



Virtual Reality in Fibromyalgia: Does Altering Visual Feedback Impact on Pain and Movement During Reaching?

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People with fibromyalgia (FM) have movement-related fear impacting on daily activities. While virtual reality has been used as a distractor to promote exercise, it can be used to manipulate visual feedback (VF) about movement, potentially influencing pain and movement. Objectives: A. To determine whether altered VF modulates pain during movement; B. To compare adaptation to an altered VF between FM participants and healthy controls (HC); C. To explore relationships between adaptation, limb position sense, kinesiophobia and pain. 20 FM participants and 20 HC performed a reaching task during two sessions in a KINARM exoskeleton including a virtual reality interface allowing to replace their arm with a virtual arm. In one session, VF was altered to show GREATER movements while in the other it showed SMALLER movements (randomized order). Pain was assessed periodically using a numerical rating scale. Movement amplitude was assessed during exposure to altered VF (adaptation) and pre-/post-exposure (without VF; after-effects). Limb position sense was assessed with a KINARM task, and kinesiophobia was assessed with the Tampa Scale for Kinesiophobia (TSK-11). Pain intensity increased slightly with movement repetitions ($p < 0.001$), but did not differ between the VF conditions (GREATER vs. SMALLER). Both groups exhibited visuomotor adaptation, as shown by VF-dependent changes in movement amplitude and speed during exposure to altered VF, and by the presence of VF-dependent after-effects ($p < 0.001$ for all variables). However, no differences were observed across groups for any of these variables, despite the fact that FM had significantly more difficulty to correctly detect VF conditions than HC ($p = 0.046$). No clear limb position sense deficits were observed in FM participants, and no significant relationships were found between TSK-11 scores and changes in pain intensity during exposure to altered VF. Altering VF did not influence pain during a reaching task in the FM group. Surprisingly, both groups adapted similarly to altered VF. Visuomotor adaptation is therefore preserved in FM, despite impairments in sensory perception and the poor ability to detect VF alterations in the present study. Further research is warranted to clarify the relationship between sensory perceptions and motor control in FM.

Keywords: upper limb, motor adaptation, altered feedback, chronic pain, kinesiophobia

INTRODUCTION

Fibromyalgia (FM) syndrome is a chronic widespread pain condition (Wolfe et al., 2016) affecting 2.7% of the population (Queiroz, 2013), mainly women (McNally et al., 2006), and requiring a combination of pharmacological and non-pharmacological treatments (Goldenberg et al., 2004). Among non-pharmacological interventions, exercise has been shown beneficial (Mannerkorpi and Iversen, 2003; Busch et al., 2008; McLoughlin et al., 2011). However, FM is often associated with kinesiophobia, i.e. pain-related fear of movement (Turk et al., 2004), that can lead to activity avoidance and disengagement in daily participation, which may in turn contribute to maintaining and aggravating disability in FM patients (Vlaeyen et al., 1995; Asmundson et al., 1999; Turk et al., 2004; Karsdorp and Vlaeyen, 2009). Thus, targeting interventions that promote movement while also reducing kinesiophobia ought to be a promising avenue of treatment for FM patients.

Virtual reality (VR) in the management of pain is known to provide distraction from pain and to increase motivation to move (Keefe et al., 2012; Wiederhold et al., 2014; Jones et al., 2016). An alternative way of using VR consists of providing altered visual feedback (VF) about movements. Introducing a visual rotation or manipulating the visual gain induces trajectory or amplitude modifications, which can extend beyond the duration of the exposure to the manipulation (after-effects) and can occur without a conscious detection by the participant (Ghahramani et al., 1996; Krakauer et al., 2000; Heuer and Hegele, 2008; Bagce et al., 2013; Cressman and Henriques, 2015; Hayashi et al., 2016; Bourdin et al., 2019).

A recent study shows that altering VF to create the perception of smaller movement amplitude in people with chronic neck pain increases actual movement amplitude despite the fact that some participants did not notice the mismatch between the actual and the displayed movement (Chen et al., 2017). Moreover, manipulating the perceived neck rotation *via* a head-mounted display influenced the onset of pain (Harvie et al., 2015), although there is mitigated evidence on this matter (Kragting et al., 2020). Thus, a VR intervention based on altered VF for people with FM could potentially promote greater movement amplitude and alleviate pain intensity, as participants would perform greater movements without necessarily noticing it.

The general aim of the study was to assess whether altered VF about movement influenced pain intensity and movement kinematics in FM. The specific aims were: A—to determine whether altered VF (GREATER or SMALLER movement) modulates pain during movements; and B—to compare adaptation to an altered VF between FM and healthy controls (HC), both upon (B.1) and after (B.2; after-effects) exposure to altered VF. We hypothesized that: A—SMALLER VF would induce less pain than GREATER VF during reaching movements, since SMALLER VF would make the reaching movement seem less threatening, thus provoking less pain compared to a GREATER VF about that same movement; and that B—both FM and HC participants would adapt their movement amplitude and average speed upon (B.1) and after (B.2) exposure to altered VF, but that FM

would adapt to a lesser extent because patients with chronic pain have a less accurate detection of movement manipulation compared to healthy participants (Roosink et al., 2015; Brun et al., 2018b). This, combined with proprioceptive deficits that are frequently reported in chronic pain populations (Lewis et al., 2010; Claeys et al., 2011; Bank et al., 2013; Brun et al., 2018b), could affect their ability to adapt to altered VF. Finally, a secondary aim (aim C) was to explore relationships between adaptation upon exposure to altered VF, limb position sense, kinesiophobia and pain.

METHODOLOGY

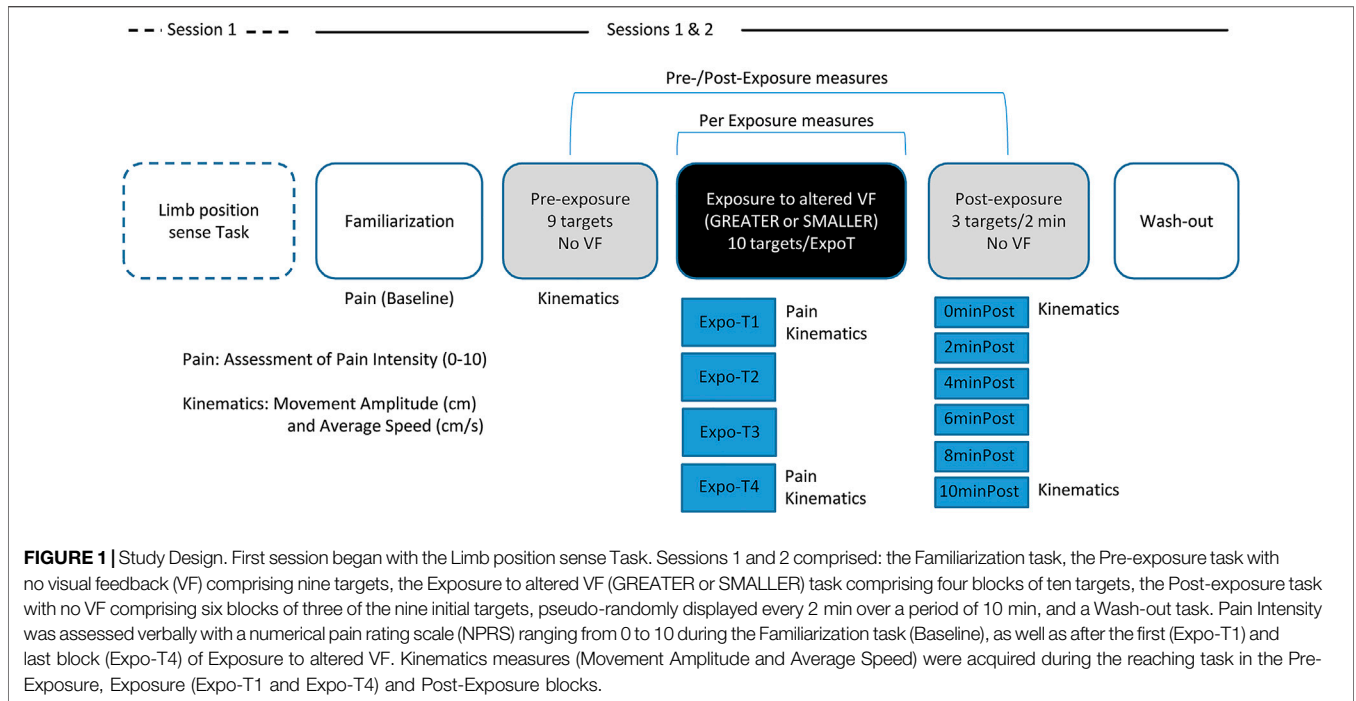
Participants and Ethics Statement

Participants with FM and age and sex matched HC participants were recruited. Inclusion criteria specific to the FM group were: adults (>18 years old) with a confirmed diagnosis of FM. Inclusion criteria specific to the HC group were: adults with no neurological or musculoskeletal disorders, including chronic pain. Exclusion criteria for both groups were: visual, motor or neurological impairment that could affect task performance, and having a body mass index over 30 (as this is usually incompatible with the robotic system employed in the study). Overall, 20 participants with FM and 20 age and sex matched HC participants were included in this study. They were recruited from Quebec City Fibromyalgia Association and from Laval University.

All participants provided their written informed consent prior to their participation to the study. The experiment was performed in accordance with the tenets of the Declaration of Helsinki and the study protocol was approved by the local ethical review board (Institut de réadaptation en déficience physique de Québec, Canada, no 2014-395).

Study Design

Participants from both groups took part in two experimental sessions separated by 7.9 ± 2.1 days. For the FM group, the first experimental session comprised an interview to gather clinical characteristics, including kinesiophobia (see Secondary Outcome Measures for details). Both groups were also required to complete a bilateral Limb position sense Task at the beginning of the first session. As for the rest of the two experimental sessions, they were identical for both groups and consisted of a visuomotor adaptation task comprising a series of target reaching movements with participants' self-reported dominant upper limb (UL) where a virtual UL replacing the actual UL displayed either a GREATER or SMALLER VF on movement. Participants were also required to complete a series of target reaching movements without VF (i.e. not seeing either their actual or virtual UL) before (PRE-) and after (POST-) exposure to altered VF (**Figure 1**). One VF condition (GREATER or SMALLER) was tested per session in a counterbalanced order for each group. Pain intensity was verbally assessed throughout the sessions (FM group only). For the FM group, the first experimental session lasted 90 min

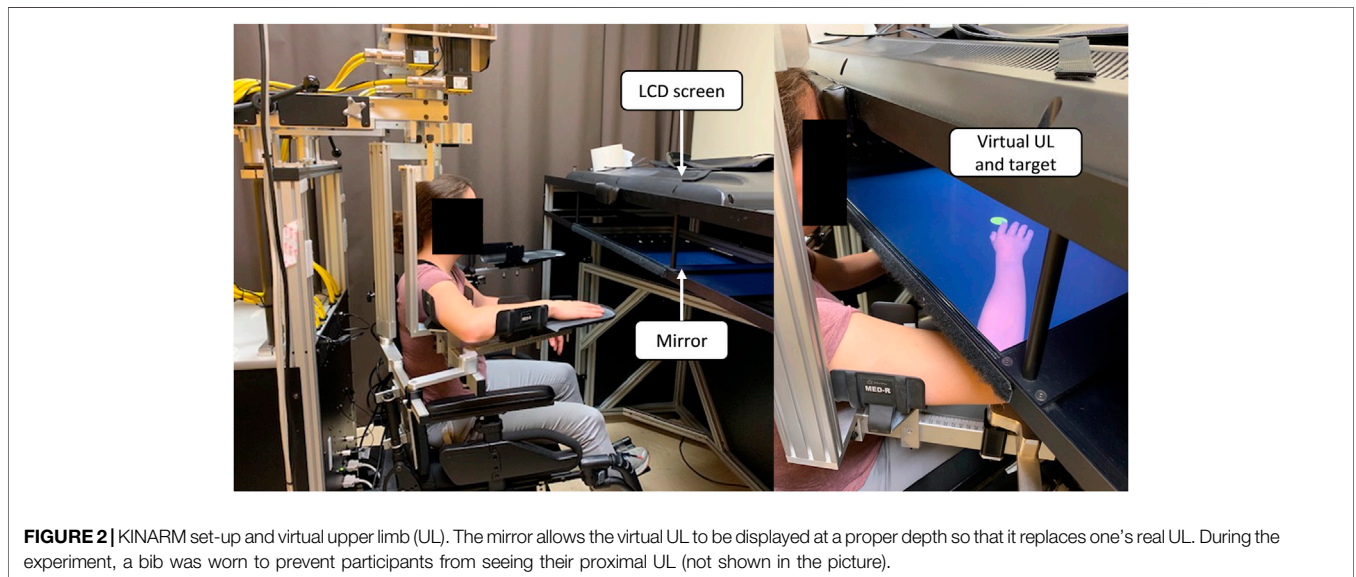


and the second session lasted 60 min. For the HC group, both sessions lasted 60 min.

Material and Procedure

The limb position sense Task and the Target Reaching Task were completed using the KINARM Exoskeleton Lab™ (KINARM, Kingston ON, Canada). The KINARM is a robotized bilateral exoskeleton allowing robot- or participant-driven movements of the elbow and shoulder joints in the horizontal plane. The robot is interfaced with a 2D virtual environment (Dexterit-E software, version 3.6) which samples participant’s elbow and shoulder

joints angles at a 1000 Hz frequency, allowing the display of a real-time feedback on movement with a virtual UL replacing the participant’s real UL (Figure 2). For the present study, actual ULs were obstructed from view in both tasks (Target Reaching Task and Limb position sense Task). For the Target Reaching Task, participants were provided with different types of VF on movement performed by a virtual UL: no VF, veridical VF, GREATER VF or SMALLER VF. This experimental set-up allowed for an immersive virtual experience. Since participants had control over the virtual ULs, which moved in accordance with their actual movements while their real ULs were concealed



from view, it enabled a sense of presence which is required in order to achieve immersion (Witmer and Singer, 1998).

Limb Position Sense Task

This task was performed using a KINARM Standard Task [Arm position matching task, version 3.6 (Dukelow et al., 2010)]. The robot randomly moved one of the participant's UL into one of four predefined positions, and the participant was required to mirror-match the position with the opposite UL. No VF was provided to the participant. Upon completion of the first round (24 trials), the opposite UL was tested. This task was used in previous studies to assess limb position sense in various clinical populations, including stroke (Dukelow et al., 2010) and a chronic pain populations (Brun et al., 2018b; Brun et al., 2020).

Target Reaching Task

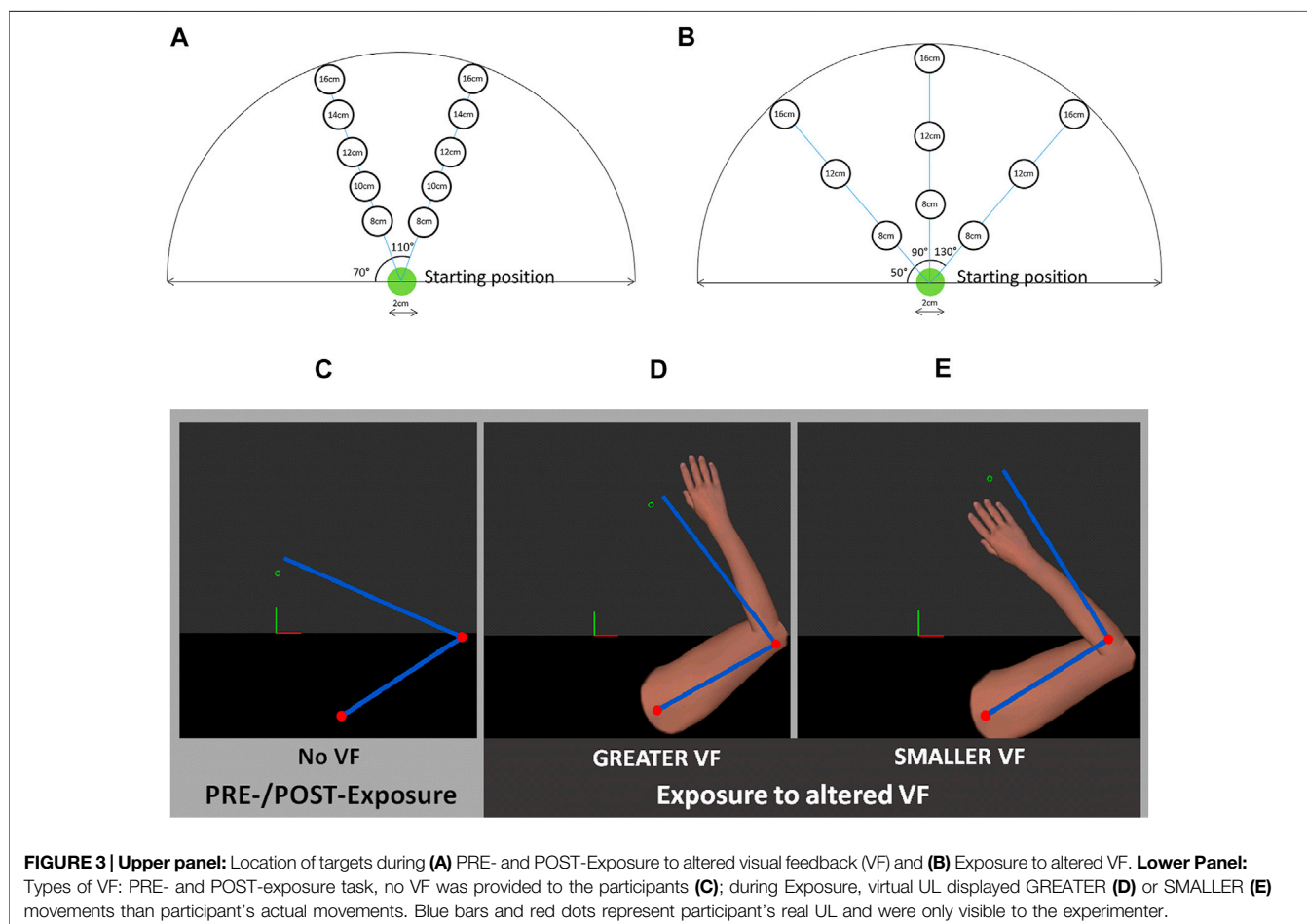
Familiarization

After a calibration procedure, participants performed a familiarization task consisting in six reaching movements toward virtual targets using a virtual UL displaying their own movements with a veridical VF on movement. This was achieved to familiarize the participants with the exoskeleton as well as with the reaching task. This task was completed again at the end of

each session (wash-out) to minimize potential carry-over effects of altered VF.

Exposure to Altered Visual Feedback

Participants were required to reach toward a series of ten randomly displayed targets (presented one by one) with their self-reported dominant hand, with a virtual UL displaying an altered VF either GREATER or SMALLER than one's own movements. Targets had a 2 cm diameter and were presented either at $\pm 20^\circ$ from midline, requiring a reaching movement of 8, 10, 12, 14 or 16 cm from the starting position, thus involving an average movement amplitude of 12 ± 3.2 cm (Figure 3A). The altered VF corresponded to a 1.5 magnification (GREATER VF—Figure 3D) or a corresponding minimization (0.67, SMALLER VF—Figure 3E) of the index fingertip position; the displayed fingertip position was scaled with respect to the starting position. Visual target display was also scaled so that the actual movement required was similar between conditions. The distance between the fingertip position and the starting position was first scaled with the desired factor (1.5 or 0.67). Then, using available code from the manufacturer, this scaled position of the fingertip position was used to retrieve angles at shoulder and elbow. These “scaled” angles were then used to display the virtual arm according to the selected scaling factor. It is important to note



that only the VF differed between conditions; the actual movement needed to reach the targets being identical for both VF conditions. Participants were instructed to reach as precisely as possible toward the center of each target with the virtual index fingertip and to move at a comfortable pace. At the beginning of the first trial, the UL was passively moved by the robot to the starting position target. At the beginning of each trial, the starting position target was displayed for 2 s (**Figure 3A**), after which one of the ten targets would appear. Participant had to reach to the target with their index fingertip and maintain this position for 2 s. Target then disappeared while the starting position target reappeared, which marked the beginning of the next trial. Participants completed a total of 40 trials, separated in four blocks (Expo-T1, Expo-T2, Expo-T3, Expo-T4). Only one target was displayed at any given time (either the starting position target or one of the ten targets).

PRE- and POST-Exposure: No Visual Feedback

Participants had to complete a series of target reaching movements with no VF on movement (**Figure 3C**). Targets had a 2 cm diameter and were presented either at midline or at $\pm 40^\circ$ from midline, and at a distance of 8, 12, or 16 cm from the starting position, thus requiring an average movement amplitude of 12 ± 4 cm (**Figure 3B**). At the beginning of the first trial, the UL was passively moved by the robot to a starting position and a visual cue was provided to the participants once this was achieved. Once the starting position had been maintained for 2 s, targets were randomly displayed one by one. Note that the position of these targets was slightly different from the ones used during the exposure to altered VF in order to assess whether the adaptation to altered VF would generalize to various movements. Participants were instructed to reach as precisely as possible toward the center of each target, moving at a comfortable pace, and to give a verbal cue once they had reached the target. Once this was achieved, participants had to go back to the starting position in order to launch the next trial.

PRE-Exposure: Prior to Exposure, participants reached once toward each of the nine targets (randomly displayed).

POST-Exposure: This task comprised the same nine targets as the Pre-Exposure task, but split into three blocks (average required movement amplitude for each block: 12 cm) which were presented in a pseudo-random order every 2 min over a 10 min period. Overall, each block was repeated twice.

Outcome Measures

Primary Outcome Measures: Pain Intensity and Kinematics (Movement Amplitude, Average Speed)

Pain Intensity

Pain Intensity was assessed verbally with a Numerical Pain Rating Scale (NPRS) ranging from 0 (no pain) to 10 (worst possible pain). This outcome was measured at rest at different time points throughout the sessions: 1- After the Familiarization task (Baseline); 2- After the first altered VF exposure block (Expo-T1) and 3- After the fourth altered VF exposure block (Expo-T4).

Kinematics

Movement Amplitude (cm) was calculated for each trial as the length of a vector between the starting position and the index

fingertip position at the end of movement. The end of movement was defined as the x and y coordinates where participant's reaching movement stopped (speed < 2 cm/s), before readjustments; **Average Speed** (cm/s) was calculated for each trial among the vector corresponding to Movement Amplitude.

Both kinematic variables were computed from the index fingertip position calculated in real-time by the Dexter-E software using custom-made MATLAB 2013 scripts (Mathworks inc., Massachusetts).

Alteration Detection

In order to assess explicit awareness of the alteration, participants were asked to identify which VF condition they had been exposed to at the end of each session. Reported answers were either "GREATER VF," "SMALLER VF" or "Don't know." Note that at the beginning of each session, participants were told that VF would either be GREATER or SMALLER. They did not know whether VF condition would be different or the same between the two sessions.

Secondary Outcome Measures: Limb Position Sense and Clinical Characteristics

For the Limb position sense Task, the mean absolute distance errors (cm) in the x- and y-axes across trials were obtained for both ULs.

Clinical characteristics for the FM group were gathered at the beginning of the first session and included a brief medical history (time since diagnosis, comorbidities, medication, Pain intensity) as well as the completion of the TSK-11. The TSK-11 is a self-reported questionnaire assessing movement-related fear among people suffering from chronic pain. Its score ranges between 11–44, with higher scores indicating greater movement-related fear of pain (George et al., 2012). A French-Canadian version of this questionnaire has been validated (French et al., 2002).

Statistical Analysis

Results are reported as mean \pm standard deviation (SD). An independent *t* test (2-tailed) was used to compare groups for age, and a Fisher's exact test was used to compare groups for handedness.

Objective A: Impact of Altered Visual Feedback on Pain

Pain Intensity was analyzed using a 2 [VF condition (GREATER or SMALLER)] \times 3 [Time (Baseline, Expo-T1, Expo-T4)] repeated-measures analyses of variance (rmANOVA). It was hypothesized that SMALLER VF would induce less pain than GREATER VF during reaching movements.

Objective B.1: Adaptation to Altered Visual Feedback Upon Exposure Across Groups

Movement Amplitude and Average Speed were analyzed for the altered VF exposure phase using 2 [Group (FM or HC)] \times 2 [VF condition (GREATER or SMALLER)] \times 2 [Time (Expo-T1, Expo-T4)] rmANOVAS. It was hypothesized that both FM and HC would adapt their movement amplitude and average speed, but to a lesser extent for the FM group. Adaptation should manifest as a

decrease in movement amplitude and speed over time when exposed to GREATER VF (and vice-versa for SMALLER VF) to ultimately achieve similar movement amplitude and average speed for both VF conditions by the end of exposure.

Alteration Detection

To assess whether participants were aware of the visual manipulation, the proportion of correct identification of both VF conditions among Groups was assessed using chi-square test of independence.

Objective B.2: Adaptation to Altered Visual Feedback: After-Effects Across Groups

For the PRE- and POST-Exposure phases, Movement Amplitude and Average Speed were analyzed using 2 [Group (FM or HC)] \times 2 [VF condition (GREATER or SMALLER)] \times 3 [Time (PRE, 0 minPOST, 10 minPOST)] rmANOVAs. It was hypothesized that both FM and HC would show after-effects, but to a lesser extent for the FM group. Expected after-effects would be a decrease in movement amplitude and average speed following exposure to a GREATER VF (and vice-versa for SMALLER VF) (Cressman and Henriques, 2015).

Two participants from the HC group and one participant from the FM had to be excluded from the Average Speed analysis as their movements were too jerky, hence it was not possible to calculate their Average Speed.

Objective C: Relationships Between Adaptation, Limb Position Sense, Kinesiophobia and Pain

Whether FM participants showed proprioceptive deficits was first established by analyzing errors in the Limb position sense task using a 2 [Groups (FM or HC)] \times 2 [Error direction (*x*-axis or *y*-axis)] rmANOVA.

The different variables of interest were assessed using Kendall's tau correlation coefficients.

Normal distribution of the data was assessed using the Kolmogorov-Smirnov goodness-of-fit test, homoscedasticity was assessed using Levene test and sphericity was assessed with Mauchly test. Greenhouse-Geisser correction was used when the assumption of sphericity was not respected. For all comparisons, $p < 0.05$ (two-sided) was considered statistically significant. Post-hoc analyses were performed using SIDAK correction.

All statistical analyses were performed using IBM SPSS Statistics software version 25.0 (IBM Corp., Armonk, New York).

RESULTS

Participants' demographic characteristics (age, handedness, gender) and FM participants' clinical characteristics (time since diagnosis, average pain intensity, and TSK-11 scores) are reported in **Table 1**. HC and FM groups did not differ in terms of age or handedness.

Objective A: Impact of Altered Visual Feedback on Pain in the Fibromyalgia Group

No main effect of VF on Pain was observed [$F(1, 19) = 0.37$, $p = 0.55$] for the FM group. There was a main effect of Time on Pain [$F(1.5, 29.1) = 17.5$, $p < 0.001$, $\eta_p^2 = 0.48$], which increased over the course of the experiment (**Figure 4**). Post-hoc analyses revealed that Pain intensity was greater at Expo-T4 compared to Expo-T1 ($p = 0.031$) and Baseline ($p < 0.001$), and that Pain intensity was greater at Expo-T1 compared to Baseline ($p = 0.001$). Notably, average Pain at Expo-T4 was comparable to that reported by participants over the last 24 h, suggesting that task-induced Pain was not worse than that associated with regular daily activities. There was no interaction between Time and VF, both VF conditions leading to similar increases in Pain [$F(2, 38) = 0.13$, $p = 0.88$].

Objective B.1: Adaptation to Altered Visual Feedback Upon Exposure Across Groups

In order to assess adaptation to altered VF upon exposure, Movement Amplitude and Average Speed changes between the beginning (Expo-T1) and the end (Expo-T4) of exposure to altered VF were analyzed.

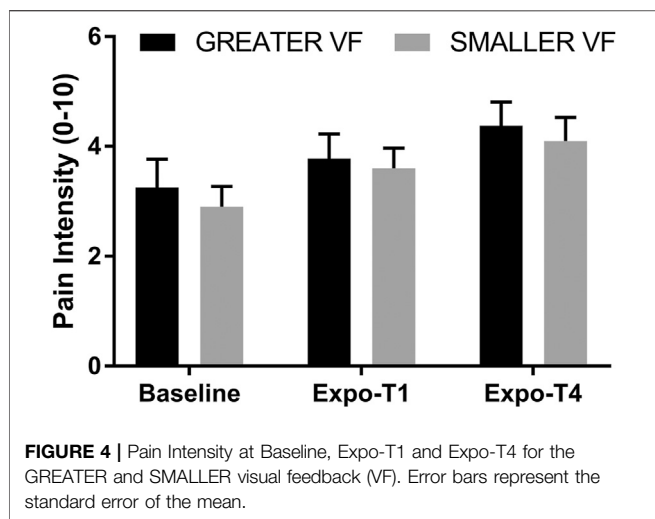
Movement Amplitude

Both groups adapted their movements to both VF conditions, as shown by changes in Movement Amplitude that were specific to the VF condition (**Figure 5A**). There was a significant interaction between Time and VF [$F(1,38) = 20.6$, $p < 0.001$, $\eta_p^2 = 0.35$]. Post-hoc analyses revealed that for the SMALLER VF condition, movement amplitude increased over time during exposure ($p < 0.001$) whereas for the GREATER VF condition, movement amplitude decreased over time during exposure ($p = 0.02$). It is also of interest to note that by the end of exposure (Expo-T4), Movement Amplitude tends to be closer to 12 cm for both VF conditions (**Figure 5A**), which is the real average amplitude required to reach the targets. There was a main

TABLE 1 | Participants' demographic characteristics.

Demographics: Mean \pm SD	FM group (n = 20)	HC group (n = 20)	Difference across groups (statistics)
Age (mean \pm SD)	46.1 \pm 11.9 years	43.4 \pm 11.9 years	$t(38): 0.70$, $p = 0.49$
Handedness	20 right-handed	18 right-handed, 2 left-handed	Fisher's exact test: $p = 0.49$
Gender (women: men)	20:0	20:0	N/A
TSK-11 scores (mean \pm SD)	26.6 \pm 6.3	N/A	N/A
Average pain in the last 24 h (mean \pm SD)	4.9 \pm 1.7	N/A	N/A
Years since diagnosis (mean \pm SD)	7 \pm 7 years	N/A	N/A

FM, Fibromyalgia; HC, Healthy controls; SD, Standard deviation; TSK, Tampa Scale for Kinesiophobia; N/A, not applicable.



effect of VF on Movement amplitude [$F(1,38) = 63.4, p < 0.001, \eta_p = 0.63$], however there was no main effect of Time [$F(1,38) = 3.72, p = 0.06$] as a result of the interaction. Altogether, these results show that participants adapted their reaching movement by altering movement amplitude in a way that is consistent with the displayed VF. Importantly however, there was no main effect of Group [$F(1,38) = 0.06, p = 0.81$], nor any significant interaction between Group and the other variables, meaning that adaptation was similar between FM and HC.

Average Speed

As for Movement Amplitude, both groups adapted their Average Speed in a way that is consistent with the displayed VF condition (Figure 5B), but this adaptation was similar across groups. There was a significant interaction between Time and VF [$F(1, 38) = 29.9, p < 0.001, \eta_p = 0.44$]; post-hoc analyses revealed that at Expo-T1, Average Speed was greater for the GREATER VF condition compared to the SMALLER VF condition ($p < 0.001$), whereas there Average speed was not statistically different between GREATER and SMALLER VF at Expo-T4

($p = 0.92$). Those results show that participants adapted their movement Speed to both VF conditions. There were also main effects of VF [$F(1, 38) = 6.28, p = 0.02, \eta_p = 0.14$] and Time [$F(1, 38) = 38.4, p < 0.001, \eta_p = 0.50$] on Average Speed. Importantly however, there was no main effect of Group [$F(1,38) = 0.20, p = 0.66$], nor any significant interaction between Group and the other variables, again indicating that adaptation was similar between FM and HC. The absence of a Group effect also indicates that even though movements were performed at a self-selected comfortable speed, FM participants produced movements that were comparable to those of HC participants.

Alteration Detection

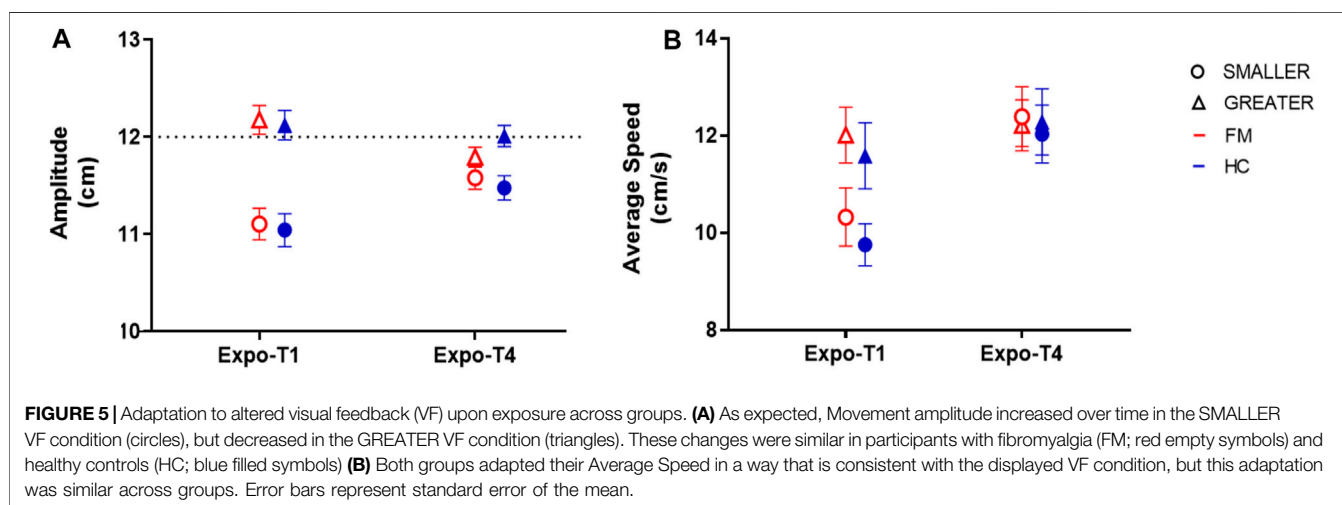
After each session, participants were asked to identify which VF condition they had been exposed to. 20% of FM participants and 50% of HC participants correctly identified both VF conditions. Chi-square test revealed a significant relation between Group and accurate identification of altered VF [$\chi^2(1, N = 40) = 3.95, p = 0.046$].

Objective B.2: Adaptation to Altered Visual Feedback: After-Effects Across Groups

In order to assess the presence of after-effects after exposure to altered VF, changes in Movement Amplitude and Average Speed between Pre- and Post-exposure (0 minPost-exposure and 10 minPost-exposure) phases were analyzed.

Movement Amplitude

Both groups displayed after-effects for both VF conditions, that is, changes in Movement Amplitude in the Post-exposure phase compared with the Pre-exposure phase (Figure 6A). There was a significant interaction between Time and VF [$F(1.7, 66.4) = 33.2, p < 0.001, \eta_p = 0.47$]; post-hoc analyses revealed that Movement Amplitude was not different between SMALLER and GREATER VF in the Pre-exposure phase ($p = 0.13$), whereas at 0minPost-exposure, Movement Amplitude was greater for the SMALLER VF condition than the GREATER VF condition ($p < 0.001$), and this difference remained present at 10minPost-exposure ($p <$



0.001). Those results are consistent with the after-effects expected Post-exposure to GREATER and SMALLER VF. There were also main effects of VF [$F(1, 38) = 99.4, p < 0.001, \eta_p = 0.72$] and Time [$F(1.4, 54.4) = 13.5, p < 0.001, \eta_p = 0.26$] on Movement Amplitude; post-hoc analyses revealed that Movement Amplitude was greater in the Pre-exposure phase compared to 0minPost-Exposure ($p = 0.005$) and to 10minPost-exposure ($p < 0.001$). However, the difference between 0minPost and 10minPost was not statistically significant ($p = 0.053$). There was no effect of Group on Movement Amplitude [$F(1,38) = 2.24, p = 0.14$], and the only significant interaction involving Group did not involve VF {Group*Time interaction [$F(1.4, 54.4) = 7.4, p = 0.004, \eta_p = 0.16$], the Control Group making slightly larger movements than FM group prior to exposure ($p = 0.013$)}. Overall, these results suggest that both groups displayed similar after-effects Post-exposure to altered VF.

Average Speed

As for Movement Amplitude, participants adapted their Average Speed Post-Exposure to both altered VF conditions (Figure 6B). There was a significant interaction between Time and VF [$F(1.8, 63.6) = 16.1, p < 0.001, \eta_p = 0.32$]; post-hoc analyses revealed that Average Speed was not different between the two VF conditions prior to exposure ($p = 0.42$). At 0minPost-exposure, Average Speed was greater after the SMALLER VF condition than the GREATER VF condition ($p < 0.001$), and this pattern was maintained at 10minPost-exposure ($p = 0.001$). There were also main effects of VF [$F(1, 35) = 30.5, p < 0.001, \eta_p = 0.47$] and Time [$F(1.6, 57.3) = 4.48, p = 0.02, \eta_p = 0.11$] on Average Speed; post-hoc analyses revealed that Average Speed was greater in the Pre-exposure phase compared to the 0minPost-exposure phase ($p = 0.04$) and the 10minPost-exposure phase ($p = 0.03$). However, the difference between 0minPost and 10minPost was not statistically significant ($p = 0.77$). There was no effect of Group on Average Speed Pre- and Post-exposure to altered VF [$F(1,35) = 1.88, p = 0.18$], nor any significant interaction between Group and the other variables, again indicating that adaptation was similar between FM and HC.

Objective C: Relationships Between Adaptation, Limb Position Sense, Kinesiophobia and Pain

Limb Position Sense

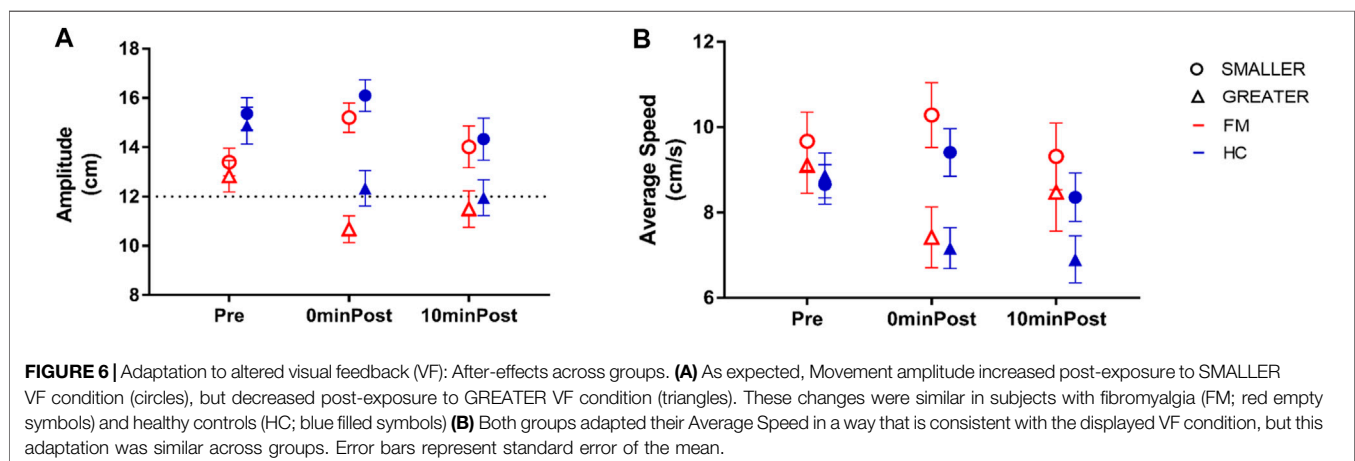
The rmANOVA revealed no main effect of Group on mean errors [$F(1,38) = 0.17, p = 0.68$], both groups displaying similar errors for a specific direction (x- or y-axis), although there was a significant main effect of the Error direction, participants displaying larger errors in the x-axis than in the y-axis [$F(1, 38) = 75.9, p < 0.001, \eta_p = 0.67$]. No significant interaction was observed between Group and Error direction [$F(1, 38) = 0.22, p = 0.64$]. Figure 7A shows an example of representative participants from each group. Figure 7B shows the mean errors in the x- and y-axes for each group. As no deficit in Limb position sense nor deficits in adaptation were observed, associations with changes in Pain were not further assessed.

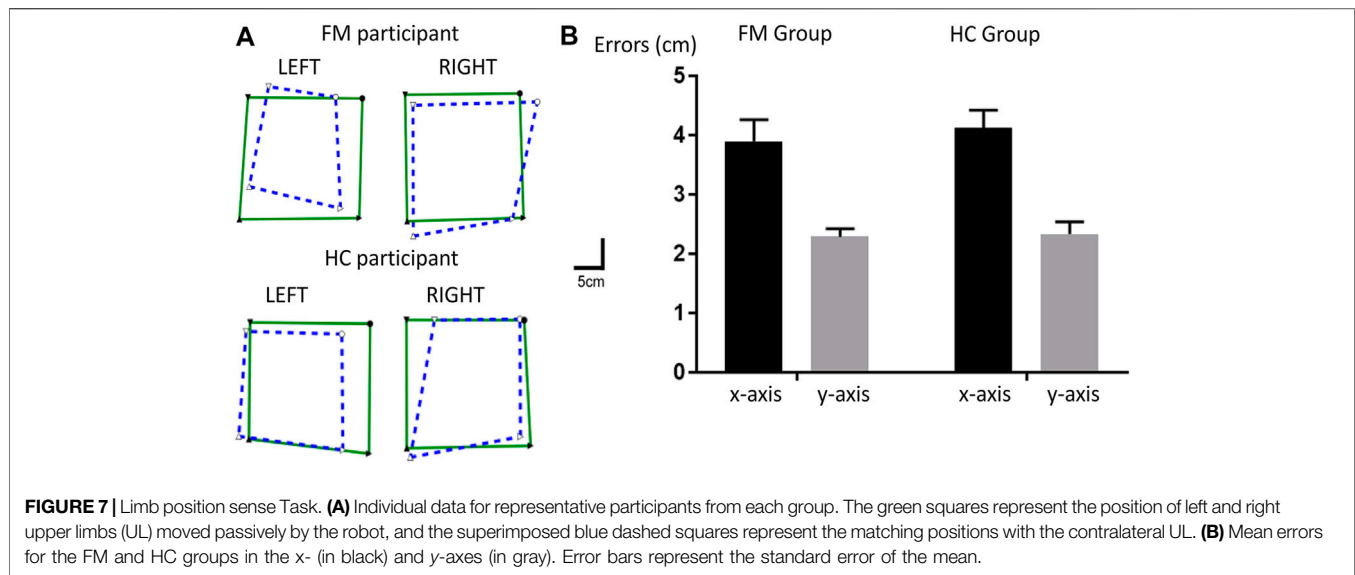
Kinesiophobia

Mean score for the TSK-11 was 26.6 ± 6.3 . Kendall's tau coefficient between TSK-11 scores and changes in Pain intensity between Expo-T1 and Expo-T4 pooled for both VF conditions was not statistically significant ($\tau = 0.048, p = 0.8$). As no deficits in adaptation were observed, no further assessment of relationship between kinesiophobia and adaptation were conducted.

DISCUSSION

The general aim of this study was to assess whether altered VF influenced pain intensity and UL kinematics in FM participants. Overall, the results showed that altered VF did not impact on pain intensity and that both FM and HC adapted their movement amplitude and speed upon and after exposure to SMALLER and GREATER VF, without any differences observed between FM and HC while FM participants had more difficulty to detect the altered VF. Interestingly, this difficulty to detect the altered feedback was observed despite the absence of significant deficits in Limb position sense in the FM group. This apparent





discrepancy could be explained by the fact that assessment of Limb position sense mainly depends on the processing of afferent feedback (the tested arm being positioned passively), while the detection of visuomotor mismatch is likely to rely not only on afferent proprioceptive feedback, but also on motor efferences. Interestingly, higher conflict sensitivity (i.e. sensory disturbances evoked when the visual feedback is altered in a very obvious manner) in fibromyalgia has been recently shown to occur mainly in sensory-motor conflicts rather than in sensory-sensory conflicts, which could reflect a deficit in updating predicted sensory feedback (Brun et al., 2020). Finally, no significant association was found between kinesiophobia and changes in pain intensity during exposure to altered VF.

Contrary to our hypothesis, altering the VF about movement amplitude and velocity during a reaching task does not impact on resting pain after each condition. This contrasts with results from previous studies in various chronic pain populations showing that various manipulations of VF induce pain reduction, such as altering the size of the limb in complex regional pain syndrome (CRPS) (Moseley et al., 2008; Matamala-Gomez et al., 2019), its transparency in peripheral nerve injury (Matamala-Gomez et al., 2019), or the perceived rotation amplitude of the neck in chronic neck pain (Harvie et al., 2015). The rationale put forward by the authors to account for these results is generally based on the presence of maladaptive reorganization within the sensorimotor cortices in these populations. For instance, functional magnetic resonance imaging and magnetoencephalography studies led with CRPS patients have shown smaller cortical representation of the affected limb within the primary somatosensory cortex (S1) contralateral to the lesion (Di Pietro et al., 2013). Similar anomalies in the somatosensory processing have also been identified in the FM population (Kim et al., 2015), although clinical pain patterns are quite different compared to the aforementioned chronic pain populations in that FM is associated with widespread pain (Wolfe et al., 1990), as opposed to regional pain, for instance in CRPS (Harden et al., 2010). In light

of the aforementioned studies, it was relevant to test whether altering the VF about movement would modulate pain, as it has been shown with other types of VF alterations. However, recently published work makes it less clear whether altering VF has an impact on pain. For instance, results from Harvie et al. were not replicated in a multicenter study undergone with a larger sample (Kragting et al., 2020). Moreover, recent systematic review (Heinrich et al., 2020) and meta-analysis (Wittkopf et al., 2018) put in light mitigated results obtained from studies altering the size of painful body parts in the treatment of chronic pain populations. One factor that could account for the discrepancies between studies is whether feedback manipulations were explicitly perceived by participants. It has been shown that activation of the primary somatosensory cortex reflects the perceived rather than the physical characteristics of the stimulus (Chen et al., 2003), highlighting the influence of perception on sensorimotor cortices activation (Chen et al., 2003; McCabe et al., 2009). It is important to note that manipulation of VF was only correctly detected by 20% of FM participants in the present study. Therefore, it can be suggested that accurate perception of visual manipulations is necessary to influence pain ratings in VR environments. Moreover, considering the fact that people with pain have more difficulty to identify visual manipulations (Roosink et al., 2015; Harvie et al., 2016; Brun et al., 2018b) than pain-free individuals, larger feedback manipulations (i.e. easier to detect than in the present study) might be needed to impact on pain. Furthermore, the fact that most FM participants did not detect the VF alterations could also explain why there was no relationship found between pain and kinesiophobia. The rationale behind the hypotheses in the present study was that a SMALLER VF would make the reaching movement seem less threatening, thus provoking less pain compared to a GREATER VF about that same movement. But, without a conscious awareness of the alteration, the only thing perceived will be the visuomotor mismatch, which will likely increase Pain since

FM are more sensitive to perceptual mismatches (Brun et al., 2020). More research is warranted to acquire a more thorough understanding of the role of awareness of visuomotor mismatch in pain modulation. FM adapted their movement amplitude and speed to the same extent as HC upon and after exposure to altered VF. Since FM participants had significantly more difficulty to correctly identify both VF alterations compared to HC participants, this result confirms that of from previous studies showing that explicit knowledge of the alteration is not a pre-requisite for visuomotor adaptation (Bourdin et al., 2019). On a clinical point of view, it is tempting to infer that abnormal sensory perceptions lead to altered motor control, but literature suggests that this relationship is not as straightforward. (Brun et al., 2018a; Brun et al., 2020). In a study involving CRPS and HC participants, both groups performed similarly in a target location task, despite differences in sensorimotor integration for the CRPS participants compared to HC (Bultitude and Petrini, 2021). Moreover, a recent study involving visuomotor conflicts in FM vs. HC demonstrated that while people with FM are more perceptually sensitive to visuomotor conflicts (i.e. reporting higher sensory disturbances), motor disturbances induced by conflict were similar between groups (Brun et al., 2020). Comparable results have been obtained in healthy people with experimental tonic pain (Brun et al., 2017), suggesting a dissociation between the effect of pain on perception and action.

Supporting that view, alterations in the treatment of sensory information and multisensory integration have been reported in FM and other chronic pain conditions (McDermid et al., 1996; McCabe et al., 2009; Martinez et al., 2018; Martínez et al., 2019), while transcranial magnetic studies have shown no evidence of sensorimotor integration deficits in either acute or chronic pain [measured with short afferent inhibition (Turton et al., 2007; Mercier et al., 2016; Vuralli et al., 2019)]. Studies looking specifically at the effect of pain on upper limb motor learning have produced mixed results, but overall do not reveal major upper limb motor learning deficits in the presence of pain (Ingham et al., 2011; Dancey et al., 2014; Dancey et al., 2016a; Dancey et al., 2016b; Lamothe et al., 2014; Bilodeau et al., 2016; Mavromatis et al., 2017; Parker et al., 2017; Salomoni et al., 2019). Importantly, most of these studies have been conducted in acute experimental pain models, the present study being one the few focusing on individuals with chronic pain. In a study conducted with painful arthritic hand patients and HC, motor performance in a motor skill training task was overall similar between groups, suggesting preserved motor function and skill learning among the patient group (Parker et al., 2017). Furthermore, in prismatic adaptation studies with CRPS patients, visuomotor adaptation was preserved as shown by large pointing errors in the first open-loop movements that faded with repetition (corresponding with visuomotor adaptation) and after-effects following removal of prismatic goggles (Bultitude and Rafal, 2010; Christophe et al., 2016), although these studies did not comprise a control group to compare adaptation with, making the results of the present study all the more relevant.

In order to assess the external validity of the present study, it is relevant to question whether our FM group was representative of

the FM population in terms of average pain, kinesiophobia and proprioceptive deficits. Since our participants were recruited from the general public—and not from a clinical facility (e.g. Pain clinic), it is likely that they displayed on average less pain and higher levels of function compared to the FM patients seen in outpatient programs, hence making them less different from HC participants than in other studies. For instance, in a study conducted with 36 FM patients recruited from outpatient pain programs, average reported pain intensity over the last 24 h was 6.9 ± 1.9 on a 0–10 visual analog scale (Brun et al., 2018c) compared to 4.9 ± 1.7 in the present study. As for kinesiophobia, in a study involving 391 FM participants (Roelofs et al., 2007), the mean TSK-11 score was 24.5 ± 6.1 , which indicates overall similar levels of kinesiophobia to that recorded in the present study (mean TSK-11 score: 26.6 ± 6.3). In terms of proprioceptive deficits, both FM and HC groups in the present study displayed similar errors in the Limb position sense. Literature supporting the presence of proprioception deficits among FM syndrome is scarce and it is unclear whether people with FM have more proprioceptive deficits than HCs. While Celenay et al. found poorer trunk position sense in FM (Toprak Celenay et al., 2019), Akyol et al. found no differences between the FM and HC group in terms of proprioceptive acuity of the knee joint (Akyol et al., 2013). Similarly, Bardal et al. found no differences between FM and HC in the shoulder joint position sense test. Most relevantly, in a previous study in our lab using the same Limb position sense Task as the present study in a different sample of participants, no differences were found between FM and HC (Brun et al., 2020). Therefore, it appears that FM participants from the present study are representative of the FM population in terms of Pain, kinesiophobia and proprioception. It is important to acknowledge however that the sample size remains limited, raising the possibility of type two errors, especially for Time*VF*Group interaction (power being between 0.07 and 0.42 for the interaction term). Therefore, while the results clearly show that participants with FM are well able to perform visuomotor adaptation, no definitive conclusion can be reached on the absence of difference from controls. Nevertheless, no trend was observed, making it unlikely that major deficits would be observed with a larger sample. A limit of the current study is that participants were asked to identify VF conditions without a two-alternative forced choice. As a result, some participants answered that it felt like the VF was true to their own movements—even though they were told that VF would be either GREATER or SMALLER than their own movements. As a result, it was only possible to identify which participants had correctly identified both VF conditions (and not the participants who had wrongly identified one or both VF conditions). In the future, it would be relevant to assess accuracy of detection with a two-alternative forced choice in order to assess whether one VF condition was more easily detected than the other, and also what is the relationship between accurate detection and Pain.

In conclusion, although FM is associated with abnormalities in sensory processing (McDermid et al., 1996; McCabe et al., 2009) and kinesiophobia, this did not seem to interfere with participants' capacity to adapt their movements to an altered

VF during a reaching task. But while visuomotor adaptation is preserved in FM, an intervention based on adaptation to SMALLER VF not did alleviate pain, nor promote greater movement amplitude compared to GREATER VF. Further research needs to be done in order to clarify the relationship between sensory perceptions and motor control in the FM population. As studies using various VR interventions continue to be conducted with chronic pain populations, one ought to be cautious when it comes to generalizing efficacy of treatment. In fact, further research shall try to clarify the mechanisms underlying pain alleviation in VR paradigms with specific chronic pain populations and the role of awareness in the modulation of pain.

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 studies involving human participants were reviewed and approved by the Comité d'éthique et de recherche du CIUSSS de la Capitale Nationale. The patients/participants provided their written informed consent to participate in this study.

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AUTHOR CONTRIBUTIONS

CM and CB designed the study; AO and MD performed data collection; CM, CB, and MD analyzed and interpreted the data; MD drafted the paper; MD, CB, AO, and CM commented on the paper and approved the final version.

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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.

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