frontiers | Frontiers in Virtual Reality

SYSTEMATIC REVIEW
published: 03 May 2022
doi: 10.3389/frvir.2022.889271

Head-Mounted Display-Based Virtual Reality and Physiological Computing for Stroke Rehabilitation: A Systematic Review

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Virtual reality (VR)-mediated rehabilitation is emerging as a useful tool for stroke survivors to recover motor function. Recent studies are showing that VR coupled with physiological computing (i.e., real-time measurement and analysis of different behavioral and psychophysiological signals) and feedback can lead to 1) more engaged and motivated patients, 2) reproducible treatments that can be performed at the comfort of the patient's home, and 3) development of new proxies of intervention outcomes and success. While such systems have shown great potential for stroke rehabilitation, an extensive review of the literature is still lacking. Here, we aim to fill this gap and conduct a systematic review of the twelve studies that passed the inclusion criteria. A detailed analysis of the papers was conducted along with a quality assessment/risk of bias evaluation of each study. It was found that the quality of the majority of the studies ranked as either good or fair. Study outcomes also showed that VR-based rehabilitation protocols coupled with physiological computing can enhance patient adherence, improve motivation, overall experience, and ultimately, rehabilitation effectiveness and faster recovery times. Limitations of the examined studies are discussed, such as small sample sizes and unbalanced male/female participant ratios, which could limit the generalizability of the obtained findings. Finally, some recommendations for future studies are given.

Keywords: stroke rehabilitation, head-mounted display (HMD), immersive virtual reality, physiological computing, feedback

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Specialty section:
This article was submitted to Virtual Reality in Medicine, a section of the journal Frontiers in Virtual Reality

Received: *04 March 2022*
Accepted: *15 April 2022*
Published: *03 May 2022*

Citation:
Amini Gougeh R and Falk TH (2022) Head-Mounted Display-Based Virtual Reality and Physiological Computing for Stroke Rehabilitation: A Systematic Review. Front. Virtual Real. 3:889271. doi: 10.3389/frvir.2022.889271

1 INTRODUCTION

Recent statistics have shown that one in every four people over the age of 25 will suffer from stroke in their lifespan, with 60% occurring in people under the age of 70 (GBD Stroke Expert Group, 2018). With over 13 million new cases being reported annually worldwide, stroke is known to cause long-term cognitive and physical disabilities, thus affecting the quality-of-life of stroke survivors (Lindsay et al., 2019). Physical impairments can range from mild (hemiparesis) to severe (hemiplegia) and commonly affect the left or right side of the body, while cognitive impairments can range from memory, language, and attention dysfunction to neuropsychiatric consequences such as post-stroke depression (Blöchl et al., 2019). To assist with improvements in performing activities of daily life, physical rehabilitation is recommended right away or within 6 months after the onset of stroke to maximize the chances of success (Lee et al., 2015). Overall, based on principles of motor learning theory, neural plasticity can be modulated greater if the training method is purposefully repeated with sufficient repetition (Kleim and Jones, 2008). In fact, the frequency of the rehabilitation sessions and their intensity have been shown to be the key factors in recovery (Tollár et al., 2021).

In many places around the world, however, access to rehabilitation professionals multiple times within the week is not possible due to either high cost, personnel availability, or insurance coverage purposes, to name a few factors. As such, routine rehabilitation sessions are seldom achieved (Carvalho et al., 2017). To overcome this limitation, forms of in-home rehabilitation tools have been explored by exploiting technology-mediated interventions. Virtual reality (VR) has emerged as a low-cost, engaging, interactive, and effective option shown to enhance functional outcomes and decrease depression levels (Szczepańska-Gieracha et al., 2020). Recently, VR combined with an exoskeleton or with physiological computing tools has been proposed to improve upper/lower limb rehabilitation, balance control, walking, and gait performance (Frisoli et al., 2011; Cikajlo et al., 2013; Comani et al., 2015; Zhang et al., 2015; Sheng et al., 2016; Berger and d'Avella, 2017; Zeiaee et al., 2017; Mubin et al., 2019). Here, physiological computing refers to the use of (multimodal) physiological data to monitor a user's psycho-physiological state. Inferred states can then be used as feedback to the user or to the machine in an adaptive manner (Jacucci et al., 2015). Dynamic and customized virtual environments can then be easily updated to accommodate user-specific interventions, can be tailored to a patient's specific rehabilitation plan, and allow for automated tracking of the patient's progression and adjusting the task accordingly. Commonly, cost-effective data acquisition devices to monitor electroencephalography (EEG), electromyography (EMG), and electrooculography (EOG) have been explored in novel interventions.

VR-based interventions have relied on the patient interacting with virtual objects through either active hand movements or imagined movements detected via a brain-computer interface (BCI) (Mizuguchi et al., 2013; Eaves et al., 2016; Ruffino et al., 2017) or via biofeedback (Levin et al., 2012). Recent research has shown that modulating neuroplasticity through VR can improve the motor function and muscle strength of stroke survivors (Ekechukwu et al., 2021). In fact, in Corbetta et al. (2015), VR was shown to be a suitable substitute for conventional rehabilitation to improve walking speed, balance, and mobility in stroke patients. With VR systems, the sense of realism and perceived immersion play key roles in stroke rehabilitation (Suzuki et al., 2017; Kritikos et al., 2020). Realistic environments can provide more engaging content and motivate stroke survivors to use the systems more frequently, with reported improvements in their quality-of-life (You et al., 2005). Moreover, virtual experiences can influence the patient's sense of ownership and agency over a virtual limb, i.e., embodiment (Perez-Marcos, 2018).

In order to provide the users with real-time feedback and a sense of control and involvement, physiological signal acquisition and processing is needed. Such signals may also be used to adjust the virtual environment autonomously, thus improving their sense of presence, especially for VR experiences based on head-mounted displays (HMDs) Sherman and Craig, (2003). Multimodal (bio)feedback, has in fact, been shown to improve rehabilitation outcomes; successful applications have been reported with motor control in children with dystonia (Casellato et al., 2012), chronic pain management (Gromala et al., 2015), and anxiety reduction (Bossenbroek et al., 2020), to name a few. The interested reader is referred to Kılıç et al. (2021) and Hao et al. (2021) for reviews on use of VR and physiological computing for fear and neural plasticity research, respectively.

Having this said, the use of HMD-based VR and physiological computing for stroke rehabilitation is also on the rise. However, no reviews summarizing the literature exist. To fill this gap, we conducted a systematic review of the existing literature to collect information about technological aspects of HMD systems, biosignal applications, and wearables (e.g., exoskeleton) that have been used for rehabilitation purposes. In particular, this study aimed to address the following questions:

(1) What physiological computing systems have been used with HMD-based VR and how effective have they been?;
(2) What equipment have been used and what advantages do certain psycho-physiological modalities offer over another?; and
(3) What clinical and non-clinical outcomes have been observed from these multimodal feedback based virtual reality interventions?

The remainder of this paper is organized as follows: **Section 2** contains the methodology used in this systematic review. Results are presented and discussed in **Section 3**, where limitations and recommendations for future studies are also described. Conclusion are finally presented in **Section 4**.

2 METHODOLOGY

This systematic review was conducted according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines (Liberati et al., 2009).

2.1 Search Strategy

A search over English language peer-reviewed journal papers was conducted across five databases, including Scopus, IEEE, Web of Science, PubMed, and Science Direct, between the years January 2015 to December 2021. The following keywords were used: (electro* OR respiration OR "galvanic skin") AND "stroke rehabilitation" AND "virtual reality." The keywords were searched in the title or abstract of the articles. Mendeley reference manager was used to remove duplicate citations across yielded results. The term "physiological computing" was not used as a keyword as it is a very specialized term that few researchers in the VR space utilize at the moment. By including all possible modalities that begin with "electro" (e.g., electrocardiogram, electroencephalogram, electromyogram, electrooculogram, electrodermal activity) we are bound to encompass all studies that utilized physiological computing systems without referring to this terminology directly.

2.2 Inclusion and Exclusion Criteria

Inclusion criteria included articles that 1) used HMD-based VR experiences, 2) included at least one feedback modality to improve the VR experience, 3) included a valid clinical measure or questionnaire to gauge the effectiveness of the intervention, and 4) developed a rehabilitation tool but tested on healthy subjects. Exclusion criteria included: 1) review papers, 2) studies not relying on HMD-based VR, and 3) studies not focusing on stroke rehabilitation applications. Eligibility criteria according to population, intervention, comparison, outcome, and study design (PICOS) has been tabulated in **Supplementary Table S1** and made available in the supplementary material section. We note that studies with healthy people have only been included if the goal of study was aligned with providing interventions to the population of interest (as described in **Supplementary Table S1**).

2.3 Screening and Data Extraction

After searching the abovementioned databases and merging the duplicated results, the authors screened titles and abstracts to exclude unrelated articles. The full-text screening was then performed on the remaining papers and aligned articles were included in this systematic review. To collect detailed information from each study, a data extraction spreadsheet was developed encompassing details across three domains: 1) study design and demographics (targeted stroke group, number of subjects, control group, gender distribution, target problem, session description, trial design), 2) technological aspects (HMD device, VR engine used, physiological modality, type of feedback, equipment, and electrode placement), and 3) outcomes (clinical/non-clinical scales, clinical results, availability of baseline information, pre- and post-intervention comparisons, and follow-up findings).

2.4 Quality Assessment

To assess the risk of bias (ROB) in the included studies, we utilized the National Institutes of Health—National Heart, Lung, and Blood Institute (NIH-NHLBI) quality assessment tool (National Institutes of Health, 2022), as well as the checklist for quasi-experimental studies based on the Joanna Briggs Institute (JBI) critical appraisal tool Tufanaru et al. (2017). For the former, articles are evaluated based on the type of the study and overall quality is judged based on "good," "fair," or "poor" categories. Categories are chosen based on replies to a number of questions, where answers can take the form of yes, no, cannot determine, not reported, or not applicable. Both NIH-NHLBI and JBI tools examine studies across three aspects, including objectives, methodology, and report of outcomes.

3 RESULTS AND DISCUSSION

3.1 Included Studies

From the 218 identified articles, 46 were from PubMed, 16 from ScienceDirect, 59 from IEEEXplore, 38 from Web of Science, and 59 from Scopus. **Figure 1** depicts a flow chart of the study selection process. After eliminating duplicates, 182 studies were left to be screened based on title and abstract. From this first pass, 130 papers were eliminated as they did not meet the inclusion criteria, resulting in 52 articles included for full-length analysis. In the end, 12 articles focusing on HMD-VR, multimodal physiological computing, and stroke motor rehabilitation were included in this review.

3.2 Study Design

Detailed information about the configuration, modalities used, study type, experiment duration, and demographics of the participants are available in **Table 1**. Detailed description of hardware used to acquire the physiological signals are described in **Table 2**.

All of the included papers followed a "pre/post study design," which refers to measuring specific metrics prior to the experiment and comparing them with recorded measures after the intervention (Thiese, 2014). As can be seen, among the included articles, four studies recruited only healthy subjects (Vourvopoulos and I Badia, 2016; Trombetta et al., 2017; Juliano et al., 2020; Achanccaray et al., 2021), three relied on patients who were in chronic stage of stroke (Vourvopoulos et al., 2019a; Vourvopoulos et al., 2019b; Marin-Pardo et al., 2020), three studies used a mixture of healthy and stroke patients (Lupu et al., 2018; Nissler et al., 2019; Stanica et al., 2020), one study used a stroke patient in sub-acute stage (Huang et al., 2018), and one study used a mixture of stroke patients in the chronic stage and patients with developmental disabilities (Elor et al., 2018). The reported numbers in **Table 1** are for participants who have completed all the sessions and satisfied all experimental protocols. Overall, 64.1% of participants were healthy subjects, and only 40% of all participants were females.

The reviewed studies relied on virtual environments to deliver rehabilitation exercises by means of gamified interventions. Ten articles focused on upper limb rehabilitation, while the remaining two studies focused on both upper and lower limbs (Juliano et al., 2020; Stanica et al., 2020). **Table 3** details the characteristics of the study (i.e., the aim of the study, target limb, and virtual environment description). As can be seen, among the included articles, only three studies used more than two different virtual environments (Huang et al., 2018; Nissler et al., 2019; Stanica et al., 2020).

3.3 Quality Assessment

As one of the reviewed papers was a case report, the NIH-NHLBI quality assessment tool for case series studies and the JBI checklist for case reports was used. For the remainder of the studies, the NIH-NHLBI quality assessment tool for before-after (pre-post) studies with no control group and the JBI checklist for quasi-experimental studies was utilized. The detailed responses obtained by both of the assessment tools are presented in **Supplementary Tables S2, S3**, respectively, both available in the supplementary materials section. **Table 4**, in turn, presents the results of the quality evaluation using the NIH-NHLBI tool.

As can be seen, from the NIH-NHLBI analysis, the majority of the pre-post studies (n = 11) were rated as fair,

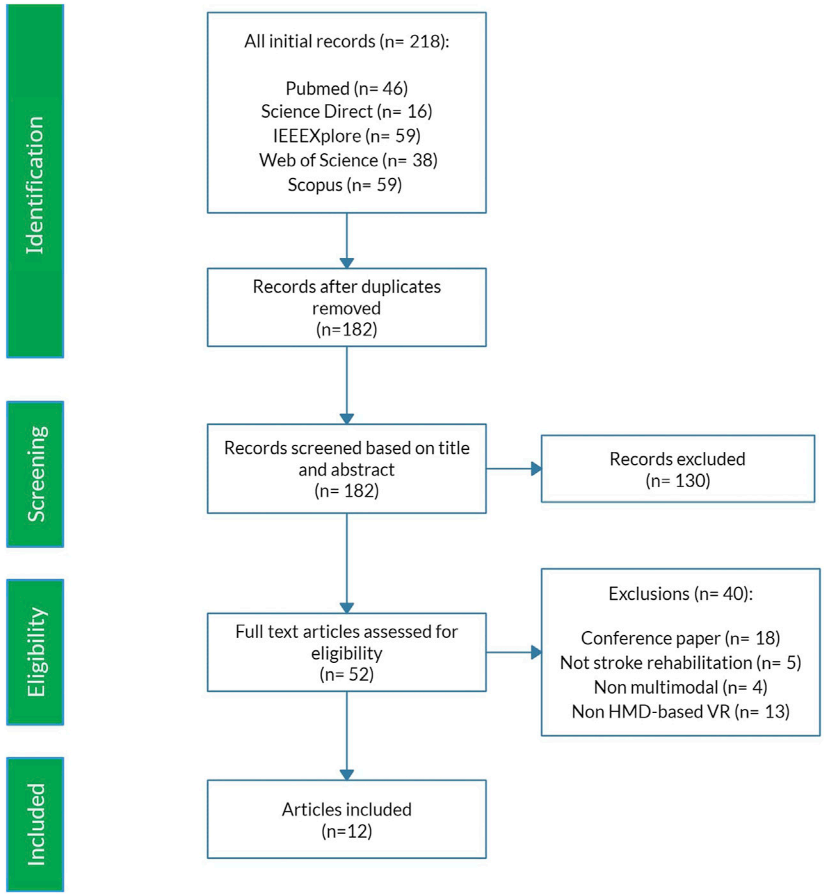

FIGURE 1 | Flow chart of paper selection steps.

while four studies were rated as good, and two as poor. The fair-rated studies showed clear objectives, eligibility criteria, selection of participants, targeting populations of interest, description of intervention, description of outcome measures, and multiple outcome measures, they reflected issues in terms of sample size, blinding of outcome assessors, and follow-up rate. Poor-rated studies, in turn, had issues concerning multiple outcome measures, statistical analysis, and group-level interventions. The case study, on the other hand, was rated good quality due to clarity of objectives, detailed description of population and intervention, valid and reliable outcome measurement, and well-described statistical method and results. In terms of JBI criteria, the issues flagged concerned lack of control group, receiving a similar treatment (except exposure to HMD-VR), and lack of follow-up plan. None of the articles showed issues with clarity of cause and effects of their study, similarity of participants, multiple measurement points of the outcome, or similar outcome measurements. Three articles, however, had issues with reliability of outcome measurements due to not using appropriate statistical analysis methods. For the case study, the JBI tool reflected "yes" responses to all of the checklist questions, thus corroborating its quality.

3.4 Technological Aspects

Overall, the included articles employed different types of technologies. **Figure 2** demonstrates an alluvial diagram of the methods, their combinations, and target aim. As evidenced, different physiological modalities and technologies have been utilized in VR-based stroke rehabilitation interventions. The following subsections highlight these methods in detail.

3.4.1 Virtual Environment

The Unity3D game engine was reported as being the most common for virtual environments design, feedback control, and integration of external devices (e.g., biosignal acquisition systems) into the game flow. Wearable HMDs, which provide stereoscopic close-to-reality experience and increased perception of depth and immersion, were widely used. In particular, three studies used the HTC Vive HMD (Valve Washington, WA, United States), (Elor et al., 2018; Nissler et al., 2019; Stanica et al., 2020), while the remaining utilized an Oculus HMD (Oculus VR, Irvine, CA, United States), likely due to its accessibility to SDKs and lower price. In the studies, varying display refresh rates from 60 to 90 Hz were reported.

To deliver targeted rehabilitation-oriented content, custom environments were typically developed, though

TABLE 1 | HMD-VR rehabilitation systems and utilized technologies, devices and study design.

Study	Hardware	Modalities	Feedback	Study Population					Experiment
				Participants	Stroke onset[a]	Age range	F/M	Duration	Tasks
Marin-Pardo et al. (2020)	Oculus Rift CV1	EEG, EMG	Visual, Hand tracking	Stroke patients (chronic stage, *n* = 4)	37 ± 48.6	13.54 ± 11.08	1/3	10 sessions	Left and right: (A) Static hold task, (B) Wrist extensor training
Lupu et al. (2018)	Oculus Rift, MotionStim 8	EEG, EOG	Visual, FES, EOG	Stroke patients (poststroke central neuromotor syndrome, *n* = 7), and controls (*n* = 3)	N/M	52 to 79	N/M	3 sessions	(A) Virtual therapist in front of user (B) Therapist/user looking at mirror
Huang et al. (2018)	Oculus Rift DK2, Tyromotion Amadeo	Finger Tracking	Visual, Audio, finger position and force	Stroke patients (subacute stage, *n* = 8)	2.18 ± 1.13	69 ± 11.48	5/3	18 sessions	(A) Passive, (B) Adaptive, (C) 2D game, (D) 3D game
Vourvopoulos et al. (2019b)	Oculus Rift, Magstim BiStim, 3T Prisma MRI scanner	EEG, EMG	Visual, Audio, Haptic, EEG	Stroke patients (chronic stage, *n* = 4)	108.5 ± 48.6	60 ± 5.8	1/3	10 sessions	Left/right wrist/elbow extension
Vourvopoulos et al. (2019a)	Oculus Rift DK1, 3T GE Signa fMRI HDxt, Arduino	EEG, EMG	Visual, Audio, Haptic, EEG	Stroke patients (chronic stage, *n* = 1)	112	60	0/1	10 sessions	Left and right hand: (A) MI with arrows-and-bars, (B) MI in VR
Juliano et al. (2020)	Oculus CV1, LSM9DS09 IMU	EEG, EMG	Visual, Audio, EEG, IMU	Healthy participants (*n* = 12)	N/A	24.4 ± 2.7	7/5	90 trials	Hand movement imagination: (A) Screen, (B) HMD-VR, (C) Exercise while using IMU
Stanica et al. (2020)	HTC Vive Cosmos Elite, Myo Armband, Mi fit 3	EMG	Visual, Audio, Haptic	Stroke patient (*n* = 1), diabetic neuropathy (*n* = 1), controls (*n* = 6)	N/M	52.62 ± 24.48	N/M	Four phases	Upper and lower limb exercises
Trombetta et al. (2017)	Oculus Rift, Kinect	Motion Tracking	Visual, Audio	healthy participants (*n* = 10)	N/A	61 to 75	8/2	1 session	Abduction movements and shoulder adduction, elbow and wrist extension with (A) Screen and (B) HMD-VR
Vourvopoulos and I Badia, (2016)	Oculus Rift DK1, Leap Motion	EEG	Visual, Audio	healthy participants (*n* = 9)	N/A	27 ± 2	1/8	3 sessions	(A) Motor execution, (B) online MI, (C) MI with arrows-and-bars
Elor et al. (2018)	HTC Vive	Hand Tracking	Visual, Audio, Haptic	Stroke patients (*n* = 9), patients with developmental disabilities (*n* = 6)	36 to 108	stroke patients: 36 to 87, developmental disabilities: 26.5 ± 3.27	6/9	1 session	Collecting scores in HMD-VR game
Achanccaray et al. (2021)	Oculus Rift, UnlimitedHand	EEG	Visual, Electrotactile	Healthy participants (*n* = 20)	N/A	26.20 ± 5.37	5/15	3 sessions	Flexion and extension MI tasks
Nissler et al. (2019)	HTC Vive, Michelangelo prosthetic hand	EMG	Visual	Healthy participants (*n* = 15), congenital right hand amputation (*n* = 1)	N/A	Healthy: 31.0 ± 7.6, Patient: 33	3/13	multiple sessions	Box and Block test with HMD-VR

HMD, head-mounted display; MRI, magnetic resonance imaging; fMRI, functional MRI; FES, functional electrical stimulation; IMU, inertial measurement unit; MI, motor imagery; DK, development kit; CV, consumer version; F/M, female/male; N/M, not mentioned.
[a]*Time after stroke onset reported in months.*

two studies relied on pre-developed games (Huang et al., 2018; Vourvopoulos et al., 2019a). For example, two studies implemented a virtual therapist to present exercises in a virtual environment (Lupu et al., 2018; Stanica et al., 2020). Nevertheless, only one study provided detailed information about the virtual environment design process, including the properties of different objects and the adjustment of feedback intensity (Elor et al., 2018). The other reviewed articles failed to provide comprehensive information about concepts of human-centered design,

TABLE 2 | Detailed information about devices used for physiological computing.

Study	EEG device	EEG sample rate	Number of channels	EEG electrode placement	EMG device	EMG sample rate	EMG electrode placement
Marin-Pardo et al. (2020)	Starstim 8	500 Hz	8	FC3, FC4. C3, C4, C5, C6, CP3, CP4	Delsys Trigno Wireless System	2,000 Hz	FCR, FCU, ECR, ECU
Lupu et al. (2018)	g.USBamp	256 Hz	12	FC1, FC2, FC5, FC6, C3, C4, C5, C6, CP1, CP2, CP5, CP6	N/A	N/A	N/A
Vourvopoulos et al. (2019b)	Starstim 8	500 Hz	8	FC3, FC4, C3, C4, C5, C6, CP3, CP4	Delsys Trigno Wireless System	2,000 Hz	EDC, FCU, BB, TB
Vourvopoulos et al. (2019a)	Enobio 8	500 Hz	8	FC5, FC6, C1, C2, C3, C4, CP5, CP6	N/A	N/A	N/A
Juliano et al. (2020)	OpenBCI	125 Hz	12	F3, F4, C1, C2, C3, C4, CP1, CP2, CP5, CP6, P3, P4	OpenBCI	125 Hz	FCR, FCU, ECR, ECU
Stanica et al. (2020)	N/A	N/A	N/A	N/A	Myo Armand	100 Hz	Forearm
Vourvopoulos and I Badia, (2016)	g.MOBIlab+	256 Hz	8	FC3, FC4, C3, C4, C5, C6, CP3, CP4	N/A	N/A	N/A
Achanccaray et al. (2021)	g.USBamp	256 Hz	16	AF3, AF4, FC3, FCz, FC4, C3, Cz, C4, T7, T8, CP3, CPz, CP4, Pz, O1, O2	N/A	N/A	N/A
Nissler et al. (2019)	N/A	N/A	N/A	N/A	Myo Armand	100 Hz	Forearm

FCR, flexor carpi radialis; FCU, flexor carpi ulnaris; ECR, extensor carpi radialis longus; ECU, extensor carpi ulnaris; EDC, extensor digitorum comunis; BB, biceps brachii; TB, triceps brachii.

TABLE 3 | Characteristic of reviewed studies, including target limbs, study aim, and virtual environment description.

Study	Target limb	Study aim	Environment description
Marin-Pardo et al. (2020)	Wrist and elbow	Reinforce activation of the wrist extensor muscles without flexor activation	Two arms are resting on a table, and users requested to push the ball off the table with the back of their hand
Vourvopoulos et al. (2019b)	Wrist and elbow	Investigate the effectiveness of BCI-VR in patients with motor disabilities	Two arms resting on a table and the task is to extend a hand toward a target where virtual hands will move via neurofeedback
Lupu et al. (2018)	Hand	Hand and fingers flexion and extension *via* a virtual therapist while leveraging mirror therapy	Virtual therapist gives hand rehabilitation exercises in a face-to-face situation and with the therapist on the left side of the user and a mirror in front
Huang et al. (2018)	Hand	Strengthen force, range of motion, finger coordination, and movement planning	Five environments including (A) Flying bird-2D, (B) Spaceship-2D, (C) VR-simulated supermarket, (D) VR-simulated kitchen, and (E) space war VR game
Vourvopoulos et al. (2019a)	Hand	Examine the efficacy of the MI-BCI paradigm with VR for post-stroke upper limb rehabilitation	NeuRow, a first-person self-paced BCI game (a boat rowing task through MI) with the goal of collecting scores in a pre-determined amount of time
Vourvopoulos and I Badia, (2016)	Hand	Increase engagement of sensory-motor networks during rehabilitation	Virtual garage where user's movement is mapped to VR to open the door *via* rotating a lever
Achanccaray et al. (2021)	Hand	Investigate the effectiveness of visual-electrotactile feedback versus visual-only feedback	Room with chairs and a desk with the user's virtual arm and a ball to present target movements
Juliano et al. (2020)	Arm and hand	Compare embodiment and motor imagery BCI performance in HMD-VR vs. screen-based VR	Hit a ball with a virtual arm using MI-BCI paradigm and active movement
Elor et al. (2018)	Arm and hand	Leverage modified constraint-induced therapy (mCIT) to influence the use of the weaker arm	Galaxy background with stars appearing. The patient's strong arm is mapped in red and weak arm in green. Patients touch stars that are falling with a goal to increase their score. More points are given if the weak arm is used
Nissler et al. (2019)	Arm and hand	Implement a VR-based version of the Box and Block test	Virtual box divided in two parts by a partition. Patients are asked to move small blocks from the right to the left partition. A virtual Jenga game, a squeezable toy, and an interactive kitchen environments were also tested
Stanica et al. (2020)	Shoulder, elbow, fist, hip, knee, ankle	Patient should imitate movements shown by a therapist	Patients observe classical rehabilitation movements performed by the virtual therapist and perform them on their own. Six VR games are tested: (A) hitting targets, (B) ball directing, (C) hitting mole, (D) boxing, (E) football, and (F) dancing
Trombetta et al. (2017)	Shoulder, elbow, fist, hip, knee, ankle	Compare HMD-VR vs. TV screen while providing motor and balance rehabilitation exercises	User movements mapped to the VR environment

TABLE 4 | NIH quality assessment results for included studies.

Study	Type	Good	Fair	Poor
Marin-Pardo et al. (2020)	Pre-post		✓	
Lupu et al. (2018)	Pre-post			✓
Huang et al. (2018)	Pre-post		✓	
Vourvopoulos et al. (2019b)	Pre-post	✓		
Vourvopoulos et al. (2019a)	Case-study	✓		
Juliano et al. (2020)	Pre-post		✓	
Stanica et al. (2020)	Pre-post		✓	
Trombetta et al. (2017)	Pre-post			✓
Vourvopoulos and I Badia, (2016)	Pre-post	✓		
Elor et al. (2018)	Pre-post		✓	
Achanccaray et al. (2021)	Pre-post	✓		
Nissler et al. (2019)	Pre-post		✓	

including signifiers, affordances, mapping, and conceptual models (Norman, 2013).

Lastly, a first-person point of view (POV) was shown to be very popular in the reviewed articles, where nine studies had a first-person perspective (patient performs from character's POV), two studies exploited third-person playing mode (patient controls a virtual avatar) (Trombetta et al., 2017; Huang et al., 2018), and one study had both settings (Lupu et al., 2018). It is known that the first-person perspective increases the sense of embodiment (limb ownership and self-location) while the third-person perspective provides space awareness (Gorisse et al., 2017).

3.4.2 Physiological Computing

Physiological computing has emerged as a powerful tool in human-computer interaction, allowing real-time physiological signal analysis and behavioral information to enhance the interaction by conveying user cognitive/mental/affective state information to the machine, as well as real-time information about patient movement, thus improving the sense of embodiment. Moreover, physiological/behavioral data can provide insights into both conscious and unconscious processes and thus may also convey information about the user's motivational and intentional states. More recently, as wearable devices burgeon, physiological computing has started to gain traction for at-home uses. This, coupled with HMD advances and a drop in costs, has resulted in the development of new in-home VR-based rehabilitation systems. **Table 2** presents technical information about the EEG and EMG wearable devices used in the reviewed papers, including a description of the devices themselves, their sample rates, and electrode placement details. Inertial measurement units (IMUs) have also been utilized for motion/behavioral tracking and EOG signals to assess if the tests were performed correctly (Lupu et al., 2018). More details about these modalities are provided below.

3.4.2.1 EEG

As seen in **Table 2**, seven articles have relied on EEG-based physiological computing methods in their VR rehabilitation studies. Since the main aim of the studies concerns motor improvement, most studies acquired EEG signals from electrodes over the motor cortex, corresponding to positions FC3, FC4, C3, C4, C5, C6, CP3, and CP4 electrodes in the 10–20 international positioning system. In terms of BCI paradigms, six studies relied on motor imagery (MI) (Vourvopoulos and I Badia, 2016; Lupu et al., 2018; Vourvopoulos et al., 2019a; Vourvopoulos et al., 2019b; Juliano et al., 2020; Achanccaray et al., 2021). The underlying hypothesis with MI is that illusions of movement and a strong feeling of embodiment could improve the neural plasticity needed for rehabilitation, with physiological computing and real-time feedback contributing to an improved embodiment. Sub-acute stroke patients, for example, who used MI-based paradigms could then improve functional outcomes (Carrasco and Aboitiz Cantalapiedra, 2016). Stronger desynchronization in the alpha (7–13 Hz) and beta (13–30 Hz) EEG bands of the ipsilesional

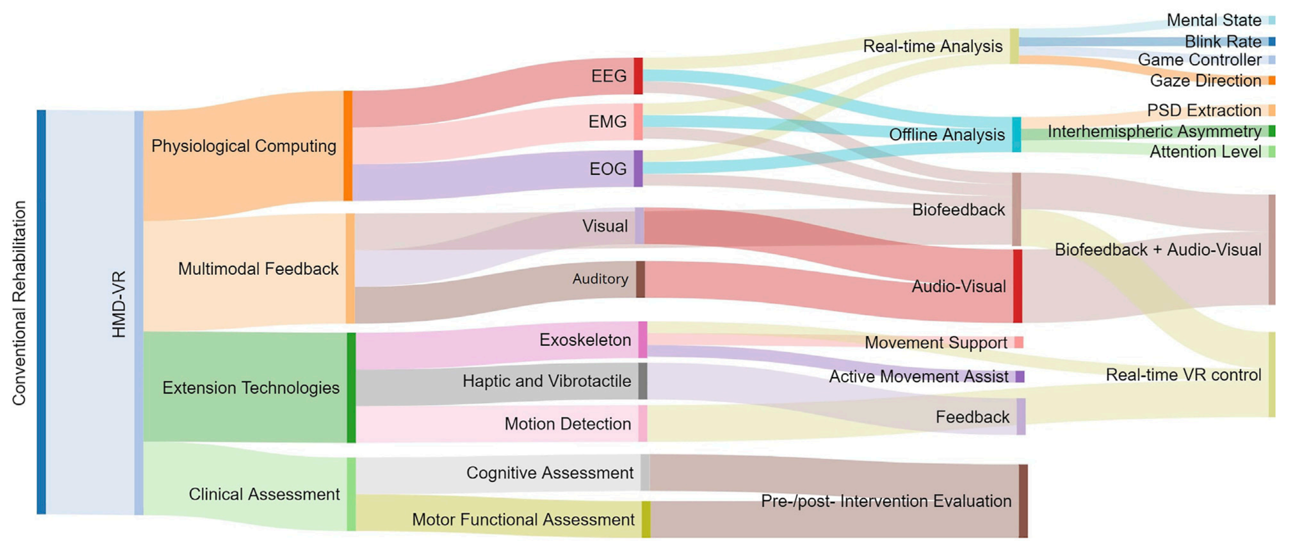

FIGURE 2 | Alluvial diagram illustrating mediated approaches and their combinations to shape significant usage within the framework of HMD-VR for rehabilitation.

hemisphere, for example, has been shown (Pichiorri et al., 2015). Additionally, increased hemispheric asymmetry has been shown in MI sessions with feedback, suggesting enhancement in fine motor task performance and modifying motor learning (Neuper et al., 1999; Garry et al., 2004). In fact, differences in interhemispheric asymmetry in stroke patients have been reported relative to a control group Berenguer-Rocha et al. (2020), thus suggesting that physiological computing could be used not only to customize the environment, but to also track intervention progress and success (Cicinelli et al., 2003). The impact of HMD-based rehabilitation has also been quantified by means of post-hoc comparisons based on event-related synchronization/desynchronization (ERS/ERD) (Vourvopoulos et al., 2019b), corticomuscular coherence (i.e., synchronization between EEG and EMG signals) (Marin-Pardo et al., 2020), resting-state alpha rhythm (Vourvopoulos et al., 2019a), and EEG rhythm power spectral analyses (Vourvopoulos and I Badia, 2016; Juliano et al., 2020; Achanccaray et al., 2021).

3.4.2.2 EMG

EMG provides information about the electrical activity of the muscles. The location of electrodes is typically determined based on the aim of the study, i.e., to improve the function of the upper or lower limb. Upper limb studies can include muscles of the hand, wrist, elbow, and rear-/fore-arm, whereas lower limbs can include the foot, ankle, knee, thigh, and hip. As shown in **Table 2**, only five of the twelve relied on EMG signals, two of which used a Delsys Trigno Wireless System (Delsys Incorporated, Natick, MA, United States) (Vourvopoulos et al., 2019b; Marin-Pardo et al., 2020), two used Myo armbands (Thalmic Labs) (Nissler et al., 2019), and one used an OpenBCI bioamplifier (Juliano et al., 2020). These systems operated at sample rates of 2,000, 100, and 125 Hz, respectively. In addition to post-hoc EMG analyses to monitor the physical improvement due to rehabilitation (e.g., EMG amplitude, rest/active state detection), three studies relied on EMG signals to map the patient's arm/hand into the VR environment to improve the sense of embodiment (Nissler et al., 2019; Marin-Pardo et al., 2020; Stanica et al., 2020).

3.4.2.3 Motion Tracking

While EMG can provide information about limb motion, it lacks details about e.g., arm/hand orientation. To this end, inertial measurement unit (IMUs) have been used as a real-time tool to map arm/hand direction onto the virtual environment. For example, Juliano et al. (2020) relied on IMUs to match the virtual arm/hand movements with the user's actual arm/hand movements. Similarly, the controllers used by VR systems can be used as a motion-tracking tool, in addition to delivering haptic feedback (Elor et al., 2018; Nissler et al., 2019). Lastly, optical tracking tools, such as a Leap Motion (Leap Motion, Inc., San Francisco, CA, United States) tracking device Vourvopoulos and I Badia, (2016) have been used to map hand orientation and finger movements into the virtual environment.

3.4.3 Feedback Modality

Feedback is known to improve the sense of embodiment and to also foster plasticity (Kumru et al., 2016; Alimardani et al., 2018), thus is widely used in neuro-rehabilitation. Visual and audio-based feedback modalities are the most classic form of feedback, but more recent studies have been exploring the use of haptic (e.g., by the controllers, as mentioned above) feedback to improve the sense of immersion and presence. Feedback needs to be easily distinguishable, especially by the patient population (Trombetta et al., 2017; Elor et al., 2018), thus the volume of audio cues, the shape and color of visual cues, and the intensity of haptic cues are of indispensable importance. In certain conditions, voluntary movement is still not possible by the patient, thus an exoskeleton is used to provide the intended feedback. Additionally, more recent methods have relied on the use of functional electrical stimulation (FES) Lupu et al. (2018) as a form of feedback, where subtle electrical charges are applied to certain muscles in order to contract them upon detection of motor activation signals from EEG, for example. In the sections below, more details are provided on exoskeleton and haptics-based feedback modalities.

3.4.3.1 Exoskeleton-Based Feedback

Exoskeleton-based rehabilitation relies on robotic or non-robotic assistive devices which help the patients perform exercises correctly, safely, and in a sustained manner with or without predefined force intensities (Mubin et al., 2019). The exoskeleton can be set in active, passive, or assistive modes (Morone et al., 2020). In the reviewed articles, only one paper relied on exoskeletons. In particular, Huang et al. (2018) used a 5-degree-of-freedom Amadeo (Tyromotion GmbH, Graz, Austria) along with audio-visual feedback. The device provided patients with control over finger movements, force, and velocity.

3.4.3.2 Haptics-Based Feedback

Haptic feedback adds the sense of touch to the virtual experience and increases the sense of immersion (Kim et al., 2017). Gloves, controllers, armbands, or even exoskeletons can be used to provide haptic feedback (Rose et al., 2018). As seen from **Table 1**, five studies relied on haptic feedback, where three used the VR system controllers to provide vibration feedback (Elor et al., 2018; Vourvopoulos et al., 2019b; Stanica et al., 2020), one proposed a custom device based on vibrating motors (Vourvopoulos et al., 2019a), one used the UnlimitedHand (H2L Inc., Tokyo, Japan) device to supply electrotactile stimulation feedback (Achanccaray et al., 2021). Haptic feedback was used primarily in these studies to inform the subject when a task was finalized and/or in response to an interaction with a specific object in the virtual environment.

3.5 Clinical/Non-Clinical Reported Outcomes

The reviewed papers relied on multiple approaches to measure the efficacy of their proposed methods. For example, several different questionnaires, physiological signal analyses, and clinical measures were explored. **Table 5**, presents a description and evaluation domains of the most-utilized clinical/non-clinical scales reported in the papers. As

TABLE 5 | Frequently used clinical measurements and questionnaires.

Name	Type	Evaluation domains	Description	Studies
Fugl–Meyer assessment (FMA)	Physical impairment	Extremities motor function, Sensory functioning, Balance, Joint range of motion, Joint pain	Reliable and validated method to evaluate upper and lower limb motor impairment Fugl-Meyer et al. (1975)	Marin-Pardo et al. (2020); Huang et al. (2018); Vourvopoulos et al. (2019a); Vourvopoulos et al. (2019b)
Action research arm test (ARAT)	Limb function	Grasp, Grip, Pinch, Gross movement	Quick and short test (only 19 items) covering important aspects of arm functional performance Yozbatiran et al. (2008)	Marin-Pardo et al. (2020)
Montreal cognitive assessment (MoCA)	Cognition impairment	Visuospatial ability, Executive functioning, Attention, Language, Orientation	Quick and short test (10 min) with ability to differentiate mild to severe range of cognitive impairments Nasreddine et al. (2005)	Vourvopoulos et al. (2019a); Marin-Pardo et al. (2020)
Motor Assessment Scale	Motor function	Supine to side lying, Supine to sitting over the edge of a bed, Balanced sitting, Sitting to standing, Walking, Upper-arm function, Hand movements, Advanced hand activities	Task-oriented evaluation of daily-life motor function Carr et al. (1985)	Huang et al. (2018)
Modified Ashworth Scale	Limb spasticity	Perceived resistance while extending limb passively from maximal flexion to maximal extension (full range of motion)	Acceptable scale to measure spasticity in muscles of both the upper or lower limbs Ashworth, 1964)	Vourvopoulos et al. (2019a); Vourvopoulos et al. (2019b)
Range of motion (ROM)	Limb extent of movement	Flexion/extension of wrist/finger/hand, Wrist deviations	Evaluate wrist, finger, or hand range of motion in three states: passive, active, assisted Gajdosik and Bohannon, (1987)	Huang et al. (2018); Marin-Pardo et al. (2020); Stanica et al. (2020)
Stroke impact scale	Quality of life	Strength, Hand function, Activities of daily living, Instrumental activities of daily living, Mobility, Communication, Emotion, Memory and thinking, Role function	Self-report assessment consists of 59 items evaluating multidimensional stroke outcomes Duncan et al. (2003)	Marin-Pardo et al. (2020); Vourvopoulos et al. (2019a); Vourvopoulos et al. (2019b)
Saltin–Grimby physical activity level scale (SGPALS)	Physical activity	Four level physical activity questionnaire during leisure time	Evaluates leisure and work time physical activity levels Saltin and Grimby, (1968)	Stanica et al. (2020)
Simulator sickness questionnaire (SSQ)	Simulator sickness	Nausea-related questions, Oculomotor, Disorientation	16 questions in three categories to evaluate severity of simulator sickness Kennedy et al. (1993)	Vourvopoulos et al. (2019b); Juliano et al. (2020); Marin-Pardo et al. (2020)
Vividness of movement imagery questionnaire (VMIQ2)	Movement imagery	Walking, Running, Kicking a stone, Bending down, Running up stairs, Jumping sideways, Throwing a stone into water, Kicking a ball in the air, Running downhill, Riding a bike, Swinging on a rope, Jumping off a high wall	Evaluates capability to perform 12 imagined movements from external perspective, internal visual imagined movements and kinesthetic imagery Roberts et al. (2008)	Vourvopoulos and I Badia, (2016); Vourvopoulos et al., 2019a)
Presence questionnaire (PQ)	Presence	Realism, Possibility to act, Possibility to examine, Quality of interface, Self-evaluation of performance	Evaluate sense of presence in the virtual environment Witmer et al. (2005)	Vourvopoulos and I Badia, (2016); Juliano et al. (2020)

interventions may have outcomes across numerous domains, it is common for studies to use more than one assessment method. As seen from the Table, seven clinical scales have been used most often, including the Fugl–Meyer assessment (FMA), action research arm test (ARAT), Montreal cognitive assessment (MoCA), motor assessment scale, modified Ashworth scale, range of motion (ROM), and stroke impact scale (SIS). Studies typically compared these metrics pre- and post-intervention to gauge the benefits of the VR therapy. Further, to assess detailed alterations in the brain and plasticity improvements, two studies relied on magnetic resonance imaging (MRI) and functional MRI (fMRI) (Vourvopoulos et al., 2019b,a). **Table 6** includes the significant final outcomes observed by the studies, as well as the time points in which clinical/non-clinical measures were taken for comparisons.

In terms of clinical measures, various metrics are observational, meaning that a clinician (or a physiotherapist) determines a score after the patient performs a specific task. Five studies relied on a certified occupational therapist or rehabilitation specialist to carry out these observational clinical measures (Huang et al., 2018; Vourvopoulos et al., 2019a; Vourvopoulos et al., 2019b; Marin-Pardo et al., 2020; Stanica et al., 2020). FMA and SIS can be seen to be the most widely used measures. However, FMA has been shown to be subject to ceiling effects (Lin et al., 2004), whereas SIS potentially has ceiling effects in hand function, memory and thinking, communication, mobility and activities of daily living (ADL), and instrumental ADL domains (Richardson et al., 2016).

In terms of non-clinical measures, post-hoc physiological computing tools have been leveraged to extract changes in the measured biosignals. For example, Vourvopoulos and I Badia, (2016) reported differences in EEG activity of motor imagery in virtual environments relative to regular imagery. In fact, the ANOVA test with a Greenhouse-Geisser correction and pairwise Wilcoxon signed-rank test showed a statistically

TABLE 6 | Measurement time points and clinical/non-clinical outcomes of each study.

Study	Measures and time points	Outcomes
Marin-Pardo et al. (2020)	FMA-UE, ARAT, MoCA, SIS-16, Wrist ROM, Grip strength, and EEG in sessions 1 and 10. SSQ evaluated in sessions 2 and 9. EMG recorded during all sessions. Enjoyment questionnaire evaluated in session 10	Improvement in SIS-16, FMA, and Wrist ROM was observed. No significant changes were seen in ARAT. Minor levels of discomfort after HMD-VR via SSQ were reported. EMG-EEG: Improved motor control, significant beta-band corticomuscular coherence during wrist extension was observed
Lupu et al. (2018)	Control error rate and satisfaction questionnaire after each session	VR-BCI-FES combination resulted in faster rehabilitation periods, increased user optimism and a desire to exercise more in order to recover lost skills
Huang et al. (2018)	FMA, MAS, active ROM, force intensity before/after training	Improvement in motor skills, including 37.5% and 38.8% increase in FMA and MAS, respectively
Vourvopoulos et al. (2019b)	fMRI, T2-weighted and diffusion-weighted MRI, single- and paired-pulse TMS, FMA-UA, MAS, and SIS in sessions 1 and 2. EMG and EEG during all sessions. SSQ and enjoyment questionnaire before and after training	Patients with severe motor impairments are shown to benefit the most from EEG-based neurofeedback. No significant differences were seen between pre- and post-intervention for all tested clinical scales. A significant negative correlation was observed between the VR task score and the FMA score. Cortical physiology changes were observed in one subject using TMS.
Vourvopoulos et al. (2019a)	fMRI, MoCA, Modified Ashworth scale, FMA, SIS, and VMIQ2 before and after training, as well as 1 month after intervention	Improvement were seen in FMA-UE (pre: 31, post: 40, follow-up: 44). An increase in brain activation plastic changes was observed in the fMRI modality
Juliano et al. (2020)	SSQ, PQ, EQ, EEG, and EMG before training, after condition 1 and after condition 2	A relationship between neurofeedback performance and sensorimotor desynchronization was observed. Higher levels of embodiment were reported in HMD-VR. Similar performance was achieved between HMD-VR and flat-screen conditions
Stanica et al. (2020)	SGPAS, VR experience Questionnaire, and ROM before and after training	Gamified exercises are reported to be useful, interesting, and entertaining. An increase in motivation was observed in gamified intervention
Trombetta et al. (2017)	Brum e Rieder questionnaire after training	Visual and aural feedback was confirmed to be more intuitive. 20% of participants showed difficulty with spatial orientation
Vourvopoulos and I Badia, (2016)	PQ, VMIQ2, NASA TLX, and EEG recording in each session	A significant difference in classification accuracy of motor execution before MI compared to standard motor imagery was observed. An increase in the mean power of all EEG rhythms in VR-based tasks has been shown
Elor et al. (2018)	Interview, scores achieved during game after each session	The reward system increased the performance of executed movements. Feedback should be strong enough to be distinguishable by all participants
Achanccaray et al. (2021)	System perception questionnaire after each session	Improved mean classification accuracy for the grasping and flexion/extension MI tasks with visual-electrotactile feedback was reported. Higher attention levels with such a hybrid feedback modality were seen
Nissler et al. (2019)	Number of moved blocks during trial	Participants using prostheses outperformed other users in the VR setting

FMA-UE, Fugl–Meyer assessment-upper extremity; ARAT, action research arm test; MoCA, Montreal cognitive assessment; SIS, stroke impact scale; ROM, range of motion; SSQ, simulator sickness questionnaire; MAS, motor assessment scale; VMIQ2, vividness of movement imagery questionnaire; PQ, presence questionnaire; EQ, embodiment questionnaire; TLX, task load index.

significant result in the alpha band ($F_{(2.524,20.191)} = 4.800$, $p < 0.05$), between "motor execution and VR (VRMP)" versus the control condition. In the theta band (4–7 Hz), the difference was reflected between motor-execution and VRMP ($F_{(1.874,14.990)} = 7.615$, $p < 0.05$). Interhemispheric interaction was also observed in several studies to be affected by visual, audio, or haptic feedback (Vourvopoulos and I Badia, 2016; Vourvopoulos et al., 2019a; Vourvopoulos et al., 2019b; Achanccaray et al., 2021). Vourvopoulos et al. (2019a) calculated ipsilateral ERD/ERS of the beta band using C3 and C4 electrodes. Subsequently, by running a t-test, a statistically significant difference was observed between the first and last session (t (199) = −16.921, $p < 0.001$). Moreover, it is known that treatments with greater engagement levels keep patients motivated and yield better outcomes (Brett et al., 2017). As there is a direct relationship between engagement and attention (Danzl et al., 2012) and attention deficits could result from strokes (Hochstenbach et al., 1998), leveraging VR tools to increase patient focus could be highly beneficial. Certain rhythms (e.g., alpha and beta bands over the parietal region for visual stimulus), for example, have been related to attention (Kamiński et al., 2012; Jurewicz et al., 2018; Thiele and Bellgrove, 2018; Magosso et al., 2019) and associated with motor function (Khanna and Carmena, 2015).

To this end, Vourvopoulos and I Badia, (2016) found a relationship between the ability to perform kinesthetic imagery and alpha-beta band modulation ($\rho = 0.50$, $p < 0.05$) and, thus potentially pointing towards improved attention levels. Furthermore, Achanccaray et al. (2021) noted higher attention levels in visual-electrotactile stimulation compared to visual-only condition, and higher attention levels were also shown to be correlated with haptic feedback and exoskeleton usage Li et al. (2021). In fact, a significant inverse Spearman correlation was found between attention level and difficulty level ($\rho = -0.45$, $p = 0.04$). However, a Spearman correlation between attention level and beta band of channels regarding somatosensory and prefrontal regions was observed in both grasping (e.g., AF3 channel: $\rho = 0.58$, $p = 0.04$) and flexion/extension (e.g., AF3 channel: $\rho = -0.5$, $p = 0.02$) MI tasks. Indeed, by adding haptic feedback, Vourvopoulos et al. (2019a) reported 9 points improvement in the FMA score at the end of the intervention (pre: 31, post: 40) in a case report on a patient with left hemiparesis. These insights suggest that haptic-based feedback could be utilized to boost attention levels in VR-based interventions and lead to improved outcomes Achanccaray et al. (2021); Stanica et al. (2020); Vourvopoulos et al. (2019a). Notwithstanding, Vourvopoulos et al. (2019b) noted that patients with more severe impairments showed the most significant improvement using motor imagery-based paradigms in a VR setting, while EMG-based feedback was shown more promising for patients with mild impairments.

VR-based solutions typically rely on their improved sense of realism (Read et al., 2021), immersion and presence (Slater, 2009), and sense of embodiment (Riva et al., 2019) to boost rehabilitation performance (Lin et al., 2001). To achieve these goals, Vourvopoulos et al. (2019b), for example, customized hand models in the virtual environment to match the patient's skin tone and gender and Stanica et al. (2020) provided close-to-reality animations of outdoor exercises. Juliano et al. (2020), in turn, leveraged linear regression to examine the relationship between neurofeedback performance and overall embodiment and reported a significant relationship in the HMD-VR experimental condition ($F_{(1,10)} = 8.293$, $p = 0.016$, $R^2 = 0.399$).

The gamification potential of VR-based solutions can also allow for reward mechanisms to be put in place to improve outcomes. For example, the reward has been shown to improve motor learning (Nikooyan and Ahmed, 2015; Chen et al., 2018) and rehabilitation outcomes (Quattrocchi et al., 2017; Widmer et al., 2017). Reinforcement feedback also induces motivation (Vassiliadis et al., 2021). This is important, as lack of motivation has been said to be one of the major barriers in conventional rehabilitation (Damush et al., 2007). As such, reward-based VR interventions improve outcomes (Abe et al., 2011), result in higher rates of satisfaction, and have increased adherence (Trombetta et al., 2017; Elor et al., 2018; Huang et al., 2018; Stanica et al., 2020). For example, Elor et al. (2018) encouraged patients to use their affected weaker limb by giving them higher scores when an action was carried out with such affected limb. Overall, only four of the reviewed articles relied on reward feedback as part of their intervention (Trombetta et al., 2017; Elor et al., 2018; Nissler et al., 2019; Stanica et al., 2020).

Notwithstanding, VR-based solutions relying on HMDs are also known to elicit in certain individuals discomfort and nausea (known as cybersickness). Trombetta et al. (2017), for example, reported a subtle improvement in the sense of comfort when screen-based tasks were given to the participants, relative to those given via an HMD. Other studies, in turn, utilized the simulator sickness questionnaire, and only very minor degrees of discomfort were reported when using HMD-VR (Vourvopoulos et al., 2019b; Marin-Pardo et al., 2020). More recently, cybersickness has been associated with activity in delta (1–4 Hz), theta, and alpha EEG frequency bands (Krokos and Varshney, 2021). Future studies could also explore the use of collected EEG signals to measure cybersickness levels; this was not performed in any of the evaluated papers. Moreover, it is known that stroke can result in a range of cognitive impairments, thus it is necessary to investigate the perception and interaction skills of patients (Sun et al., 2014) in virtual environments. To this end, Nissler et al. (2019) implemented a clinical assessment method called Box and Block test in a virtual environment to measure gross manual dexterity and compared the performance of the patients in both conventional and VR-based settings. The results showed better control of a virtual prosthesis by a patient compared to the healthy control group.

Lastly, one additional advantage of a VR-based intervention with physiological computing is that it enables automated, repeatable, and reliable interventions. Such factors are crucial for treatment fidelity, which has been directly linked with intervention quality (Hildebrand et al., 2012). For example, Resnick et al. (2011) proposed a treatment fidelity plan based on design, training, delivery, receipt, and enactment for stroke exercise interventions. In non-VR-based interventions, there is a great chance of inconsistency in delivering the treatment by a physiotherapist. VR-based treatments, in turn, are programmed, thus system functionality could be used as a proxy for treatment fidelity (Coons et al., 2011). While the study by Stanica et al. (2020) utilized a specific order for all of the participants to assure consistency in the treatment, none of the reviewed articles used a fidelity checklist explicitly.

3.6 Limitations and Future Study Recommendations

The included articles show the potential of VR-based interventions, coupled with physiological computing, for improved rehabilitation outcomes for stroke survivors. Notwithstanding, none of the articles followed a "randomized control trial" study design, which is preferred to investigate clinical results. Moreover, studies frequently reported a small sample size as a limitation, and only two articles reported a gender-balanced participant pool, thus making generalization of the results difficult (Miller et al., 1993; Butler et al., 2009). Moreover, several studies investigated the efficacy of an HMD-based intervention received in parallel with conventional therapy, thus making it difficult to truly gauge the benefits of the VR intervention per se. Overall, nonetheless, the results suggest that an additional VR-based intervention (in addition to the conventional treatment) is better than having two conventional treatments. Moreover, patient involvement is crucial for successful rehabilitation outcomes (Kristensen et al., 2016). As the majority of stroke patients will be older in age, they may be strangers to burgeoning VR and physiological computing (e.g., wearables) tools. Future studies should assure that sufficient training sessions and/or tutorials are provided and that the tasks can be achieved even by those with cognitive impairments resultant from the stroke. Incorporating some principles from iterative designing (Nielsen and Molich, 1990) and gamer user experience into the virtual environment could be beneficial (Tondello et al., 2016; Rajanen and Rajanen, 2018). Integrating many of the physiological computing tools directly into the VR headset could also alleviate some of these issues; such instrumented HMDs are already emerging (Cassani et al., 2018; Cassani et al., 2020a; Moinnereau et al., 2020).

Moreover, the examined studies measured intervention efficacy pre and post-intervention, thus providing limited insights on the long-term effects of VR-based rehabilitation. Future studies should focus on the long-term effects of these interventions. Moreover, the reviewed articles relied on "passive" physiological computing tools, in the sense that signals were measured and used to either change the virtual environment or to gauge intervention outcomes. More "active" tools, such as non-invasive brain stimulation (e.g., transcranial magnetic stimulation and transcranial direct current stimulation, tDCS), have recently emerged and shown to provide some success in rehabilitation when coupled with VR (Cassani et al., 2020b). Future studies could couple passive and active physiological computing (e.g., *via* an EEG-tDCS headset) and explore the benefits that such hybrid architectures could bring. As observed herein, the majority of the studies utilized EEG sensors to measure neural responses and plasticity. Functional near-infrared spectroscopy (fNIRS) is also emerging as a useful tool for plasticity monitoring (Balconi, 2016) and hybrid fNIRS-EEG headsets are already available in the market. As such, future studies could explore the advantages of integrating the improved spatial resolution advantages of fNIRS with the improved temporal resolution of EEG for stroke rehabilitation. Alternate feature representations, beyond simple ERD/ERS and EEG frequency subband powers, could also be explored as proxies of brain plasticity and intervention outcomes (Papadopoulos et al., 2021).

Regarding the effects of feedback type, studies herein showed that as more senses were stimulated, improved outcomes and attention could be observed. Recently, olfactory feedback has emerged as an additional feedback modality, as tools such as the OVR ION (OVR Tech, Burlington, VT, United States) have appeared in the market. Integrating olfactory feedback may further boost attention, sense of embodiment, and presence, which could show improvements in outcomes, as was the case in other allied domains (Gim et al., 2015; Longobardi et al., 2020). Additionally, none of the studies used glove-based haptic feedback systems. Such systems could provide finger tracking capabilities and individual finger and full hand vibrations, thus potentially also benefiting interventions of the upper limbs (Caeiro-Rodríguez et al., 2021; Gast et al., 2021). Lastly, the reviewed studies did not report experiments with patients suffering from post-stroke visual impairment/disturbances. Such patients may be incapable of benefiting completely from audio-visual VR-based interventions, thus multisensory experiences should be explored. The work of Wedoff et al. (2019) and Real and Araujo (2020), for example, leveraged the use of auditory and haptic stimuli to make VR experiences more accessible to those with visual impairments. In fact, VR interventions could potentially be used soon after the stroke to identify the risk of visual after-effects (Besic et al., 2019).

4 CONCLUSION

This paper systematically reviewed the recent literature on HMD-based VR stroke rehabilitation treatments, which leveraged the use of physiological computing. We described and discussed the technological aspects of existing solutions, study design, and intervention outcomes, as reported in the reviewed papers. Limitations of existing solutions are also described, and recommendations for future studies are provided. Ultimately, VR-based interventions coupled with physiological computing have been shown to improve patient attention and engagement, improve the sense of embodiment, allow for rewards to be given, thus increasing motivation, and allow for repeatable and consistent treatment. Combined, these factors could lead to improved rehabilitation outcomes.

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.

AUTHOR CONTRIBUTIONS

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

FUNDING

This work was funded by the Natural Sciences and Engineering Council (NSERC) of Canada (RGPIN-2021-03246).

ACKNOWLEDGMENTS

We thank Dr. Lucas R. Trambaiolli, Dr. Raymundo Cassani and Belmir de Jesus Junior for useful insights, comments, and discussions.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/frvir.2022.889271/full#supplementary-material

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