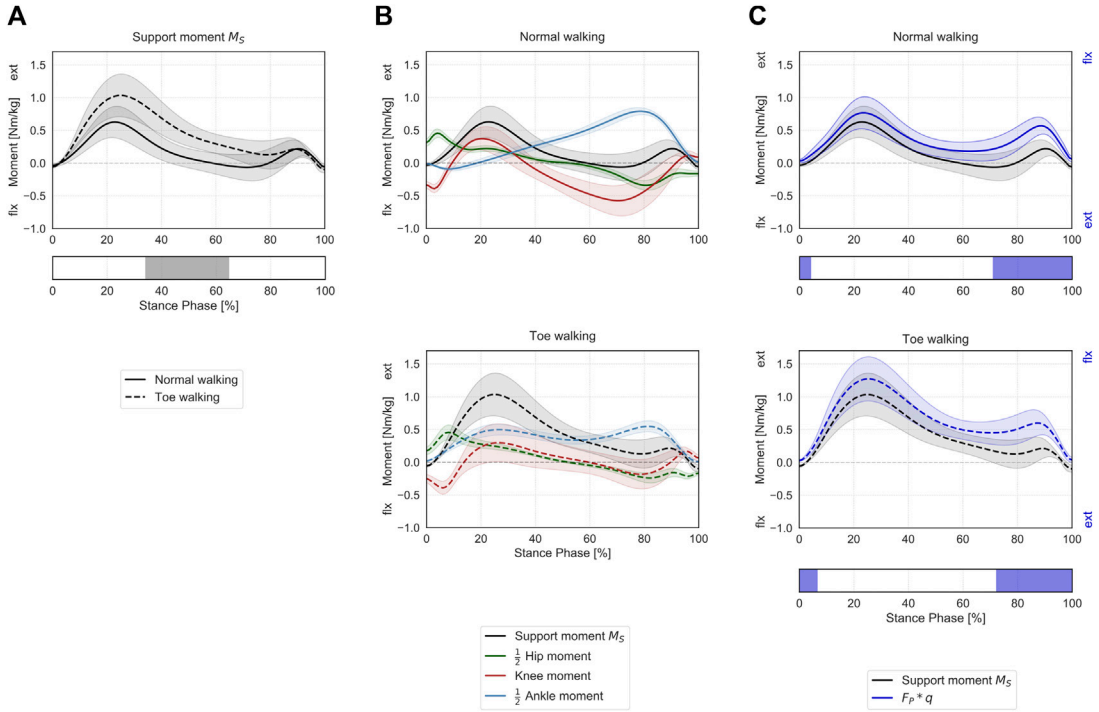

FIGURE 4 | Support moment in the sagittal plane during ST. **(A)** Mean ± 1SD support moment (black/grey) is reported during normal walking (solid line) and toe-walking (dashed line). The phase of ST for which a statistically significant difference in the SPM paired *t*-test was found is indicated as a grey bar below. **(B)** Mean ± 1SD support moment (black/grey), ankle (blue), knee (red), and hip (green) internal net sagittal moments, weighted according to the definition by A.L. Hof (Hof, 2000), are reported for normal walking (top, solid lines) and toe-walking (bottom, dashed lines). **(C)** Comparison between support moment and the external forces acting on the stance limb. Mean ± 1SD support moment (black/grey) compared to the product of the GRF component acting in the direction of the hip-ankle line FP times knee eccentricity q (violet-blue), during normal walking (solid line, top) and toe-walking (dashed line, bottom). The support moment is acting in the opposite direction compared to the moment produced by the GRF. The phases of ST for which a statistically significant difference in the SPM two-sample *t*-test was found are indicated as violet-blue bars below.

20% ST, the soleus also starts providing a positive contribution to the support moment, and it becomes the dominant contributor from mid-stance until push-off. From mid-to terminal-stance, the rectus femoris also plays a significant supporting role. During terminal stance, the mean support moment across the cohort becomes negative (~60–80% ST), corresponding with the peak knee flexion moment (**Figure 4B**). During this phase, the hamstrings and the gastrocnemius provide a net negative contribution to the support moment. During pre-swing, the vasti work again synergistically with the rectus femoris and the soleus to provide a net positive support moment.

During toe-walking, the hamstrings provide a prolonged negative contribution during the initial foot contact until loading response. This is counteracted by a synchronous positive contribution from the gluteus maximus and the adductor magnus. The soleus is required to provide a positive and large contribution already during loading response and lasting until push-off. The vasti remain the largest contributors to the support moment, and their activation is also continuously required from load acceptance throughout ST. The rectus femoris contribution is also qualitatively reduced, particularly during push-off. The mean support moment remains positive throughout ST when toe-walking, despite a negative contribution from the hamstring during terminal stance. The gastrocnemius provides a small positive contribution during terminal stance.

Progression Moment

Toe-walking was associated with a significantly reduced peak backward progression moment during the initial foot contact and loading response (0–40% ST) (**Figure 5A**). The mean progression moment becomes forward-oriented at 14% ST during toe-walking, compared to normal walking when this transition occurs at 31% ST. This was determined by an earlier forward contribution by the ankle sagittal moment (**Figure 5B**). From mid- to terminal-stance, toe-walking was characterized by a significantly reduced peak forward progression moment (53–89% ST).

The progression moment, defined as a corollary of Hof's interpretation, showed a similar trend and comparable magnitude with the product of the GRF component acting transversally to the direction of the hip-ankle line (F_T) times the distance between hip and ankle (p) (**Figure 5C**). Statistically significant differences between M_P and $F_T{*}p$ were found during the transitions between stance and swing phases (0–2% and 92–100% ST for normal walking, 0–2% and 93–100% ST for

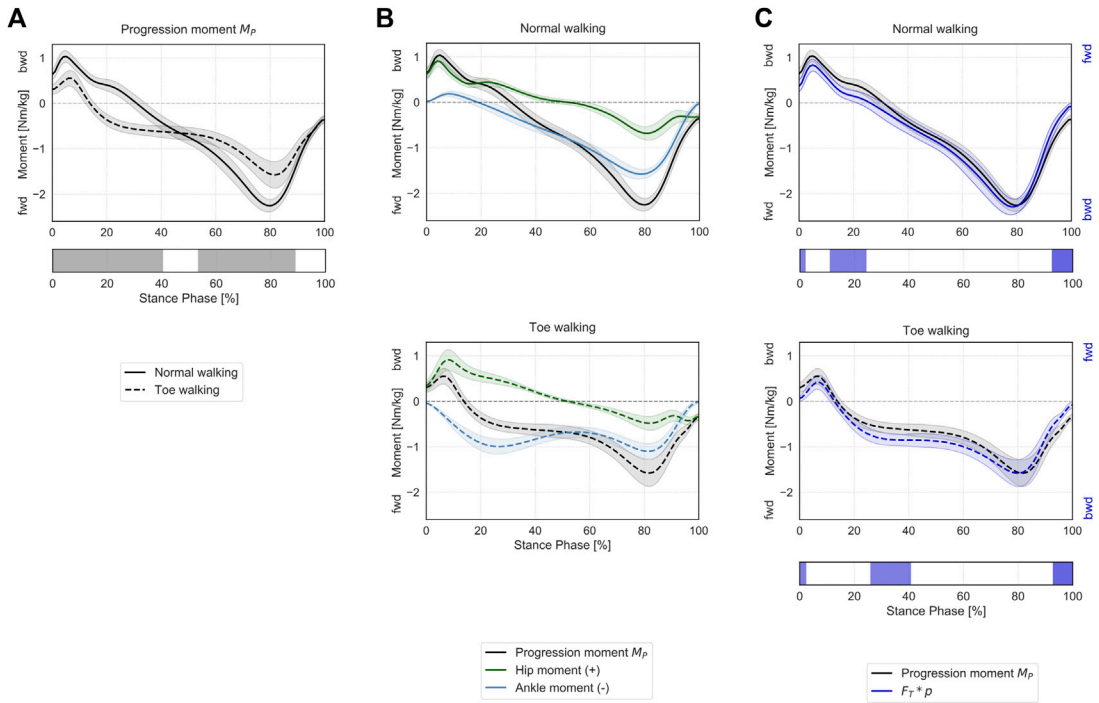

FIGURE 5 | Progression moment in the sagittal plane during ST. **(A)** Mean ± 1SD progression moment (black/grey) is reported during normal walking (solid line) and toe-walking (dashed line). The phases of ST for which a statistically significant difference in the SPM paired *t*-test was found are indicated as grey bars below. **(B)** Mean ± 1SD progression moment (black/grey), ankle (blue), and hip (green) internal net sagittal moments, weighted according to the definition derived from A.L. Hof (Hof, 2000), are reported for normal walking (top, solid lines) and toe-walking (bottom, dashed lines). **(C)** Comparison between support moment and the external forces acting on the stance limb. Mean ± 1SD progression moment (black/grey) compared to the product of the GRF component acting transversally to the direction of the hip-ankle line FT times the distance between hip and ankle p (violet-blue), during normal walking (solid line, top) and toe-walking (dashed line, bottom). The progression moment is acting in the opposite direction compared to the moment produced by the GRF. The phases of ST for which a statistically significant difference in the SPM two-sample *t*-test was found are indicated as violet-blue bars below.

toe-walking), as well as during 11–24% ST for normal walking and 26–41% ST for toe-walking. This suggests that only ankle- and hip-spanning muscles are counteracting the external forces acting transversally to the stance leg.

The muscles' contributions to the progression moment were qualitatively different between normal walking and toe-walking (**Figure 6B**). During normal walking, in order to counteract the forward-oriented $F_T{*}p$ (**Figure 5C**), the hamstrings provide a backward contribution during the initial heel-strike. Their contribution remains present albeit reduced during most of the stance phase. The other hip extensors – gluteus maximus and adductor magnus – immediately follow and provide a backward contribution during loading response, together with the tibialis anterior. This highlights a synergistic effect of hip extensors and ankle dorsiflexors in early stance in slowing down the anterior motion of the leg. From mid-stance, the ankle plantarflexors – soleus and gastrocnemius – provide a forward contribution to the progression moment (counteracting the posteriorly oriented $F_T{*}p$), as does the iliopsoas during pre-swing. The forward contribution of the rectus is smaller compared to the iliopsoas. There is an overall synergistic action of ankle plantarflexors and hip flexors in rotating the leg forward.

During toe-walking, the hamstring provided a relatively larger backward contribution for a prolonged period of ST. The lack of tibialis anterior backward contribution is compensated by a larger relative contribution of all hip extensors during early stance. At the same time, the soleus and the gastrocnemius provide a forward contribution already during the early stance. The hip extensors and the ankle plantarflexors are therefore acting antagonistically during the initial phases of ST when toe-walking. During mid-stance to late stance, the forward contribution to the progression moment of the plantarflexors remains substantial, and it is strengthened by a synergistic effect of the iliopsoas and to a smaller extent of the rectus femoris during pre-swing.

Muscle Forces on Patella and Achilles Tendon

Toe-walking was associated with significantly larger muscle forces exerted by the quadriceps to the patella during mid-stance (49–56% ST) (**Figure 7A**). The significantly higher muscle forces during initial foot contact (0–3% ST) were of negligible magnitude.

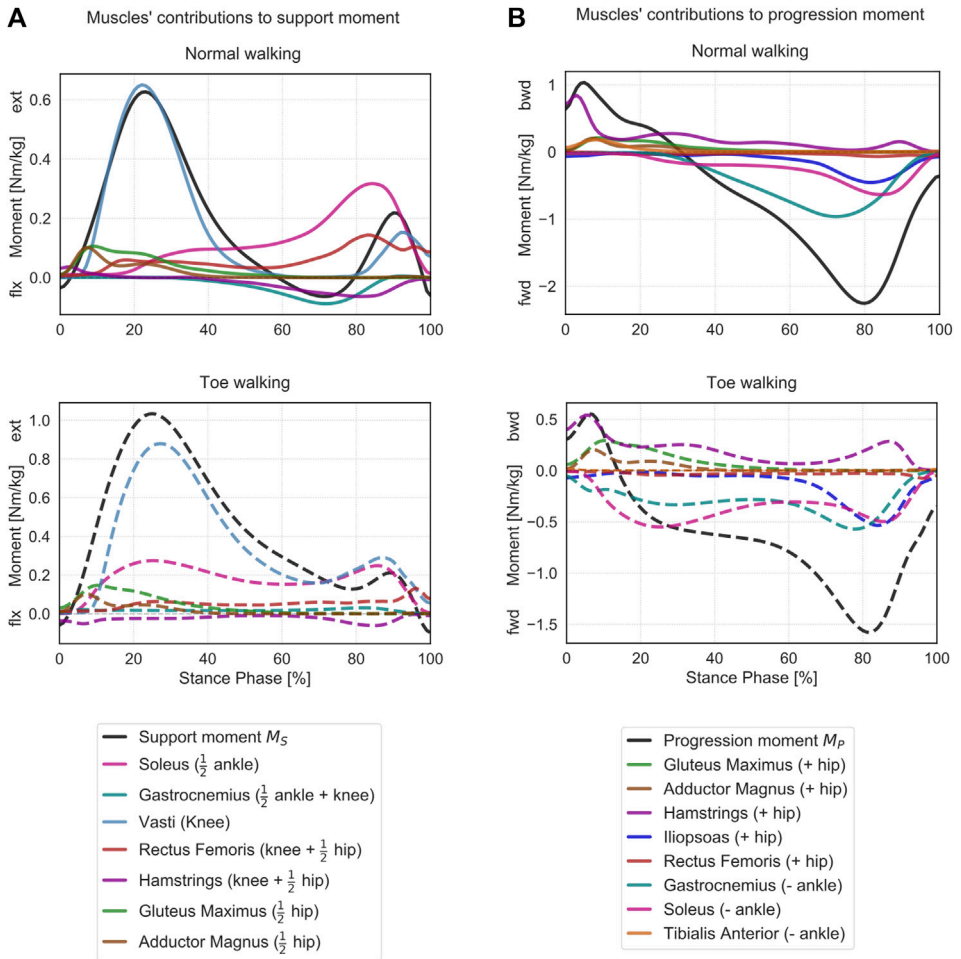

FIGURE 6 | Contributions of the lower limb muscles to support and progression moments. **(A)** Mean support moment (black) and sagittal moment contributions of the major lower-limb muscles are reported for normal walking (top, solid lines) and toe-walking (bottom, dashed lines). For each muscle, the contribution to the support moment is calculated as a weighted sum of its contributions to the joints it spans, as indicated in **Eq. 4**. Weighing factors are reported in brackets (+1/2 for ankle and hip, +1 for the knee). **(B)** Mean progression moment (black) and sagittal moment contributions of the major lower-limb muscles are reported for normal walking (top, solid lines) and toe-walking (bottom, dashed lines). For each muscle, the contribution to the progression moment is calculated as a weighted contribution to the joint it spans, as indicated in **Eq. 5**. Weighing factors are reported in brackets (–1 for the ankle, +1 for the hip).

Regarding the muscle forces exerted from the triceps surae to the calcaneus (**Figure 7B**), toe-walking was also characterized by a prolonged force transmission through the Achilles tendon, with higher forces during early stance (2–39% ST) and a reduced peak force during terminal-stance (48–92% ST).

DISCUSSION

The objective of this study was to describe the gait deviations occurring in a cohort of healthy subjects when they are voluntarily walking on their toes compared to their normal heel-to-toe gait pattern. The focus was to characterize the functional adaptations of the major lower-limb muscles which are required in order to toe walk. The role and importance of each muscle to the kinetics of gait was assessed by estimating its required contribution to the joint net sagittal moments using musculoskeletal modeling. Additionally, the concept of the support moment was used to evaluate the overall muscular effort necessary to maintain stance limb stability and prevent the collapse of the knee due to external forces (winter 1980, 2009; Hof, 2000).

Compared to a normal heel-to-toe gait pattern, toe-walking was characterized by significantly different lower-limb joint kinematics and kinetics (**Table 1**). The altered kinetic demands at each joint translated into different required moment contributions from most flexor and extensor muscles. In particular, an earlier and prolonged ankle plantarflexion contribution was required from the soleus and gastrocnemius during most of the stance phase. On the other hand, the tibialis anterior did not provide any dorsiflexion contribution during the initial stance phase when toe-walking. At the knee, a reduced net

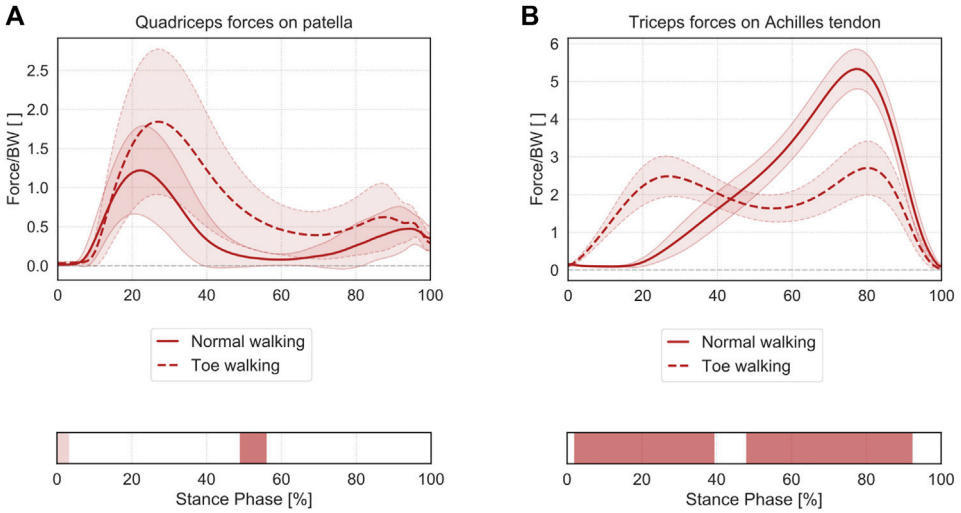

FIGURE 7 | Mean ± 1SD magnitude of the muscle forces transmitted from the quadriceps muscle to the patella **(A)** and from the triceps surae to the calcaneus through the Achilles tendon **(B)**, during normal walking (solid lines) and toe-walking (dashed lines), normalized to body weight (BW). The phases of ST for which statistically significant differences in the SPM paired *t*-tests were found are indicated as red bars below each subplot. ST phases in which statistically significant differences were observed but the muscle forces were characterized by negligible magnitudes are reported in a lighter tint.

TABLE 1 | Overview of most important differences in sagittal kinematics and kinetics occurring in toe-walking compared to normal walking during different periods of the stance phase.

Major sagittal kinematic and kinetic differences of toe-walking compared to normal walking during stance phase					
	Initial contact	***Loading response***	***Mid-stance***	***Terminal stance***	***Pre-swing***
Kinematics	Toe-contact (vs heel); Plantarflexed ankle (vs neutral); Larger knee flexion; Larger hip flexion	Toe-contact (vs heel); Plantarflexed ankle (vs dorsiflexed); Larger knee flexion; Larger hip flexion	Toe-contact (vs flat foot); Plantarflexed ankle (vs dorsiflexed); Larger knee flexion; Larger hip flexion	Toe-contact (vs flat foot); Plantarflexed ankle (vs dorsiflexed); Larger knee flexion; Larger hip flexion; Larger anterior pelvic tilt	Larger foot-floor inclination angle; Larger ankle plantarflexion; Lower peak hip extension; Larger anterior pelvic tilt
Ankle kinetics	Net plantarflexion (vs dorsiflexion) moment; Gastrocnemius plantarflexion contribution; Lack of tibialis anterior dorsiflexion contribution	Net plantarflexion (vs dorsiflexion) moment; Gastrocnemius plantarflexion contribution; Soleus plantarflexion contribution; Lack of tibialis anterior dorsiflexion contribution	Larger net plantarflexion moment; Prolonged and initially larger gastrocnemius plantarflexion contribution; Prolonged and larger soleus plantarflexion contribution	Lower net plantarflexion moment; Lower gastrocnemius plantarflexion contribution	Lower peak net plantarflexion moment; Lower gastrocnemius plantarflexion contribution
Knee kinetics	Lower net flexion moment; Lower hamstring flexion contribution	Prolonged and larger net flexion moment; Gastrocnemius flexion contribution; prolonged hamstring flexion contribution	Prolonged net extension moment; Lower gastrocnemius flexion contribution; Larger vasti extension contribution	Lower net flexion moment; Lower gastrocnemius flexion contribution	Lower gastrocnemius flexion contribution
Hip kinetics	Lower net extension moment; Lower hamstring extension contribution; Larger gluteus maximus extension contribution	Prolonged net extension moment; prolonged and larger hamstring extension contribution; Larger gluteus maximus extension contribution; Larger adductor magnus extension contribution		Lower net peak flexion moment	
Support moment			Larger extensive support moment	Larger extensive support moment	
Progression moment	Lower backward progression moment	Early transition backward to forward progression moment	Larger forward progression moment	Lower forward progression moment	Lower peak forward progression moment

flexion moment during mid-to terminal-stance corresponded with a significantly larger knee extension contribution required from the vasti during mid-stance, while the hamstrings provided a reduced but longer-lasting knee flexion contribution during loading response when toe-walking. All hip extensors provided a larger extensive moment during loading response. Overall, different muscular activations are therefore functionally required at every joint level in order to toe-walk compared to normal walking.

The higher support moment during the stance phase indicates that an overall higher muscular effort is required during toe-walking to support the stance limb. The computed muscle contributions to the support moment reveal that different muscles effectively work to maintain a stable leg during different phases of walking. In particular, when toe-walking, a higher extensive contribution is required by the soleus during initial stance, and by the vasti, which present a prolonged extensive activity during mid-stance while the contribution of the rectus during pre-swing is reduced compared to normal walking. The hamstrings, which provide an extensive contribution to the support moment in a normal heel-to-toe gait pattern, are instead providing a flexing contribution during initial contact when toe-walking. These changes indicate an overall different support strategy to maintain a stable leg during the stance phase and prevent the knee from collapsing.

The analysis of the progression moment, which was derived as a corollary of A.L. Hof formulations (Hof, 2000), showed that during normal walking, forward-oriented external forces are counteracted by hip extensors and ankle dorsiflexors (initial ST) while backward-oriented external forces are balanced by activation of ankle plantarflexors and hip flexors (mid- and terminal ST). During toe-walking, this activation pattern is altered, with the hip extensors and ankle plantarflexors being simultaneously activated during the initial phases of ST. The altered activation of gastrocnemius and soleus during early stance seems to be required to maintain a force balance transversally to the leg axis when toe-walking.

Furthermore, toe-walking was characterized by significantly larger muscle forces exerted by the quadriceps to the patella and prolonged force transmission through the Achilles tendon during the stance phase.

Prolonged muscular effort and overuse may lead to fatigue, pain, and a reduced HR-QoL (Balemans et al., 2015; Williams and Haines, 2015; Alriksson-Schmidt and Hägglund, 2016; Eken et al., 2019). In particular, the higher loads required from the vasti may explain the high prevalence of knee pain and patellofemoral symptoms observed in CP patients, especially with increasing age (Jahnsen et al., 2004; Rethlefsen et al., 2015). Overactive quadriceps muscles may lead to an overstretched patellar tendon and a further loss of functionality (Villani et al., 1988; Jahnsen et al., 2004). Similarly, the prolonged force transmission through the Achilles tendon in a plantarflexed position may be associated with tendon shortening and contractures (Tardieu et al., 1989; Solan et al., 2010). Optimal treatment options should therefore aim at addressing the primary neuromuscular disorders which are associated with an altered gait pattern in order to avoid secondary long-term adverse consequences.

The restoration of a heel-to-toe gait pattern may improve the functionality and the gait efficiency of toe-walking patients while reducing the long-term risks associated with compensatory mechanisms (Brunner et al., 2021). Several treatments aiming at restoring a heel-strike pattern are available (Graham et al., 2016), ranging from conservative options, such as physical therapy (Palmer et al., 2010), casting, and orthotic devices (Totah et al., 2019), to the use local medication (Botulinum toxin-A) (Strobl et al., 2015) and bone and soft tissue corrective surgeries (McGinley et al., 2012). Physiotherapy could also benefit from a better understanding of the compensatory mechanisms to define targeted strengthening and rehabilitation programs (Damiano and Abel, 1998; Booth et al., 2018). Therefore, the choice of treatment depends on a correct understanding of the underlying pathology and on the individual biomechanics of walking.

This study was limited to a cohort of nine healthy volunteers who were asked to mimic a pathological toe-walking pattern. Through the analysis of healthy individuals, this study isolated the influence of a specific motion pattern on the optimally-required muscular loads, without additional assumptions of altered neuromuscular control (Steele et al., 2015). Musculoskeletal modeling addresses the muscle redundancy problem by identifying an optimal set of muscle activations that can provide the necessary forces and torques to reproduce an experimentally measured motion (Crowninshield and Brand, 1981; Rasmussen et al., 2001; Andersen, 2021). The timing of the predicted muscle contributions for both walking modalities in this study is in qualitative agreement with the EMG data reported for the same healthy cohort (Romkes and Brunner, 2007), further confirming the validity of the modeling predictions in a healthy cohort. These assumptions, however, might not always hold true when analyzing the motion of patients with aberrant motor control, such as those affected by CP (Veerkamp et al., 2019).

Romkes and Brunner (2007) observed similar gastrocnemius and tibialis anterior EMG activity between voluntary (healthy) and obligatory (pathological) unilateral toe-walking. These measured activations of gastrocnemius and soleus during toe-walking may therefore be interpreted as dictated by the biomechanics of toe-walking, rather than by the pathology alone. Such muscle activations, which have a direct correspondence with the measured kinematic pattern, can also be predicted through musculoskeletal modeling. It is also expected that similar gait patterns would lead to similar predicted activation patterns in healthy and pathological subjects. These predicted activations in pathological subjects could be interpreted as optimal and minimally required activity in order to perform a given motion. In reality, patients may also present additional muscle activity in the form of antagonist or stabilizing co-activations (Solomonow et al., 1988; Unnithan et al., 1996; Ikeda et al., 1998), which cannot be predicted adequately within the current musculoskeletal modeling framework (Mortensen et al., 2018). For instance, different activations of the rectus femoris during the swing phase were previously observed between voluntary and obligatory toe-walking (Romkes and Brunner, 2007). However, the kinetic analysis in this study was limited to the stance phase. A

better understanding of the functional role of different muscles during swing phase motion is also necessary (Arnold et al., 2007; Brunner and Rutz, 2013).

Overall, the analysis of healthy individuals provides a unique insight into the gait-pattern-related muscular demands. Nevertheless, the generalization of these findings to a pathological population should be carried out cautiously. Despite being able to mimic a typical unilateral toe-walking pattern, the gait of the healthy participants in this study was characterized by slight differences in spatiotemporal parameters, leg length discrepancy, and joint kinematics compared to obligatory toe-walking CP patients (Romkes and Brunner, 2007). Future research should aim at investigating gait data of actual toe-walking patients characterized by different neuromuscular conditions to confirm whether they show similar kinetic patterns and required muscular demands. Other commonly-observed pathological gait patterns and deviations (Winters et al., 1987; Rodda and Graham, 2001) may also present altered kinetic strategies (Steele et al., 2013) and should therefore be investigated further in addition to toe-walking.

The modeling framework developed in this study was based on 3-dimensional optical motion-capture gait data and an accurate 3-dimensional geometrical representation of the lower-limb based on cadaveric data (Carbone et al., 2015; De Pieri et al., 2018). However, due to the reduced number of markers on the foot segment, the motions of the ankle joint complex were simplified by neglecting subtalar inversion and eversion, which could affect the prediction of muscle activations (Jinha et al., 2006). Additionally, bone morphology variability in the transversal and frontal planes could also affect the prediction of muscle activations and forces (Passmore et al., 2018; Kainz et al., 2020; Martelli et al., 2020; De Pieri et al., 2021; Modenese et al., 2021; Veerkamp et al., 2021).

The lower-limb muscles were modeled as Hill-type actuators (Heinen et al., 2016) characterized by a muscle strength that followed force-length and force-velocity relationships (Hill, 1938; Zajac, 1989; Heinen et al., 2016; Andersen, 2021). Previous work underlined the importance of accounting for force-length relationships as a result of non-optimal contractile conditions associated with altered joint positions when toe-walking (Neptune et al., 2007). Specifically, the ankle plantarflexors are shortened during toe-walking and present, therefore, a reduced force-generating capacity (Herman and Bragin, 1967; Hoy et al., 1990; Perry et al., 2003). Patients with spasticity, prolonged equinus postures, and/or fixed muscular contractures may also present alteration of the underlying muscle morphology and intrinsic mechanical properties (Tardieu et al., 1982; Delp, 2003; Weidensteiner et al., 2021), even though it was shown that children with diplegic CP were able to generate maximum ankle torques at similar joint angles (Engsberg et al., 2000; Neptune et al., 2007). Therefore, restoring a more optimal foot and ankle position, as during heel-to-toe gait, may lead to improvements in muscle functionality and strength. On the other hand, muscle weakness is a commonly observed symptom in pathological populations (Hanssen et al., 2021) which can lead to inefficient and compensatory activations of other muscles, thus increasing the overall energetic cost of walking (van der Krogt et al., 2012). While the muscle strength of the participants in this study could be considered unimpaired, accounting for subject-specific scaling of muscle strength and mechanical properties may play a more important role in pathological populations (Kainz et al., 2018; Vandekerckhove et al., 2021).

The definition of the support moment as the weighted sum of the lower-limb joints sagittal extensive moments was derived from the mechanical interpretation provided by A.L. Hof (Hof, 2000) rather than the original formulation by D. Winter (Winter, 1980). According to this definition, the support moment counteracts the moment generated by the vertical component of the GRF times knee eccentricity and thus prevents the collapse of the knee (Hof, 2000). The comparison between the support moment and the vertical GRF moment showed good agreement for both walking modalities, with a similar overall trend and statistically significant differences limited to heel strike and pre-swing. This strengthens the interpretation that the support moment counteracts the external forces that would flex the knee. A higher support moment during toe-walking compared to normal walking indicates an overall higher muscular effort required when walking on the toes, as suggested by previous EMG analyses (Rose et al., 1999; Perry et al., 2003). It has to be mentioned that **Eqs 2**, **3** was derived under the approximation of equal shank and thigh lengths and while assuming massless legs (Hof, 2000). Neglecting the inertial contributions to the joint moments might therefore have affected the accuracy of the identity between the support moment and the moment produced by the external force. For more dynamic motions, such as running and jumping, this model might no longer be valid (Hof, 2000). The self-selected walking speed and the foot-floor inclination angle may further influence the resulting balance of forces and the predicted muscle contributions. This analysis was limited to the sagittal plane. Frontal plane balance and mediolateral stability are fundamental aspects of any support and locomotion strategy (Pandy et al., 2010). The lack of trunk markers did not allow to identify support strategies associated with upper-body control (Wyers et al., 2021). The control of the contralateral limb could also play an important role in forward propulsion while maintaining stability (Bovonsunthonchai et al., 2012). Nevertheless, the support moment can serve as a synthetic parameter to identify inefficient gait patterns and quantify the overall muscular demands associated with walking in pathological populations (Holsgaard-Larsen et al., 2019; Wyers et al., 2021).

The relationship between the progression moment M_P, defined as the difference between hip and ankle extensive moments, and the moment generated by the transversal GRF component (F_T) times the distance between hip and ankle (p) was also further evaluated. A good agreement between these two quantities was found for both walking modalities. This suggests that the forces acting transversally to the stance leg are counteracted by muscular contributions around the ankle and the hip, and not around the knee, as already suggested by Hof (2000). During toe-walking, altered activation of ankle and hip muscles is also required to maintain a force balance

transversally to the leg axis. The relationship between these altered muscle activation patterns counteracting transversal forces during gait and different balance strategies, known from postural analyses, should be further evaluated (Horak and Nashner, 1986).

Muscle-induced acceleration analysis is another computational approach that can reveal how much each muscle supports the weight of the body and contributes to a forward acceleration during walking (Neptune et al., 2001; Neptune et al., 2004; Arnold et al., 2005; Liu et al., 2006; Sasaki et al., 2008; Hamner and Delp, 2013; Steele et al., 2013; Uchida and Delp, 2021). In addition to calculating the muscle-induced accelerations on the body center of mass, Neptune et al. (Neptune et al., 2001) computed the accelerations that the lower-limb muscles induce around the knee joint during walking. They observed that the vasti were the main contributors to knee stability during early stance while the rectus contributed towards terminal ST. The gastrocnemius induced the knee into flexion around mid-stance, while the soleus was the only muscle that provided knee stability throughout single-leg stance. These observations are in line with the muscle contributions to the support moment during normal walking presented in this study, further indicating that the support moment should be interpreted with a focus on knee stability rather than center of mass acceleration. The knee-extending effect of the triceps surae was previously explained through dynamic coupling (Zajac and Gordon, 1989; Uchida and Delp, 2021). This effect is clinically known as plantar flexion—knee extension couple (Gage, 1995; Brunner and Rutz, 2013; Sangeux et al., 2015). While the soleus causes an extension of the knee by accelerating the shank backwards (Anderson, 2006), the gastrocnemius can induce either a net knee flexion or extension, depending on ankle and knee positions (Zajac, 1993; Uchida and Delp, 2021). The analysis of the soleus contribution to the support moment confirmed an overall net knee-extensive activity for both walking modalities. On the other hand, the gastrocnemius worked as a net knee flexor during normal walking while it provided a small extensive contribution when walking on the toes. Neptune et al. (Neptune et al., 2001) further suggested that impaired soleus activity would require compensatory mechanisms to prevent the knee from collapsing, most probably through prolonged activation of the vasti, in agreement with clinical observations (Murray et al., 1978; Sutherland et al., 1980). The analysis of the muscle contributions to the individual joint moments and the support moment confirmed the important role of the vasti.

Nevertheless, the physical meaning of the muscle contributions determined through induced-acceleration analysis is not well-defined and should be interpreted carefully (Chen, 2006). The support and the progress moment definitions used in this study were also derived from simplified force equilibrium equations. While this study provides an intuitive interpretation of muscle forces as counteracting external forces to provide a net force and moment balance, conclusions about muscle functionality should also be drawn with caution in light of the previously-stated limitations. Further comparisons between support moment and induced-acceleration analyses of toe-walking are required to elucidate the physical meaning of the outcome measures of both analyses. Simulation frameworks able to predict *de novo* kinematics based on a mathematical model of the neuro-musculoskeletal system may overcome such limitations. These novel computational tools could better clarify muscle functionality by highlighting causal relationships between muscle characteristics or surgical intervention and the resulting overall motion pattern (Geijtenbeek, 2019; De Groote and Falisse, 2021; K.; Veerkamp et al., 2021).

The muscular demands and joint loads experienced during different motions and activities of daily living should also be the focus of further studies. In particular, sports activities that involve repetitive forefoot contact, such as running (Besier et al., 2009; Fredericson and Misra, 2012; Neal et al., 2016), jumping (Ferretti et al., 1983; Lian et al., 2017), or ballet (Prisk et al., 2008; Smith et al., 2015; Sobrino et al., 2015), may also lead to overuse injuries, such as patellofemoral pain syndrome, patellar tendonitis, Achilles tendonitis, and forefoot injuries. Similarly to toe-walking, the use of high-heeled shoes also leads to a plantarflexed position of the foot during walking, thus determining alterations of joint kinetics and muscle activations (Stefanyshyn et al., 2000; Simonsen et al., 2012).

CONCLUSION

Musculoskeletal modeling allows investigating the kinetic requirements placed on individual muscles in association with a specific kinematic pattern, such as toe-walking. Walking on the toes, compared to a normal heel-to-toe gait pattern, induces altered kinetic balances at each joint level, thus determining functional adaptations for most lower-limb muscles, as shown in the analysis of a cohort of healthy volunteers mimicking a unilateral toe-walking pattern. Overall, the analysis of healthy individuals provides a unique insight on the muscular demands solely related to the specific gait pattern, independently of any underlying neuromuscular control disorder. It can be expected that similar activation patterns would be predicted through musculoskeletal modeling in both healthy and pathological subjects with similar gait patterns. Modeling predictions can be interpreted as the most optimal activation pattern required from the lower-limb muscles in order to walk in a specific manner. While a generalization of these conclusions to pathological populations should still be done cautiously, the method presented in this study has the potential to provide meaningful information for the clinical management of conditions characterized by altered gait patterns.

The support moment for instance can serve as a synthetic parameter to quantify the overall muscular demands associated with specific gait patterns. A higher support moment during toe-walking indicates an overall higher muscular effort necessary to maintain stance limb stability and prevent the collapse of the knee. Higher muscular demands during gait may lead to fatigue, pain, and reduced quality of life. Musculoskeletal modeling predictions suggest that toe-walking is indeed associated with significantly larger muscle forces exerted by the quadriceps to the patella, and prolonged force transmission through the Achilles tendon during the stance phase. The restoration of a normal heel-

to-toe gait pattern may improve muscle functionality and gait efficiency, while reducing potential long-term adverse consequences, such as knee extensor overload. Optimal treatment options should therefore account for muscular demands and potential overloads associated with specific compensatory mechanisms.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusion of this article will be made available by the authors without undue reservation.

ETHICS STATEMENT

The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

EDP contributed to study conceptualization, study design, method development, software, data curation, data visualization, data analysis, data interpretation and writing. JR contributed to study conceptualization, data acquisition, data curation, data interpretation and writing. CW contributed to study design, method development, software, data interpretation and writing. RB and EV contributed to study conceptualization, study design, data interpretation and writing. All the authors contributed to the article and approved the submitted version.

FUNDING

EDP was partially funded by the University of Basel Research Fund for Excellent Junior Researchers.

REFERENCES

Alriksson-Schmidt, A., and Hägglund, G. (2016). Pain in Children and Adolescents with Cerebral Palsy: a Population-based Registry Study. *Acta Paediatr.* 105 (6), 665–670. doi:10.1111/APA.13368

Andersen, M. S., Damsgaard, M., and Rasmussen, J. (2009). Kinematic Analysis of Over-determinate Biomechanical Systems. *Comp. Methods Biomech. Biomed. Eng.* 12 (4), 371–384. doi:10.1080/10255840802459412

Andersen, M. S. (2021). "Introduction to Musculoskeletal Modelling," in *Computational Modelling of Biomechanics and Biotribology in the Musculoskeletal System* (Elsevier), 41–80. doi:10.1016/b978-0-12-819531-4.00004-3

Anderson, F. (2006). "Simulation of Walking," in *Human Walking* (Lippincott Williams & Wilkins), 195–210.

Arnold, A. S., Anderson, F. C., Pandy, M. G., and Delp, S. L. (2005). Muscular Contributions to Hip and Knee Extension during the Single Limb Stance Phase of normal Gait: a Framework for Investigating the Causes of Crouch Gait. *J. Biomech.* 38 (11), 2181–2189. doi:10.1016/J.JBIOMECH.2004.09.036

Arnold, A. S., Thelen, D. G., Schwartz, M. H., Anderson, F. C., and Delp, S. L. (2007). Muscular Coordination of Knee Motion during the Terminal-Swing Phase of normal Gait. *J. Biomech.* 40 (15), 3314–3324. doi:10.1016/J.JBIOMECH.2007.05.006

Balaban, B., and Tok, F. (2014). Gait Disturbances in Patients with Stroke. *PM&R* 6 (7), 635–642. doi:10.1016/J.PMRJ.2013.12.017

Balemans, A. C. J., van Wely, L., Becher, J. G., and Dallmeijer, A. J. (2015). Longitudinal Relationship Among Physical Fitness, Walking-Related Physical Activity, and Fatigue in Children with Cerebral Palsy. *Oxford Acad.* 95 (7), 996–1005. doi:10.2522/PTJ.20140270

Bertsch, C., Unger, H., Winkelmann, W., and Rosenbaum, D. (2004). Evaluation of Early Walking Patterns from Plantar Pressure Distribution Measurements. First Year Results of 42 childrenGait & Posture. *Gait & Posture* 19 (3), 235–242. doi:10.1016/S0966-6362(03)00064-X

Besier, T. F., Fredericson, M., Gold, G. E., Beaupré, G. S., and Delp, S. L. (2009). Knee Muscle Forces during Walking and Running in Patellofemoral Pain Patients and Pain-free Controls. *J. Biomech.* 42 (7), 898–905. doi:10.1016/J.JBIOMECH.2009.01.032

Booth, A. T. C., Buizer, A. I., Meyns, P., Oude Lansink, I. L. B., Steenbrink, F., and van der Krogt, M. M. (2018). The Efficacy of Functional Gait Training in Children and Young Adults with Cerebral Palsy: a Systematic Review and Meta-Analysis. *Dev. Med. Child. Neurol.* 60 (9), 866–883. doi:10.1111/DMCN.13708

Boudarham, J., Roche, N., Pradon, D., Bonnyaud, C., Bensmail, D., and Zory, R. (2013). Variations in Kinematics during Clinical Gait Analysis in Stroke Patients. *PLoS ONE* 8 (6), e66421. doi:10.1371/JOURNAL.PONE.0066421

Bovonsunthonchai, S., Hiengkaew, V., Vachalathiti, R., Vongsirinavarat, M., and Tretriluxana, J. (2012). Effect of Speed on the Upper and Contralateral Lower Limb Coordination during Gait in Individuals with Stroke. *Kaohsiung J. Med. Sci.* 28 (12), 667–672. doi:10.1016/J.KJMS.2012.04.036

Brunner, R., and Rutz, E. (2013). Biomechanics and Muscle Function during Gait. *J. Children's Orthopaedics* 7 (5), 367–371. doi:10.1007/s11832-013-0508-510.1007/S11832-013-0508-5

Brunner, R., Taylor, W. R., and Visscher, R. M. S. (2021). Restoration of Heel-Toe Gait Patterns for the Prevention of Asymmetrical Hip Internal Rotation in Patients with Unilateral Spastic Cerebral Palsy. *Children* 88 (9), 773773. doi:10.3390/CHILDREN8090773

Carbone, V., Fluit, R., Pellikaan, P., van der Krogt, M. M., Janssen, D., Damsgaard, M., et al. (2015). TLEM 2.0 - A Comprehensive Musculoskeletal Geometry Dataset for Subject-specific Modeling of Lower Extremity. *J. Biomech.* 48 (5), 734–741. doi:10.1016/j.jbiomech.2014.12.034

Chen, G. (2006). Induced Acceleration Contributions to Locomotion Dynamics Are Not Physically Well Defined. *Gait & Posture* 23 (1), 37–44. doi:10.1016/J.GAITPOST.2004.11.016

Crowninshield, R. D., and Brand, R. A. (1981). A Physiologically Based Criterion of Muscle Force Prediction in Locomotion. *J. Biomech.* 14 (11), 793–801. doi:10.1016/0021-9290(81)90035-X

Damiano, D. L., and Abel, M. F. (1998). Functional Outcomes of Strength Training in Spastic Cerebral Palsy. *Arch. Phys. Med. Rehabil.* 79 (2), 119–125. doi:10.1016/S0003-9993(98)90287-8

Damsgaard, M., Rasmussen, J., Christensen, S. T., Surma, E., and de Zee, M. (2006). Analysis of Musculoskeletal Systems in the AnyBody Modeling System. *Simulation Model. Pract. Theor.* 14 (8), 1100–1111. doi:10.1016/j.simpat.2006.09.001

Davids, J. R., Foti, T., Dabelstein, J., and Bagley, A. (1999). Voluntary (Normal) versus Obligatory (Cerebral Palsy) Toe-Walking in Children: A Kinematic, Kinetic, and Electromyographic Analysis. *J. Pediatr. Orthopaedics* 19 (4), 461–469. doi:10.1097/01241398-199907000-00008

De Groote, F., and Falisse, A. (2021). Perspective on Musculoskeletal Modelling and Predictive Simulations of Human Movement to Assess the Neuromechanics of Gait. *Proc. R. Soc. B.* 288. doi:10.1098/RSPB.2020.2432

De Pieri, E., Friesenbichler, B., List, R., Monn, S., Casartelli, N. C., Leunig, M., et al. (2021). Subject-Specific Modeling of Femoral Torsion Influences the Prediction of Hip Loading during Gait in Asymptomatic Adults. *Front. Bioeng. Biotechnol.* 9, 551. doi:10.3389/fbioe.2021.679360

De Pieri, E., Lund, M. E., Gopalakrishnan, A., Rasmussen, K. P., Lunn, D. E., and Ferguson, S. J. (2018). Refining Muscle Geometry and Wrapping in the TLEM 2 Model for Improved Hip Contact Force Prediction. *PLoS ONE* 13 (9), e0204109. doi:10.1371/journal.pone.0204109

De Pieri, E., Lunn, D. E., Chapman, G. J., Rasmussen, K. P., Ferguson, S. J., and Redmond, A. C. (2019). Patient Characteristics Affect Hip Contact Forces during Gait. *Osteoarthritis and Cartilage* 27 (6), 895–905. doi:10.1016/j.joca.2019.01.016

Dean, J. C., and Kautz, S. A. (2015). Foot Placement Control and Gait Instability Among People with Stroke. *J. Rehabil. Res. Dev.* 52 (5), 577–590. doi:10.1682/JRRD.2014.09.0207

Delp, S. L. (2003). *What Causes Increased Muscle Stiffness in Cerebral Palsy?* 27. United States: Muscle & nerve, 131–132. doi:10.1002/mus.10284

Derrick, T. R., van den Bogert, A. J., Cereatti, A., Dumas, R., Fantozzi, S., and Leardini, A. (2020). ISB Recommendations on the Reporting of Intersegmental Forces and Moments during Human Motion Analysis. *J. Biomech.* 99, 109533. doi:10.1016/j.jbiomech.2019.109533

Eken, M. M., Braendvik, S. M., Bardal, E. M., Houdijk, H., Dallmeijer, A. J., and Roeleveld, K. (2019). Lower Limb Muscle Fatigue during Walking in Children with Cerebral Palsy. *Dev. Med. Child. Neurol.* 61 (2), 212–218. doi:10.1111/DMCN.14002

Engelbert, R., Gorter, J. W., Uiterwaal, C., van de Putte, E., and Helders, P. (2011). Idiopathic Toe-Walking in Children, Adolescents and Young Adults: a Matter of Local or Generalised Stiffness? *BMC Musculoskelet. Disord.* 12 (1), 1–8. doi:10.1186/1471-2474-12-61

Engsberg, J. R., Ross, S. A., Olree, K. S., and Park, T. S. (2000). Ankle Spasticity and Strength in Children with Spastic Diplegic Cerebral Palsy. *Dev. Med. Child Neurol.* 42 (1), 42–47. doi:10.1111/J.1469-8749.2000.TB00023.X

Erdemir, A., McLean, S., Herzog, W., and van den Bogert, A. J. (2007). Model-based Estimation of Muscle Forces Exerted during Movements. *Clin. Biomech.* 22 (2), 131–154. doi:10.1016/j.clinbiomech.2006.09.005

Ferretti, A., Ippolito, E., Mariani, P., and Puddu, G. (1983). Jumper's Knee. *Am. J. Sports Med.* 11 (2), 58–62. doi:10.1177/036354658301100202

Fock, J., Galea, M. P., Stillman, B. C., Rawicki, B., and Clark, M. (2009). Functional Outcome Following Botulinum Toxin A Injection to Reduce Spastic Equinus in Adults with Traumatic Brain Injury. *Brain Inj.* 18 (1), 57–63. doi:10.1080/02699050310001494 98

Fredericson, M., and Misra, A. K. (2007). Epidemiology and Aetiology of Marathon Running Injuries. *Sports MedicineSpringer* 3737 (4), 4437–4439. doi:10.2165/00007256-200737040-00043

Friston, K. J., Holmes, A. P., Worsley, K. J., Poline, J.-P., Frith, C. D., and Frackowiak, R. S. J. (1994). Statistical Parametric Maps in Functional Imaging: A General Linear Approach. *Hum. Brain Mapp.* 2 (4), 189–210. doi:10.1002/hbm.460020402

Gage, J. R. (1995). The Clinical Use of Kinetics for Evaluation of Pathologic Gait in Cerebral Palsy. *Instr. Course Lect* 44, 507–515.

Geijtenbeek, T. (2019). SCONE: Open Source Software for Predictive Simulation of Biological Motion. *Joss* 4 (38), 1421. doi:10.21105/JOSS.01421

Graham, H. K., Rosenbaum, P., Paneth, N., Dan, B., Lin, J.-P., Damiano, D. L., et al. (2016). Cerebral Palsy. *Nat. Rev. Dis. Primers* 2, 1–25. doi:10.1038/nrdp.2015.82

Hallemans, A., De Clercq, D., Dongen, S. V., and Aerts, P. (2006). Changes in Foot-Function Parameters during the First 5 Months after the Onset of Independent Walking: a Longitudinal Follow-Up Study. *Gait & Posture* 23 (2), 142–148. doi:10.1016/J.GAITPOST.2005.01.003

Hamner, S. R., and Delp, S. L. (2013). Muscle Contributions to Fore-Aft and Vertical Body Mass center Accelerations over a Range of Running Speeds. *J. Biomech.* 46 (4), 780–787. doi:10.1016/J.JBIOMECH.2012.11.024

Hanssen, B., Peeters, N., Vandekerckhove, I., De Beukelaer, N., Bar-On, L., Molenaers, G., et al. (2021). The Contribution of Decreased Muscle Size to Muscle Weakness in Children with Spastic Cerebral Palsy. *Front. Neurol.* 12, 692582. doi:10.3389/FNEUR.2021.692582

Heinen, F., Lund, M. E., Rasmussen, J., and de Zee, M. (2016)., 230. London, England, 976–984. doi:10.1177/095441191665989410.1177/0954411916659894Muscle-tendon Unit Scaling Methods of Hill-type Musculoskeletal Models: An Overview*Proc. Inst. Mech. Eng. H*10

Herman, R., and Bragin, S. J. (1967). Function of the Gastrocnemius and Soleus Muscles: A Preliminary Study in the Normal Human Subject. *Oxford Acad.* 47 (2), 105–113. doi:10.1093/PTJ/47.2.105

Hill, A. V. (1938). The Heat of Shortening and the Dynamic Constants of Muscle. *Ser. B-Biological Sci.* 126 (843), 136–195.

Hof, A. L. (2000). On the Interpretation of the Support Moment. *Gait & Posture* 12 (3), 196–199. doi:10.1016/S0966-6362(00)00084-9

Holsgaard-Larsen, A., Thorlund, J. B., Blackmore, T., and Creaby, M. W. (2019). Changes in Total Lower Limb Support Moment in Middle-Aged Patients Undergoing Arthroscopic Partial Meniscectomy - A Longitudinal Observational Cohort Study. *The Knee* 26 (3), 595–602. doi:10.1016/J.KNEE.2019.04.004

Horak, F. B., and Nashner, L. M. (1986). Central Programming of Postural Movements: Adaptation to Altered Support-Surface Configurations. *J. Neurophysiol.* 55 (6), 1369–1381. doi:10.1152/jn.1986.55.6.136910.1152/JN.1986.55.6.1369

Hoy, M. G., Zajac, F. E., and Gordon, M. E. (1990). A Musculoskeletal Model of the Human Lower Extremity: The Effect of Muscle, Tendon, and Moment Arm on the Moment-Angle Relationship of Musculotendon Actuators at the Hip, Knee, and Ankle. *J. Biomech.* 23 (2), 157–169. doi:10.1016/0021-9290(90)90349-8

Ikeda, A. J., Abel, M. F., Granata, K. P., and Damiano, D. L. (1998). Quantification of Cocontraction in Spastic Cerebral Palsy. *Electromyogr. Clin. Neurophysiol.* 38 (8), 497–504.

Imani Nejad, Z., Khalili, K., Hosseini Nasab, S. H., Schütz, P., Damm, P., Trepczynski, A., et al. (2020). The Capacity of Generic Musculoskeletal Simulations to Predict Knee Joint Loading Using the CAMS-Knee Datasets. *Ann. Biomed. Eng.* 48 (4), 1430–1440. doi:10.1007/S10439-020-02465-5/FIGURES/6

Jahnsen, R., Villien, L., Aamodt, G., Stanghelle, J., and Holm, I. (2004). Musculoskeletal Pain in Adults with Cerebral Palsy Compared with the General Population. *J. Rehabil. Med.* 36 (2), 78–84. doi:10.1080/16501970310018305

Jinha, A., Ait-Haddou, R., and Herzog, W. (2006). Predictions of Co-contraction Depend Critically on Degrees-Of-freedom in the Musculoskeletal Model. *J. Biomech.* 39 (6), 1145–1152. doi:10.1016/J.JBIOMECH.2005.03.001

Kadaba, M. P., Ramakrishnan, H. K., and Wootten, M. E. (1990). Measurement of Lower Extremity Kinematics during Level Walking. *J. Orthop. Res.* 8 (3), 383–392. doi:10.1002/jor.1100080310

Kainz, H., Goudriaan, M., Falisse, A., Huenaerts, C., Desloovere, K., De Groote, F., et al. (2018). The Influence of Maximum Isometric Muscle Force Scaling on Estimated Muscle Forces from Musculoskeletal Models of Children with Cerebral Palsy. *Gait & Posture* 65, 213–220. doi:10.1016/J.GAITPOST.2018.07.172

Kainz, H., Killen, B. A., Wesseling, M., Perez-Boerema, F., Pitto, L., Garcia Aznar, J. M., et al. (2020). A Multi-Scale Modelling Framework Combining Musculoskeletal Rigid-Body Simulations with Adaptive Finite Element Analyses, to Evaluate the Impact of Femoral Geometry on Hip Joint Contact Forces and Femoral Bone Growth. *PLoS ONE* 15 (7 July), e0235966. doi:10.1371/journal.pone.0235966

Kalen, V., Adler, N., and Bleck, E. E. (1986). Electromyography of Idiopathic Toe Walking. *J. Pediatr. Orthopaedics* 6 (1), 31–33. doi:10.1097/01241398-198601000-00006

Kelly, I. P., Jenkinson, A., Stephens, M., and O'Brien, T. (1997). The Kinematic Patterns of Toe-Walkers. *J. Pediatr. Orthopaedics* 17 (4), 478–480. doi:10.1097/01241398-199707000-00013

Kerrigan, D. C., Riley, P. O., Rogan, S., and Burke, D. T. (2000). Compensatory Advantages of Toe Walking. *Arch. Phys. Med. Rehabil.* 81 (1), 38–44. doi:10.1016/S0003-9993(00)90219-3

Kinsella, S., and Moran, K. (2008). Gait Pattern Categorization of Stroke Participants with Equinus Deformity of the Foot. *Gait & Posture* 27 (1), 144–151. doi:10.1016/J.GAITPOST.2007.03.008

Lian, Ø. B., Engebretsen, L., and Bahr, R. (2017). Prevalence of Jumper's Knee Among Elite Athletes from Different Sports: A Cross-Sectional Study. *Am. J. Sports Med.* 33 (4), 561–567. doi:10.1177/0363546504270454

Liu, M. Q., Anderson, F. C., Pandy, M. G., and Delp, S. L. (2006). Muscles that Support the Body Also Modulate Forward Progression during Walking. *J. Biomech.* 39 (14), 2623–2630. doi:10.1016/J.JBIOMECH.2005.08.017

Lund, M. E., Andersen, M. S., de Zee, M., and Rasmussen, J. (2015). Scaling of Musculoskeletal Models from Static and Dynamic Trials. *Int. Biomech.* 2 (1), 1–11. doi:10.1080/23335432.2014.993706

Lund, M. E., de Zee, M., Andersen, M. S., and Rasmussen, J. (2012). On Validation of Multibody Musculoskeletal Models. *Proc. Inst. Mech. Eng. H* 226 (2), 82–94. doi:10.1177/0954411911431516

Lund, M., Rasmussen, J., and Andersen, M. (2019). AnyPyTools: A Python Package for Reproducible Research with the AnyBody Modeling System. *Joss* 4 (33), 1108. doi:10.21105/joss.01108

Lundh, S., Nasic, S., and Riad, J. (2018). Fatigue, Quality of Life and Walking Ability in Adults with Cerebral Palsy. *Gait & Posture* 61, 1–6. doi:10.1016/J.GAITPOST.2017.12.017

Lunn, D. E., De Pieri, E., Chapman, G. J., Lund, M. E., Redmond, A. C., and Ferguson, S. J. (2020). Current Preclinical Testing of New Hip Arthroplasty Technologies Does Not Reflect Real-World Loadings: Capturing Patient-specific and Activity-Related Variation in Hip Contact Forces. *The J. Arthroplasty* 35 (3), 877–885. doi:10.1016/j.arth.2019.10.006

Manca, M., Ferraresi, G., Cosma, M., Cavazzuti, L., Morelli, M., and Benedetti, M. G. (20142014). "Gait Patterns in Hemiplegic Patients with Equinus Foot Deformity," in *BioMed Research International*. Editor G. Morone, 2014, 1–7. doi:10.1155/2014/939316

Marra, M. A., Vanheule, V., Fluit, R., Koopman, B. H. F. J. M., Rasmussen, J., Verdonschot, N., et al. (2015). A Subject-specific Musculoskeletal Modeling Framework to Predict *In Vivo* Mechanics of Total Knee Arthroplasty. *ASME* 137 (2), 020904. doi:10.1115/1.4029258

Martelli, S., Sancisi, N., Conconi, M., Pandy, M. G., Kersh, M. E., Parenti-Castelli, V., et al. (2020). The Relationship between Tibiofemoral Geometry and Musculoskeletal Function during normal Activity. *Gait & Posture* 80, 374–382. doi:10.1016/J.GAITPOST.2020.06.022

McGinley, J. L., Dobson, F., Ganeshalingam, R., Shore, B. J., Rutz, E., and Graham, H. K. (2012). Single-event Multilevel Surgery for Children with Cerebral Palsy: a Systematic Review. *Dev. Med. Child. Neurol.* 54 (2), 117–128. doi:10.1111/J.1469-8749.2011.04143.X

Modenese, L., Barzan, M., and Carty, C. P. (2021). Dependency of Lower Limb Joint Reaction Forces on Femoral Version. *Gait & Posture* 88, 318–321. doi:10.1016/J.GAITPOST.2021.06.014

Morgan, P., and McGinley, J. (2013). Gait Function and Decline in Adults with Cerebral Palsy: a Systematic Review. *Disabil. Rehabil.* 36 (1), 1–9. doi:10.3109/09638288.2013.77535910.3109/09638288.2013.775359

Mortensen, J., Trkov, M., and Merryweather, A. (2018). Exploring Novel Objective Functions for Simulating Muscle Coactivation in the Neck. *J. Biomech.* 71, 127–134. doi:10.1016/J.JBIOMECH.2018.01.030

Murray, M. P., Guten, G. N., Sepic, S. B., Gardner, G. M., and Baldwin, J. M. (1978). Function of the Triceps Surae during Gait. Compensatory Mechanisms for Unilateral Loss. *The J. Bone Jt. SurgeryAmerican volume* 60 (4), 473–476. doi:10.2106/00004623-197860040-00007

Neal, B. S., Barton, C. J., Gallie, R., O'Halloran, P., and Morrissey, D. (2016). Runners with Patellofemoral Pain Have Altered Biomechanics Which Targeted Interventions Can Modify: A Systematic Review and Meta-Analysis. *Gait & Posture* 45, 69–82. doi:10.1016/J.GAITPOST.2015.11.018

Neptune, R. R., Burnfield, J. M., and Mulroy, S. J. (2007). The Neuromuscular Demands of Toe Walking: A Forward Dynamics Simulation Analysis. *J. Biomech.* 40 (6), 1293–1300. doi:10.1016/J.JBIOMECH.2006.05.022

Neptune, R. R., Kautz, S. A., and Zajac, F. E. (2001). Contributions of the Individual Ankle Plantar Flexors to Support, Forward Progression and Swing Initiation during Walking. *J. Biomech.* 34 (11), 1387–1398. doi:10.1016/S0021-9290(01)00105-1

Neptune, R. R., Zajac, F. E., and Kautz, S. A. (2004). Muscle Force Redistributes Segmental Power for Body Progression during Walking. *Gait & Posture* 19 (2), 194–205. doi:10.1016/S0966-6362(03)00062-6

Opheim, A., Jahnsen, R., Olsson, E., and Stanghelle, J. K. (2009). Walking Function, Pain, and Fatigue in Adults with Cerebral Palsy: a 7-year Follow-Up Study. *Dev. Med. Child Neurol.* 51 (5), 381–388. doi:10.1111/J.1469-8749.2008.03250.X

Palmer, F. B., Shapiro, B. K., Wachtel, R. C., Allen, M. C., Hiller, J. E., Harryman, S. E., et al. (2010). The Effects of Physical Therapy on Cerebral Palsy. A Controlled Trial in Infants with Spastic Diplegia. *N. Engl. J. Med.* 318 (13), 803–808. doi:10.1056/NEJM198803131813021056/NEJM198803313181302

Pandy, M. G., Lin, Y.-C., and Kim, H. J. (2010). Muscle Coordination of Mediolateral Balance in normal Walking. *J. Biomech.* 43 (11), 2055–2064. doi:10.1016/J.JBIOMECH.2010.04.010

Passmore, E., Graham, H. K., Pandy, M. G., and Sangeux, M. (2018). Hip- and Patellofemoral-Joint Loading during Gait Are Increased in Children with Idiopathic Torsional Deformities. *Gait & Posture* 63, 228–235. doi:10.1016/j.gaitpost.2018.05.003

Pataky, T. C. (2012). One-dimensional Statistical Parametric Mapping in Python. *Comp. Methods Biomech. Biomed. Eng.* 15 (3), 295–301. doi:10.1080/10255842.2010.527837

Pataky, T. C., Vanrenterghem, J., and Robinson, M. A. (2015). Zero- vs. One-Dimensional, Parametric vs. Non-parametric, and Confidence Interval vs. Hypothesis Testing Procedures in One-Dimensional Biomechanical Trajectory Analysis. *J. Biomech.* 48 (7), 1277–1285. doi:10.1016/J.JBIOMECH.2015.02.051

Perry, J., Burnfield, J. M., Gronley, J. K., and Mulroy, S. J. (2003). Toe Walking: Muscular Demands at the Ankle and Knee. *Arch. Phys. Med. Rehabil.* 84 (1), 7–16. doi:10.1053/APMR.2003.50057

Prisk, V. R., O'Loughlin, P. F., and Kennedy, J. G. (2008). Forefoot Injuries in Dancers. *Clin. Sports Med.* 27 (2), 305–320. doi:10.1016/J.CSM.2007.12.005

Rasmussen, J., Damsgaard, M., and Voigt, M. (2001). Muscle Recruitment by the Min/max Criterion - a Comparative Numerical Study. *J. Biomech.* 34 (3), 409–415. doi:10.1016/S0021-9290(00)00191-3

Rethlefsen, S. A., Nguyen, D. T., Wren, T. A. L., Milewski, M. D., and Kay, R. M. (2015). Knee Pain and Patellofemoral Symptoms in Patients with Cerebral Palsy. *J. Pediatr. Orthopaedics* 35 (5), 519–522. doi:10.1097/BPO.0000000000000304

Rodda, J., and Graham, H. K. (2001). Classification of Gait Patterns in Spastic Hemiplegia and Spastic Diplegia: A Basis for a Management Algorithm. *Eur. J. Neurol.* 8 (s5), 98–108. doi:10.1046/j.1468-1331.2001.00042.x

Romkes, J., and Brunner, R. (2007). An Electromyographic Analysis of Obligatory (Hemiplegic Cerebral Palsy) and Voluntary (normal) Unilateral Toe-Walking. *Gait & Posture* 26 (4), 577–586. doi:10.1016/J.GAITPOST.2006.12.010

Rose, J., Martin, J. G., Torburn, L., Rinsky, L. A., and Gamble, J. G. (1999). Electromyographic Differentiation of Diplegic Cerebral Palsy from Idiopathic Toe Walking: Involuntary Coactivation of the Quadriceps and Gastrocnemius. *J. Pediatr. Orthopaedics* 19 (5), 677–682. doi:10.1097/01241398-199909000-00025

Sangeux, M., Rodda, J., and Graham, H. K. (2015). Sagittal Gait Patterns in Cerebral Palsy: The Plantarflexor-Knee Extension Couple index. *Gait & Posture* 41 (2), 586–591. doi:10.1016/J.GAITPOST.2014.12.019

Sasaki, K., Neptune, R. R., Burnfield, J. M., and Mulroy, S. J. (2008). Muscle Compensatory Mechanisms during Able-Bodied Toe Walking. *Gait & Posture* 27 (3), 440–446. doi:10.1016/J.GAITPOST.2007.05.012

Schlough, K., Andre, K., Owen, M., Adelstein, L., Hartford, M. C., Javier, B., et al. (2020). Differentiating between Idiopathic Toe Walking and Cerebral Palsy: A Systematic Review. *Lippincott Williams and Wilkins* 32 (1), 2–10. doi:10.1097/PEP.0000000000000659

Schwachmeyer, V., Damm, P., Bender, A., Dymke, J., Graichen, F., and Bergmann, G. (2013). *In Vivo* hip Joint Loading during post-operative Physiotherapeutic Exercises. *PloS one* 8 (10), e77807. doi:10.1371/journal.pone.0077807

Schweizer, K., Romkes, J., and Brunner, R. (2013). The Association between Premature Plantarflexor Muscle Activity, Muscle Strength, and Equinus Gait in Patients with Various Pathologies. *Res. Dev. Disabilities* 34 (9), 2676–2683. doi:10.1016/J.RIDD.2013.05.025

Seth, A., Hicks, J. L., Uchida, T. K., Habib, A., Dembia, C. L., Dunne, J. J., et al. (2018). OpenSim: Simulating Musculoskeletal Dynamics and Neuromuscular Control to Study Human and Animal Movement. *Plos Comput. Biol.* 14 (7), e1006223. doi:10.1371/JOURNAL.PCBI.1006223

Simonsen, E. B., Svendsen, M. B., Nørreslet, A., Baldvinsson, H. K., Heilskov-Hansen, T., Larsen, P. K., et al. (2012). Walking on High Heels Changes Muscle Activity and the Dynamics of Human Walking Significantly. *J. Appl. Biomech.* 28 (1), 20–28. doi:10.1123/JAB.28.1.20

Sloot, L. H., and van der Krogt, M. M. (2018). *Interpreting Joint Moments and Powers in Gait BT - Handbook of Human Motion*. Cham: Springer International Publishing, 625–643. doi:10.1007/978-3-319-14418-4_32

Smith, P. J., Gerrie, B. J., Varner, K. E., McCulloch, P. C., Lintner, D. M., and Harris, J. D. (2015). Incidence and Prevalence of Musculoskeletal Injury in Ballet. *Orthopaedic J. Sports Med.* 3 (7), 232596711559262. doi:10.1177/232596711559262110.1177/2325967115592621

Smith, S. H. L., Coppack, R. J., van den Bogert, A. J., Bennett, A. N., and Bull, A. M. J. (2021). Review of Musculoskeletal Modelling in a Clinical Setting: Current Use in Rehabilitation Design, Surgical Decision Making and Healthcare Interventions. *Clin. Biomech.* 83, 105292. doi:10.1016/J.CLINBIOMECH.2021.105292

Sobrino, F. J., de la Cuadra, C., and Guillén, P. (2015). Overuse Injuries in Professional Ballet. *Orthopaedic J. Sports Med.* 3 (6), 232596711559011. doi:10.1177/2325967115590114

Solan, M. C., Kohls-Gatzoulis, J., and Stephens, M. M. (2010). Idiopathic Toe Walking and Contractures of the Triceps Surae. *Foot Ankle Clin.* 15 (2), 297–307. doi:10.1016/J.FCL.2010.01.002

Solomonow, M., Baratta, R., Zhou, B. H., and D'Ambrosia, R. (1988). Electromyogram Coactivation Patterns of the Elbow Antagonist Muscles during Slow Isokinetic Movement. *Exp. Neurol.* 100 (3), 470–477. doi:10.1016/0014-4886(88)90032-5

Steele, K. M., Rozumalski, A., and Schwartz, M. H. (2015). Muscle Synergies and Complexity of Neuromuscular Control during Gait in Cerebral Palsy. *Dev. Med. Child. Neurol.* 57 (12), 1176–1182. doi:10.1111/dmcn.12826

Steele, K. M., Seth, A., Hicks, J. L., Schwartz, M. H., and Delp, S. L. (2013). Muscle Contributions to Vertical and Fore-Aft Accelerations Are Altered in Subjects with Crouch Gait. *Gait & Posture* 38 (1), 86–91. doi:10.1016/J.GAITPOST.2012.10.019

Stefanyshyn, D. J., Nigg, B. M., Fisher, V., O'Flynn, B., and Liu, W. (2000). The Influence of High Heeled Shoes on Kinematics, Kinetics, and Muscle EMG of Normal Female Gait. *J. Appl. Biomech.* 16 (3), 309–319. doi:10.1123/JAB.16.3.309

Strobl, W., Theologis, T., Brunner, R., Kocer, S., Viehweger, E., Pascual-Pascual, I., et al. (2015). Best Clinical Practice in Botulinum Toxin Treatment for Children with Cerebral Palsy. *Toxins* 7 (5), 1629–1648. doi:10.3390/toxins7051629

Sun, D., Fekete, G., Baker, J. S., Mei, Q., István, B., Zhang, Y., et al. (20202020). A Pilot Study of Musculoskeletal Abnormalities in Patients in Recovery from a Unilateral Rupture-Repaired Achilles Tendon. *Ijerph* 1717 (13), 46424642. doi:10.3390/IJERPH17134642

Sutherland, D. H., Cooper, L., and Daniel, D. (1980). The Role of the Ankle Plantar Flexors in normal Walking. *J. Bone Jt. SurgeryAmerican volume* 62 (3), 354–363. doi:10.2106/00004623-198062030-00005

Sylvester, A. D., Lautzenheiser, S. G., and Kramer, P. A. (2021). A Review of Musculoskeletal Modelling of Human Locomotion. *Interf. Focus.* 11 (5), 20200060. doi:10.1098/RSFS.2020.0060

Tardieu, C., Huet de la Tour, E., Bret, M. D., and Tardieu, G. (1982). Muscle Hypoextensibility in Children with Cerebral Palsy: I. Clinical and Experimental Observations. *Arch. Phys. Med. Rehabil.* 63 (3), 97–102.

Tardieu, C., Lespargot, A., Tabary, C., and Bret, M.-D. (1989). Toe-Walking in Children with Cerebral Palsy: Contributions of Contracture and Excessive Contraction of Triceps Surae Muscle. *Oxford Acad.* 69 (8), 656–662. doi:10.1093/PTJ/69.8.656

Thelen, D. G., Lenz, A., and Hernandez, A. (2011). Measurement and Simulation of Joint Motion Induced via Biarticular Muscles during Human Walking. *Proced. IUTAM* 2, 290–296. doi:10.1016/J.PIUTAM.2011.04.026

Totah, D., Menon, M., Jones-Hershinow, C., Barton, K., and Gates, D. H. (2019). The Impact of Ankle-Foot Orthosis Stiffness on Gait: A Systematic Literature Review. *Gait & Posture* 69, 101–111. doi:10.1016/J.GAITPOST.2019.01.020

Uchida, T. K., and Delp, S. L. (2021). *Biomechanics of Movement: The Science of Sports, Robotics, and Rehabilitation*. MIT Press.

Unnithan, V. B., Dowling, J. J., Frost, G., Volpe Ayub, B., and Bar-Or, O. (1996). Cocontraction and Phasic Activity during GAIT in Children with Cerebral Palsy. *Electromyogr. Clin. Neurophysiol.* 36 (8), 487–494.

van der Krogt, M. M., Delp, S. L., and Schwartz, M. H. (2012). How Robust Is Human Gait to Muscle Weakness? *Gait & Posture* 36 (1), 113–119. doi:10.1016/j.gaitpost.2012.01.017

Vandekerckhove, I., Wesseling, M., Kainz, H., Desloovere, K., and Jonkers, I. (2021). The Effect of Hip Muscle Weakness and Femoral Bony Deformities on Gait Performance. *Gait & Posture* 83, 280–286. doi:10.1016/j.gaitpost.2020.10.022

Veerkamp, K., Kainz, H., Killen, B. A., Jónasdóttir, H., and van der Krogt, M. M. (2021). Torsion Tool: An Automated Tool for Personalising Femoral and Tibial Geometries in OpenSim Musculoskeletal Models. *J. Biomech.* 125, 110589. doi:10.1016/J.JBIOMECH.2021.110589

Veerkamp, K., Schallig, W., Harlaar, J., Pizzolato, C., Carty, C. P., Lloyd, D. G., et al. (2019). The Effects of Electromyography-Assisted Modelling in Estimating Musculotendon Forces during Gait in Children with Cerebral Palsy. *J. Biomech.* 92, 45–53. doi:10.1016/j.jbiomech.2019.05.026

Veerkamp, K., Waterval, N. F. J., Geijtenbeek, T., Carty, C. P., Lloyd, D. G., Harlaar, J., et al. (2021). Evaluating Cost Function Criteria in Predicting Healthy Gait. *J. Biomech.* 123, 110530. doi:10.1016/J.JBIOMECH.2021.110530

Vigotsky, A. D., Zelik, K. E., Lake, J., and Hinrichs, R. N. (2019). Mechanical Misconceptions: Have We Lost the "mechanics" in "sports Biomechanics"? *J. Biomech.* 93, 1–5. doi:10.1016/J.JBIOMECH.2019.07.005

Villani, C., Pappalardo, S., Meloni, C., Amorese, V., and Romanini, L. (1988). Patellofemoral Dysplasia in Infantile Cerebral Palsy. *Ital. J. Orthop. Traumatol.* 14 (2), 201–210.

Weidensteiner, C., Madoerin, P., Deligianni, X., Haas, T., Bieri, O., Akinci D'Antonoli, T., et al. (2021). Quantification and Monitoring of the Effect of Botulinum Toxin A on Paretic Calf Muscles of Children with Cerebral Palsy with MRI: A Preliminary Study. *Front. Neurol.* 12, 390. doi:10.3389/FNEUR.2021.630435

Williams, C., and Haines, T. (2015). Idiopathic Toe Walking May Impact on Quality of Life. *J. Foot Ankle Res.* 8 (Suppl. 2), O40. doi:10.1186/1757-1146-8-S2-O40

Williams, G., Morris, M. E., Schache, A., and McCrory, P. R. (2009). Incidence of Gait Abnormalities after Traumatic Brain Injury. *Arch. Phys. Med. Rehabil.* 90 (4), 587–593. doi:10.1016/J.APMR.2008.10.013

Winter, D. A. (2009). *Biomechanics and Motor Control of Human Movement*. John Wiley & Sons.

Winter, D. A. (1980). Overall Principle of Lower Limb Support during Stance Phase of Gait. *J. Biomech.* 13 (11), 923–927. doi:10.1016/0021-9290(80)90162-1

Winters, T. F., Gage, J. R., and Hicks, R. (1987). Gait Patterns in Spastic Hemiplegia in Children and Young Adults. *J. Bone Jt. Surg AmAmerican volume* 69 (3), 437–441.

Wu, G., Siegler, S., Allard, P., Kirtley, C., Leardini, A., Rosenbaum, D., et al. (2002). ISB Recommendation on Definitions of Joint Coordinate System of Various Joints for the Reporting of Human Joint Motion-Part I: Ankle, Hip, and Spine. *J. Biomech.* 35 (4), 543–548. doi:10.1016/S0021-9290(01)00222-6

Wyers, L., Verheyen, K., Ceulemans, B., Schoonjans, A.-S., Desloovere, K., Van de Walle, P., et al. (2021). The Mechanics behind Gait Problems in Patients with Dravet Syndrome. *Gait & Posture* 84, 321–328. doi:10.1016/J.GAITPOST.2020.12.029

Zajac, F. E. (1989). Muscle and Tendon: Properties, Models, Scaling, and Application to Biomechanics and Motor Control. *Crit. Rev. Biomed. Eng.* 17 (4), 359–411.

Zajac, F. E., and Gordon, M. E. (1989). Determining Muscle??s Force and Action in Multi-Articular Movement. *Exerc. Sport Sci. Rev.* 16, 187–230. doi:10.1249/00003677-198900170-00009

Zajac, F. E. (1993). Muscle Coordination of Movement: A Perspective. *J. Biomech.* 26 (Suppl. 1), 109–124. doi:10.1016/0021-9290(93)90083-Q

Zeininger, A. D., Jensen, J. L., and Shapiro, L. J. (2018). Ontogenetic Changes in Foot Strike Pattern and Calcaneal Loading during Walking in Young Children. *Gait & Posture* 59, 18–22. doi:10.1016/J.GAITPOST.2017.09.027

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors, and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Advantages of publishing in Frontiers

OPEN ACCESS
Articles are free to read for greatest visibility and readership

FAST PUBLICATION
Around 90 days from submission to decision

HIGH QUALITY PEER-REVIEW
Rigorous, collaborative, and constructive peer-review

TRANSPARENT PEER-REVIEW
Editors and reviewers acknowledged by name on published articles

Frontiers
Avenue du Tribunal-Fédéral 34
1005 Lausanne | Switzerland

Visit us: www.frontiersin.org
Contact us: frontiersin.org/about/contact

REPRODUCIBILITY OF RESEARCH
Support open data and methods to enhance research reproducibility

DIGITAL PUBLISHING
Articles designed for optimal readership across devices

FOLLOW US
@frontiersin

IMPACT METRICS
Advanced article metrics track visibility across digital media

EXTENSIVE PROMOTION
Marketing and promotion of impactful research

LOOP RESEARCH NETWORK
Our network increases your article's readership