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The Contribution of Motor Commands to the Perturbations Induced by Sensorimotor Conflicts in Fibromyalgia

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Abstract—Individuals with pain report higher sensory disturbances during sensorimotor conflicts compared to pain-free individuals. In the pain field, it is frequently assumed that disturbances arise from a discordance between sensory and efference copies (defined as *sensory-motor* conflict), while in the sensorimotor control field they are considered to result from the incongruence between sensory modalities (defined as *sensory-sensory* conflict). The general aim of this study was to disentangle the relative contribution of motor efferences and sensory afferences to the increased sensitivity to sensorimotor conflicts in individual with fibromyalgia (n = 20) compared to controls (n = 20). We assessed sensory and motor disturbances during *sensory-sensory* and *sensory-motor* conflicts using a robotized exoskeleton interfaced with a 2D virtual environment. There was a significant interaction between the group and the type of conflict (p = 0.03). Moreover, the increase in conflict sensitivity from *sensory-sensory* to *sensory-motor* conflicts in fibromyalgia was related to conflict-induced motor disturbances (r = 0.57; p < 0.01), but did not result from a poorer proprioception (r = 0.12; p = 0.61). Therefore, it appears that higher conflict sensitivity in fibromyalgia is mainly explained by a *sensory-motor* conflict rather by a *sensory-sensory* conflict. We suggest this arises due to a deficit in updating predicted sensory feedback rather than in selecting appropriate motor commands.

Key words: sensorimotor conflict, chronic pain, fibromyalgia, sensorimotor control, virtual reality.

INTRODUCTION

Sensorimotor integration is crucial for the planning of our movements as well as their online monitoring and correction, but also to build a unified representation of our body. To this end, afferent signals (as visual and proprioceptive information) and efferent copies of motor commands are optimally integrated. According to the Bayesian integration framework, the contribution of each signal is weighted based on its reliability, thus meaning that a signal with low variance (i.e. reliable) is weighted more heavily than a signal with high variance (i.e. noisy) (Ernst and Banks, 2002; van Beers et al., 2002; Scott, 2004; Reuschel et al., 2010; Metral et al., 2013). Under certain circumstances, these different signals (sensory afferences and efference copies) might convey incongruent information, creating a sensorimotor conflict. In this article, sensorimotor conflict is a general term that incorporates both *sensory-sensory* conflicts (conflicts between various sensory modalities) and *sensory-motor* conflicts (conflicts between sensory and efference copies of motor commands). Such sensorimotor conflicts have been shown to induce both sensory and motor disturbances (i.e. altered perception or motor performance when compared to conditions without conflict) (Brun et al., 2017, 2018a; Katayama et al., 2018; Osumi et al., 2018), providing some insight into the role of sensorimotor integration in perception and action. It has been proposed that the brain tries to minimize the occurrence of such conflicts in three ways: (1) by selectively ignoring the sensory input and/or modifying the gain of each sensory input; (2) generating new sensations to match what it expects (for example by moving the body to generate the predicted sensory feedback issued from the efference copies) and (3) by updating the sensory prediction (Barrett and Simmons, 2015).

An example of sensorimotor conflict that has been studied is the one occurring when people do a drawing

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Abbreviations: EEG, electroencephalography; FM, Fibromyalgia; VF, visual feedback.

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task while looking at their hand in a mirror. In such case, the predicted sensory feedback based on efference copies is congruent with the proprioceptive information, but in conflict with the visual information, and this results in motor disturbances (i.e. altered motor performance compared to a condition with congruent visual feedback). These disturbances are considered to arise mainly from a conflict between vision and proprioception (i.e. arise from a *sensory-sensory conflict*) (Lajoie et al., 1992; Holmes et al., 2006; Snijders et al., 2007) based on the fact that deafferented patients (i.e. with limited proprioceptive feedback) show fewer motor disturbances than healthy controls in this task (Lajoie et al., 1992; Miall and Cole, 2007). Consistent with the view that decreasing proprioceptive information is an effective strategy to resolve the conflict, electroencephalography (EEG) studies in healthy individuals have shown that during exposure to a conflict, the somatosensory gain is reduced relative to the visual gain (Bernier et al., 2009; Lebar et al., 2017). Some authors suggest that motor errors might result from an updated proprioceptive map (Bernier et al., 2009; Lebar et al., 2017) while other suggest that the sensory prediction is updated thereby reducing the prediction error (Hinder et al., 2007; Riek et al., 2012). These two hypotheses allow to explain why motor disturbances decrease with time (Lajoie et al., 1992; Hinder et al., 2007; Miall and Cole, 2007; Riek et al., 2012), but they are not exclusive.

In parallel to motor disturbances, sensorimotor conflicts generate sensory disturbances. In healthy individuals, conflict-evoked sensory disturbances mainly involve the impression of having an extra limb and feelings of peculiarity (McCabe et al., 2005b; Foell et al., 2013; Nishigami et al., 2015; Katayama et al., 2016; Brun et al., 2017, 2018c). It has been suggested that sensorimotor conflicts might cause pain and other sensory abnormalities in chronic pain conditions with no clear explanations, or contribute to their maintenance (Harris, 1999; McCabe et al., 2000, 2009; Don et al., 2016). Phantom limb pain occurring after amputation is the most frequently cited example to support this hypothesis, as in this case the proprioceptive feedback is systematically incongruent with the predicted sensory feedback based on motor commands toward the missing limb. Since this theory was proposed, several studies showed that in the presence of chronic or acute pain, sensorimotor conflicts induce a transient increase in pain and discomfort, as well as other sensory disturbances (McCabe et al., 2007; Cohen et al., 2010; Daenen et al., 2010, 2012; Roussel et al., 2015; Kooning et al., 2016; Brun et al., 2017, 2018c). These results reinforce the idea that sensorimotor conflicts could contribute to pain in various pain populations, and suggest that the presence of pain lowers the detection threshold of sensorimotor conflicts (McCabe et al., 2007; Brun et al., 2018c). A recent study in fibromyalgia, complex regional pain syndrome, arthritis and healthy participants showed that the intensity of clinical pain is a strong predictor of the intensity of conflict-induced sensory disturbances, but not the origin of the pathology or other clinical variables (Brun et al., 2018c). While studies in the field of motor control have shown an important contribution of proprioceptive information in conflict-induced motor disturbances (i.e. motor disturbances are considered to arise from a *sensory-sensory conflict*), it is noteworthy that in the field of pain, conflict-induced sensory disturbances have been generally assumed to arise from a discrepancy between predicted sensory feedback and actual sensory feedback (i.e. from a *sensory-motor conflict*). However, no study in pain populations so far has attempted to distinguish between the contributions of motor efferences *vs.* proprioceptive afferences during sensorimotor conflicts.

To address this gap, the general aim of the present study was to start to disentangle the relative contribution of motor efferences and sensory afferences to the increase in sensitivity to sensorimotor conflicts in chronic pain. Fibromyalgia (FM) was selected as the chronic pain population of interest as two previous studies showed that FM participants report higher sensory disturbances than controls during sensorimotor conflicts (McCabe et al., 2007; Brun et al., 2018c). To explore whether their increased sensitivity to sensorimotor conflicts arises mainly from proprioceptive afferences or also depend on motor efferences (in conflict with the visual feedback), two experimental conditions were contrasted: a conflict evoked by Passive movements (i.e. a *sensory-sensory conflict* between visual and proprioceptive information only) *vs*. a conflict evoked by Active movements (i.e. *sensory-motor conflict* between visual and efferent + proprioceptive information). The primary objective was to compare the sensory disturbances induced by each type of conflict in FM compared to Controls. We hypothesized that FM participants would be more sensitive to conflicts during Active (i.e. *sensory-motor conflict*) than Passive (i.e. *sensory-sensory conflict*) movements compared to Controls (i.e. would have a different relative contribution of efferent information), based on the common assumption in the pain field that the higher conflict sensitivity in chronic pain is the result of a discordance between the sensory prediction and the actual sensory feedback (Harris, 1999; McCabe et al., 2000, 2009; Don et al., 2016).

Two secondary objectives were to investigate whether the relative contribution of motor efferences (expressed as the difference between Active and Passive condition) to conflict-evoked sensory disturbances is in relation to motor disturbances and/or proprioceptive deficits in FM. First, motor disturbances evoked by the conflict (in the Active condition only) were compared between groups, and their relationship with the amount of the difference in sensory disturbances between Active and Passive movement was assessed. Second, proprioception was compared between groups, and its association with the amount of difference in sensory disturbances between Active and Passive movement was assessed.

EXPERIMENTAL PROCEDURES

Participants and ethics statement

Adults with FM and healthy controls, matched for age, sex and self-reported laterality, were included in the study.

For the FM group, participants were included if they had received a confirmed diagnostic of fibromyalgia. Participants were excluded if they had any motor impairment interfering with the task performance, which necessitated 85 degrees shoulder abduction and reaching movements with an amplitude of 30 cm, the arm being fully supported. Exclusion criteria for Controls were the presence of acute pain in the last 3 months or of chronic pain in the last year. Finally, the presence of non-corrected visual impairments was an exclusion criterion for both groups.

Twenty women with FM (17 right-handed; mean ± standard deviation (SD) age: 43.1 ± 15.1 years; all Caucasian) and twenty healthy women (16 right-handed, mean ± SD age: 42.9 ± 12.3 years; all Caucasian) were recruited over a one-year period in the Quebec City area. FM participants were recruited from Laval University mailing lists and the fibromyalgia association from Quebec City. Controls were recruited from Laval University. Details of the FM group are reported in Table 1.

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).

All participants provided written informed consent before enrollment. This study was approved by the local Ethical Review Board (Institut de réadaptation en déficience physique de Québec, Canada, n°2015-461) and conformed with the Declaration of Helsinki.

In the FM group, a brief history of each patient's condition, including pain manifestations, pain treatments (pharmaceutical and non-pharmaceutical) and comorbidities was obtained from a semi-structured interview. FM participants were also asked to rate their mean pain intensity over the last 24 h on an 11-point numerical rating scale ranging from 0 (no pain) to 10 (worst pain imaginable).

Table 1. Characteristics of FM participants

	Age (years)	Laterality	Pain Intensity (/10)	Time since diagnostic (years)	Pharmacological treatments	Non-pharmacological treatments	Actual comorbidities
FM01	23	Right	6	6	Ibuprofen; Pregabalin; Doxepin; Escitalopram	Physiotherapy; Occupational therapy	–
FM02	33	Right	3	5.75	–	Physiotherapy	–
FM03	47	Right	5	25	Paracetamol; Ibuprofen	–	–
FM04	21	Right	6.5	2.5	Vitamins	Psychotherapy; Physiotherapy	–
FM05	45	Left	6	2	Pregabalin	Kinesiology	Chronic fatigue syndrome
FM06	57	Right	5.5	32	Duloxetine	Osteopathy	Depression
FM07	55	Right	4.5	1.6	Duloxetine; Morphine	Massage	–
FM08	60	Right	4.5	14.5	–	Kinesiology; Massage Acunpuncture; Physiotherapy; Chirotherapy	–
FM09	63	Right	5.5	26	Ibuprofen; Paracetamol; Pregabalin	Kinesiology	–
FM10	59	Right	6	15	Ibuprofen; Tapentadol; Esomeprazole; Paracetamol	Physiotherapy	Knee osteoarthritis
FM11	60	Right	3.5	15	Tramadol; Benzodiazepine	Physiotherapy; Chirotherapy; Acupuncture; Massage	–
FM12	29	Right	6	3.5	Benzodiazepine; Duloxetine; Paracetamol	Physiotherapy; Chirotherapy; Acupuncture; Massage	–
FM13	31	Left	5.5	3	Paracetamol; Ibuprofen	Kinesiology	–
FM14	31	Right	7	10	Benzodiazepine; Paracetamol	Physiotherpay; Psychotherapy	–
FM15	49	Right	5	0.5	Pregabiline	Occupational therapy; Kinesiology	–
FM16	51	Right	6	0.8	Duloxetine	–	–
FM17	62	Right	6	0.9	–	Physiotherapy; Osteotherapy	
FM18	43	Right	5	8	Duloxetine; Candesartan	Acupuncture; Chirotherapy; Massage	High blood pressure
FM19	21	Right	6	3.5	–	–	–
FM20	25	Right	6	1	Ibuprofen; Paracetamol; Pregabalin	Physiotherapy	–
Mean		+ SD	43.2 ± 15.1		5.6 ± 0.9	12.1 ± 10.5	

Study design

Each participant took part in one experimental session and was exposed to two independent experimental tasks. All participants completed Task 1 first, and then Task 2. Task 1 assessed proprioception using a position matching task (in absence of vision of the arm). Task 2 assessed motor and sensory disturbances induced by four experimental conditions (Active_Congruent, Active_Incongruent, Passive_Congruent, Passive_Incongruent; see Procedure for details). For Task 1 and Task 2, both arms were tested separately in a counterbalanced order across participants.

Instrumentation

Task 1 and Task 2 were conducted with a KINARM robotized exoskeleton (BKIN Technologies, Kingston ON, Canada; see Fig. 1A) that allows shoulder abduction–adduction and elbow flexion–extension in order to move the ULs in the transversal plane (the weight of the UL being fully supported). Movement of the endpoint (index fingertip) in this plane are described on the anteroposterior axis and the mediolateral axis. The movement of the tested arm was either active or passive, i.e. moved by the robot. The robot is interfaced with a 2D virtual environment (47 inches, refreshing rate: 60 Hz) creating the illusion of a virtual arm at the same location as the participant's arm (Dexterit-E software version 3.5.3; Fig. 1B), while the participant's arm is obstructed from view. For Task 2 only, according to the visual feedback (VF) condition, the virtual arm was either driven in real time by the participant's actual movement or followed a pre-defined trajectory incongruent with the actual movement. Joint angular positions for both the shoulder and elbow were obtained from KINARM motor encoders and sampled at 1 kHz, and the position of the index fingertip was computed in real time. Data processing was made with Matlab (MathWorks, R2011b).

Procedure

Task 1 (Proprioception). This task comprised the KINARM Arm position matching task (Scott and Brown, 2013), a standard test that has previously been used to characterize proprioceptive alterations in stroke (Dukelow et al., 2010) and in complex regional pain syndrome (Brun et al., 2018b) participants.

During this task, no visual feedback is provided, therefore participants had only proprioceptive feedback to complete the task. Proprioception for left and right UL were tested in counterbalanced order across

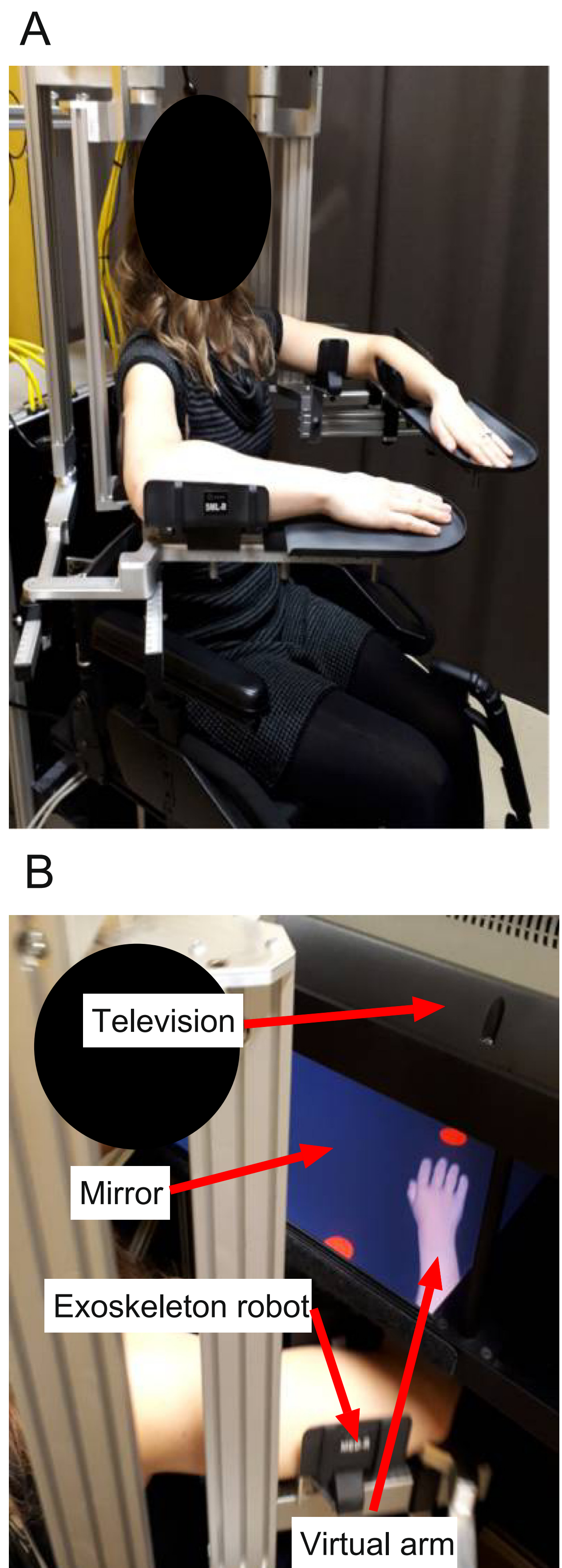

Fig. 1. Experimental set up. The KINARM consists of an exoskeleton robot **(A)** and a 2D virtual environment **(B)**. **(A)** Before the experiment, the exoskeleton is fitted to the anthropometric characteristics of the participant's arm. **(B)** The 2D virtual environment consists in the projection of a virtual upper limb on a semi-transparent mirror (47″) using a television. The arms are obstructed from view and rest on the exoskeleton under a semi-transparent mirror.

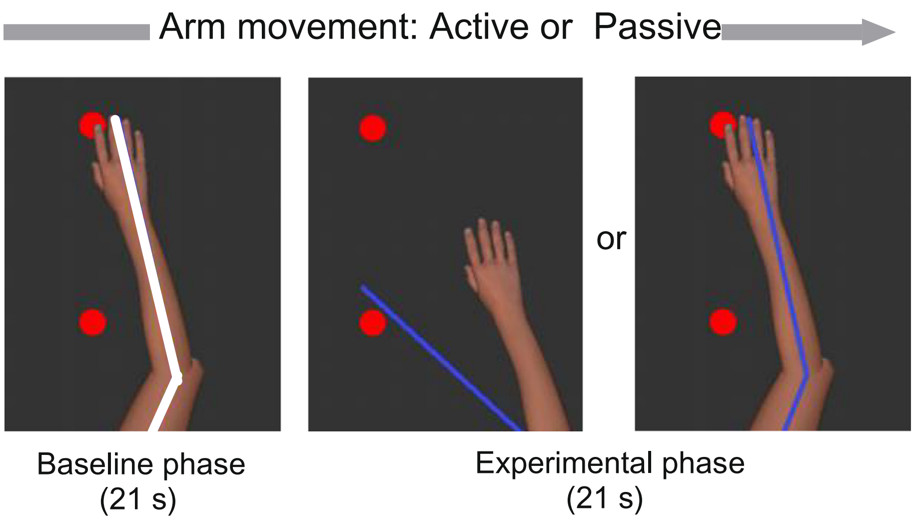

Fig. 2. Task 1 – proprioception assessment. This figure is a screenshot from a standard report (Dexterit-E software version 3.5.3) of one control participant. Respectively, the left and right panel represents the assessment of the left and right arm. The four corners of the green square represent the four predefined position where the left and right arm are passively moved. The four corners of the blue square represent the match position by the contralateral arm (the dotted blue line is a mirroring of the solid blue line).

participants. Respectively, for the right (left) UL assessment, the robot passively moves the right (left) UL to one of four predefined positions in the right (left) hemispace (Fig. 2). Then, the participant reproduces the position with the left (right) UL (i.e. making a mirror image of the position of the right (left) UL). Each position is repeated six times in a pseudo-randomized order (total of 24 trials). For each participant, the values of the four predefined positions are relative to angular positions of shoulder (30 degrees) and elbow (90 degrees) and the four targets are in a 20 cm wide square grid around that point. Between each target, the robot moved the arm in a linear path using a bell-shaped speed profile (max speed < 1 m/s) (Dukelow et al., 2010). Participants are required to match only the final position of the contralateral UL (not to reproduce the trajectory/speed of displacement toward that final position). For a video of Task 1 see Supplementary Material S1.

Task 2 (Sensorimotor conflicts). This custom task designed in our lab was used to assess motor and sensory disturbances induced by sensorimotor conflicts during passive and active movements (Brun et al., 2018a). For a video of Task 2 see Supplementary Material S2.

Before each trial, participants were informed of the Movement condition (Active or Passive). In each trial, two red targets were presented on the screen, one at (0, 15) coordinates (in cm) and the other at (0, −15) from the initial position (0, 0), and remained until the end of the trial. Participants were required to successively reach each target without stopping on them, in order to create a cyclic movement as fluid and straight-lined as possible in the anteroposterior axis. A metronome beat was provided to help the participant maintain the required movement frequency (0.33 Hz). Each trial was divided in two phases (Fig. 3).

In the Baseline phase (21 s), the virtual arm reproduced faithfully the movement of the participant's UL.

In the Experimental phase (21 s), the Congruent or the Incongruent VF condition was presented to the participant. During the Congruent VF condition, the virtual UL reproduced faithfully the participant's UL movement. During the Incongruent VF condition, the virtual UL was pre-programmed (video) to move in in the mediolateral axis of the transversal plane. This pre-programmed video was used rather than applying a 90° angular deviation to the actual UL movement in order to have similar VF during Passive and Active movements in the Incongruent VF condition. In a previous study, we showed that viewing a virtual UL moving incongruently with our own movement induces motor and sensory disturbances, no matter whether the virtual upper limb is driven by our actual movement or not (Brun et al., 2018b). The movement amplitude of the virtual UL in Incongruent VF conditions (from the left to the right and vice versa) was at 30 cm. In the Active condition, participants were required to continue to reach each target as in the Baseline phase (in the anteroposterior axis), even if the Incongruent VF was disturbing. In the Passive condition, participants were required to relax their UL. Participants were not allowed to close their eyes or to look away during the Incongruent VF, to ensure that a conflict between vision and proprioception/motor intention occurred.

After each trial, participants had to respond to a questionnaire about their perception of their arm (for more details, see Measures and data analyses).

Measures and data analyses

Task 1 (Proprioception). Mean absolute distance error in the mediolateral and anteroposterior axes across trials were obtained from Dexterit-E software (Arm position matching task (Scott and Brown, 2013), version 3.5.3).

Task 2 (Sensorimotor conflicts). For both sensory and motor disturbances, the test–retest reliability has been previously shown to be very good (Brun et al., 2018a).

Sensory disturbances. At the end of each trial, participants verbally rated eight items assessing changes in the perception of their arm on a scale from 0

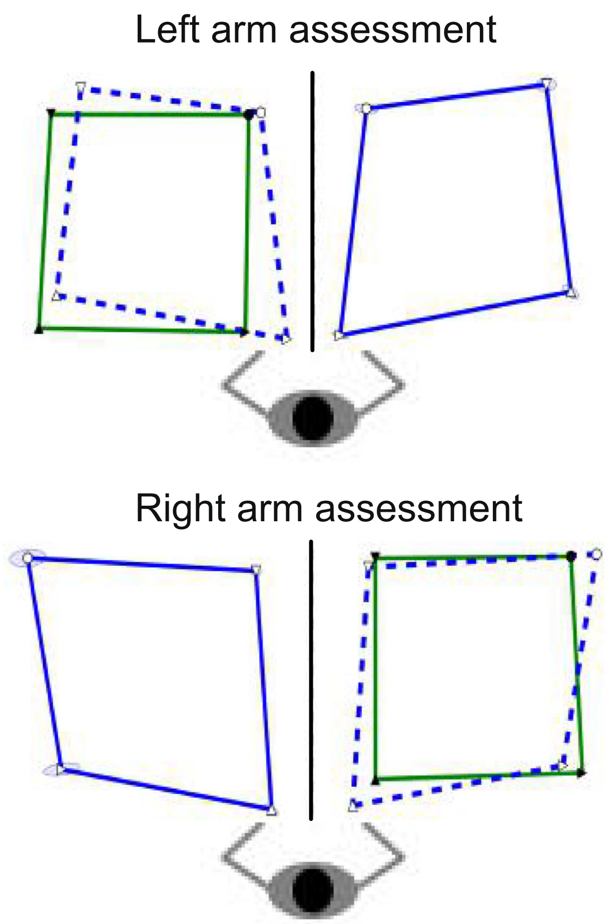

Fig. 3. Task 2 – Timeline and experimental conditions. Participants saw exclusively one virtual arm (left or right) and the red targets. White line depicts the actual position of the arm, but this information was not provided to the participant. During all the trial, the movement of the upper limb could be either Active or Passive. During the Active condition, participants had to reach one of the targets following a metronome beat (0.33 Hz) in order to create a cyclic movement. In the Passive condition, the same movement frequency was created by the robot. In the Baseline phase, the virtual arm movement was always congruent with the actual participant movement. In the Experimental phase, the movement of the virtual upper limb was either Congruent or Incongruent, depending on the experimental condition.

(no change) to 3 (important change). Participants had to rate the perceived changes from the Baseline to the Experimental phase. Items were related to pain, discomfort, the perception of losing a limb, temperature, weight, the perception of having an extra-limb, the perception of losing control and feelings of peculiarity (McCabe et al., 2005a, 2007; Foell et al., 2013; Brun et al., 2017, 2018a, 2018c). A total score was computed using the mean of the eight items.

Sensory disturbances were expressed as a change between the Congruent and the Incongruent VF. Hereafter, the difference between the Congruent and Incongruent VF is termed Conflict sensitivity. A positive value of Conflict sensitivity indicates higher sensory disturbances in the Incongruent VF condition compared to the Congruent VF.

Motor disturbances. Two outcomes were used to assess motor disturbances (Brun et al., 2017, 2018a) based on the position of the index fingertip (see Fig. 6A for an example): amplitude and mediolateral drift. The position of the index was computed by the KINARM according the angular position of the elbow and shoulder. For amplitude, anteroposterior coordinates were encoded for each peak of flexion and extension. For each movement half-cycle, the amplitude on the y-axis was extracted. For medio-lateral drift, for each movement half-cycle, the mediolateral coordinates of the maximal deviant point (from the virtual straight line between the two red targets) was extracted.

Both motor outcomes were expressed as a change relative to the Baseline phase (Experimental phase – Baseline phase), as we were not interested in the effect of Group on motor performance per se, but rather in the motor disturbances induced by the conflict. A positive value indicates motor disturbances in the Experimental phase compared to the Baseline phase.

Statistics

The mean ± SD is reported in the results. The threshold for statistical significance was set to $p < 0.05$. The normality of data was tested with the Shapiro-Wilk test (all $p > 0.29$). Homoscedasticity was assessed with the Brown-Forsythe test (all $p > 0.08$). When necessary, Tukey corrections were used for post-hoc tests. Eta-partial squared (η_p^2) indicates size effect. As no difference between the dominant and the non-dominant arm was observed on any variable in each group (all $p > 0.18$), all statistical analyses were performed on the mean of both arms.

Proprioception. Errors in Task 1 were analyzed using a 2*2 mixed-design analyses of variance (rmANOVA): [*Error direction* (Mediolateral or Anteroposterior) × *Group* (FM or Controls)].

Conflict-induced sensory disturbances. For the sensory disturbances, a paired t-test was first performed for each group in order to test whether there was a difference between the Congruent and Incongruent VF conditions. Then, a 2*2 mixed-design ANOVA [*Movement* (Active or Passive) by *Group* (FM or Controls)] was performed to assess the effect of Passive and Active movements on the Conflict sensitivity according to the group.

Conflict-induced motor disturbances. A 2*2 mixed-design ANOVA [*Visual feedback* (Congruent or Incongruent) by *Group* (FM or Controls)] was performed to assess the effect of the VF and the Group on motor disturbances.

Correlation analyses. Pearson correlation coefficients were used to test whether the relative contribution of efferent information, i.e. the change in Conflict sensitivity during Incongruent VF from the Passive to the Active condition (in both FM and Controls) is associated with motor disturbances induced by conflicts and errors in proprioception.

RESULTS

Sensory disturbances induced by sensorimotor conflicts

FM participants and Controls reported higher sensory disturbances during Incongruent VF compared to the Congruent condition in both Active and Passive movements (all $p < 0.05$).

Fig. 4 displays the results for the Conflict sensitivity. A significant interaction was observed between Group and Movement conditions ($F(1,38) = 4.7$; $p = 0.03$; $\eta^2_p = 0.38$). Post-hoc comparisons revealed a higher Conflict sensitivity for FM compared to Controls in the Active condition ($p < 0.01$), but not in the Passive condition ($p = 0.88$), suggesting that the difference between FM and Controls in Conflict sensitivity is explained by the *sensory-motor* conflict rather than the *sensory-sensory* conflict condition. Moreover, FM participants were more sensitive to conflicts during Active than Passive movements ($p < 0.01$), while this difference was not significant in Controls ($p = 0.79$). In other words, only FM participants were more sensitive to *sensory-motor* conflict compared to *sensory-sensory* conflict. Main effects of Group ($F(1,38) = 4.1$; $p = 0.04$; $\eta^2_p = 0.11$) and Movement were observed ($F(1,38) = 8.7$; $p < 0.001$; $\eta^2_p = 0.51$). However, these main effects were better explained by the interaction effect (FM being more sensitive to Controls in the Incongruent condition only, and Active movement creating higher Conflict sensitivity in FM participants only).

Fig. 5 displays each sensory disturbance according the group for the Incongruent VF in Active and Passive conditions.

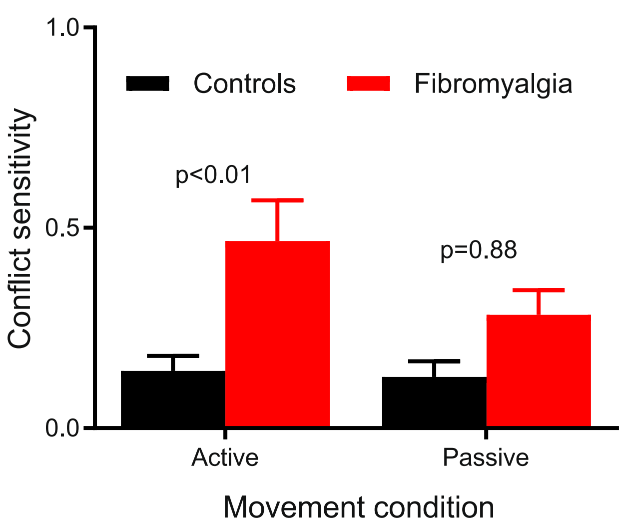

Fig. 4. Mean of Conflict sensitivity (sensory disturbances) for each Group according the Movement condition. Conflict sensitivity represents the difference between the Congruent and Incongruent Visual Feedback condition. A positive value indicates that higher sensory disturbances were reported during the Incongruent VF condition. Error bars represent the standard error of the mean.

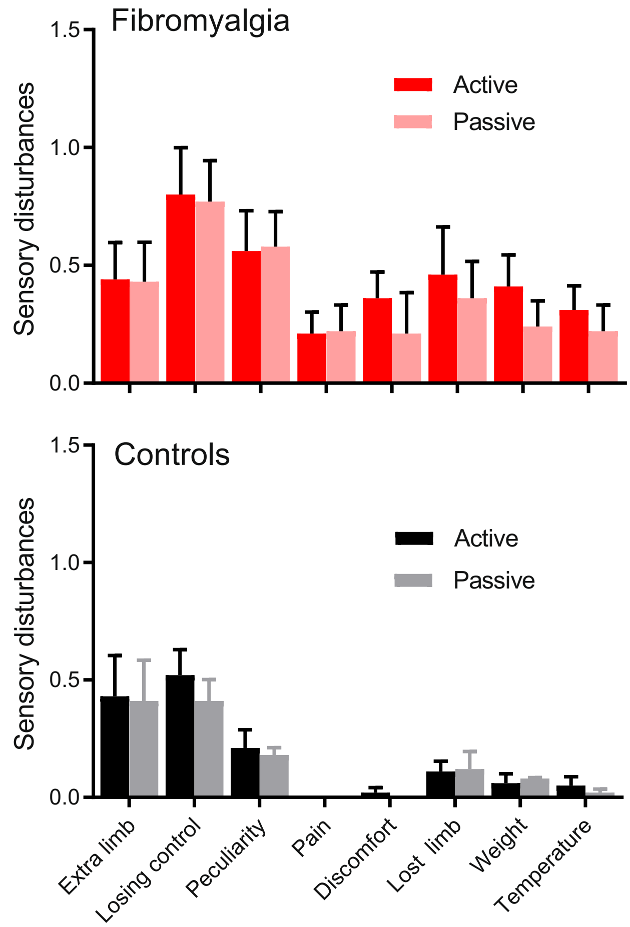

Fig. 5. Mean and SEM of each item of the sensory disturbance questionnaire for the Incongruent VF in the Active and Passive conditions.

Motor disturbances induced by sensorimotor conflicts and their relation with sensory disturbances

Fig. 6A displays the motor behaviour of one representative participant in the Fibromyalgia group for the Congruent and Incongruent VF conditions. Fig. 6B, C respectively represent the mean and standard errors of the mean for the Amplitude and Mediolateral drift for each group during Congruent and Incongruent VF conditions.

Amplitude. During the Incongruent VF condition the movement amplitude was smaller than during the Congruent VF condition ($F(1,38) = 12.9$; $p < 0.001$; $\eta^2_p = 0.25$). However, there was no significant difference between groups ($F(1,38) < 1$; $p = 0.89$) and no interaction ($F(1,38) < 1$; $p = 0.58$). Correlation analyses revealed that the relative contribution of motor efferences (i.e. the change in Conflict sensitivity during Incongruent VF from the Passive to the Active condition) was not associated with amplitude during the Incongruent VF in Active condition in FM ($r = -0.14$; $p = 0.53$) and in Controls ($r = 0.07$; $p = 0.14$).

Mediolateral drift. As shown in Fig. 6A, C, the mediolateral drift was higher in the Incongruent VF (*F*

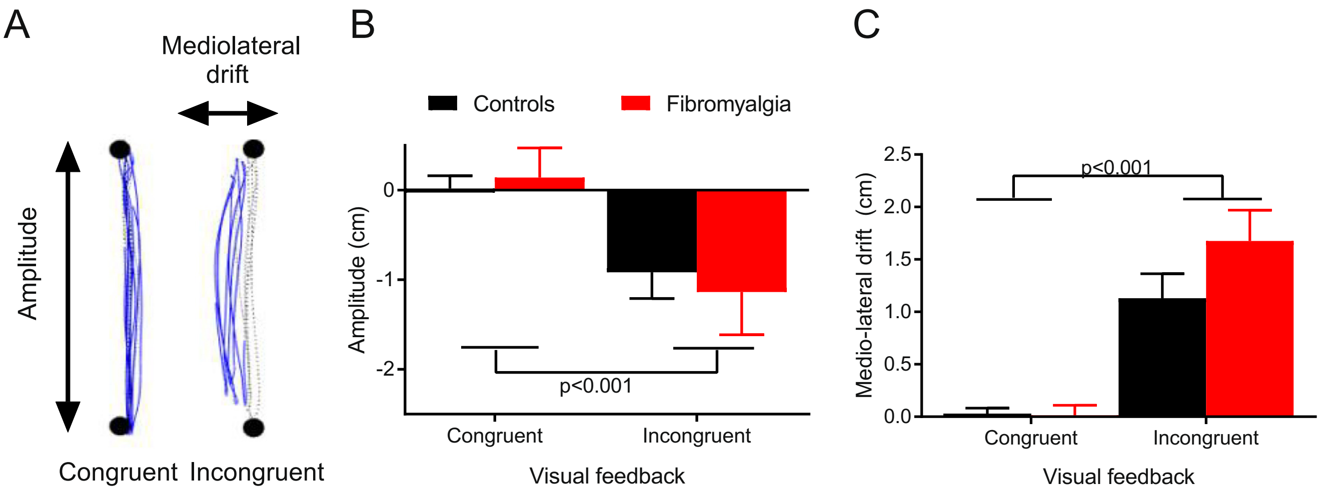

Fig. 6. Motor disturbances according the Visual feedback conditions. **(A)** Individual data for a representative participant in the Fibromyalgia group for the Congruent and Incongruent VF. The dotted black and the solid red lines represent respectively the trajectory of the right upper limb during the Baseline phase and the Experimental phase. **(B)** Amplitude. A positive value indicates higher amplitude in the Experimental phase compared to the Baseline phase, and a negative value indicates lower amplitude. **(C)** Mediolateral drift. A positive value indicates higher mediolateral drift in the Experimental phase compare to the baseline phase. Error bars represent standard error of the mean.

(1,38) = 51.83; $p < 0.001$; $\eta_p^2 = 0.39$) compared to the Congruent VF condition. However, there was no significant difference between groups ($F(1,38) = 1.7$; $p = 0.19$) and no interaction ($F(1,38) = 2.1$; $p = 0.15$). Correlation analyses revealed that relative contribution of motor efferences (i.e. the change in Conflict sensitivity during Incongruent VF from the Passive to the Active condition) was positively related to the mediolateral drift induced by conflicts during Active movements in FM ($r = 0.57$; $p < 0.01$) but not in Controls ($r = 0.03$; $p = 0.87$).

Proprioception and its relation with sensory disturbances

As shown in Fig. 7, no significant difference was found between groups ($F(1,38) < 1$; $p = 0.81$). A main effect of Error direction ($F(1,38) = 99$; $p < 0.001$) indicates that errors were higher in the mediolateral direction compared to the anteroposterior direction. Finally, there was no significant interaction between Group and Error direction ($F(1,38) < 1$; $p = 0.61$). Correlation analyses showed that errors in proprioception were not related to relative contribution of efferent information (i.e. the change in Conflict sensitivity during Incongruent VF from the Passive to the Active condition) in both FM ($r = 0.12$; $p = 0.61$) and Controls ($r = 0.02$; $p = 0.92$).

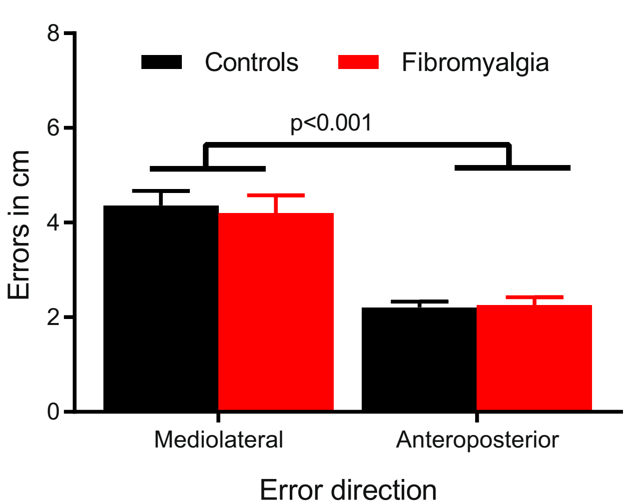

Fig. 7. Mean error for the mediolateral and anteroposterior axis for the Fibromyalgia and the Control groups. Error bars represent the standard error of the mean.

DISCUSSION

An extensive literature shows that individuals with acute or chronic pain report higher sensory disturbances in the presence of sensorimotor conflicts compared to healthy pain-free individuals (McCabe et al., 2007; Cohen et al., 2010; Daenen et al., 2010, 2012; Roussel et al., 2015; Kooning et al., 2016; Brun et al., 2017, 2018c). In the pain field it is frequently assumed that these conflicts arise from a discordance between sensory afferences and efference copies, despite the fact that studies in the field of motor control have shown an important contribution of proprioceptive information in conflict-induced motor disturbances. The general aim of this study was to dissociate the relative contribution of proprioceptive afferences and motor efferences (discordant with the visual feedback) in Conflict sensitivity, in individuals with FM compared to healthy individuals. Results show that a conflict arising from Active movements (generating a sensory-motor conflict) induces higher sensory disturbances than one arising from Passive movements (generating a sensory-sensory conflict) in FM, but not in Controls. Moreover, this increase in Conflict sensitivity from Passive to Active movements in FM was related to conflict-induced motor disturbances, but did was not related to a poorer proprioception. Therefore, it appears that the discordance between motor efferences and the visual feedback is the key component explaining greater Conflict sensitivity in FM.

Our results suggest that sensory-motor conflicts in FM induce higher sensory disturbances without provoking higher motor disturbances compared to healthy pain-free individuals. However, this statement does not necessarily imply that sensory and motor disturbances depend on distinct processes. Indeed, we observed a strong and positive association between the relative contribution of motor efferences in sensory disturbances and motor disturbances in FM participants, meaning that the more they were sensitive to sensory-motor conflict compared to sensory-sensory conflict, the more they exhibited motor disturbances. These apparently discrepant results might be reconciled based on internal models of motor control explaining the relation between sensory afferences and motor efferences in the perception and the control of action (Fig. 8) (Frith et al., 2000). On the one hand, the predictors (also referred to as forward models) are used to predict the sensory consequences of motor commands and to support the perception of action. On the other hand, the controllers (also referred to as inverse models) are involved in the generation of the motor commands and therefore support the control of action. When a discordance arises between the actual and the predicted sensory feedback, both internal models (predictors and controllers) are updated (Frith et al., 2000; Scott, 2004). Clinical arguments have been advanced to demonstrate that perception and control of action might be altered independently (Frith et al., 2000). For example, apraxia might result from an alteration in controllers while perturbation in feelings of agency in schizophrenia would be the results of an alteration in predictors (Frith et al., 2000). Therefore, based on our results, we suggest that both sensory and motor disturbances depend on the detection of the discordance between the actual and the predicted sensory feedback (explaining the significant correlation between sensory and motor disturbances). However, the fact that only the

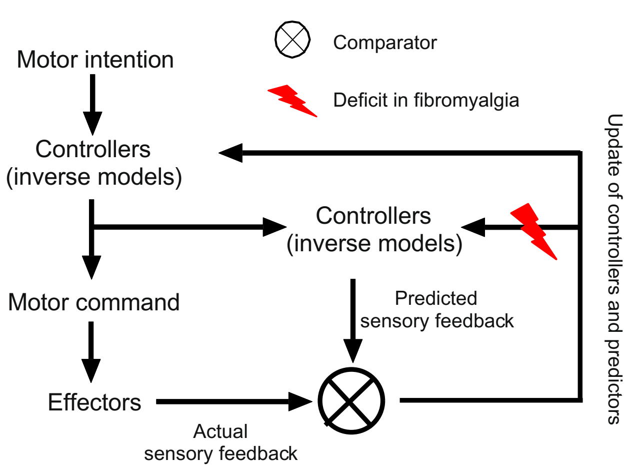

Fig. 8. Internal models of motor control. Errors issued from the comparison between the actual and the predicted sensory feedback are used to update the controllers (the control of action) and the predictors (the perception of action).

sensory disturbances in the Active condition differed between FM participants and Controls suggest that FM have a deficit in updating the predictors but not the Controllers (no significant difference between FM and controls in motor disturbances; Fig. 8). From a clinical point of view, these results suggests that alterations in body awareness, that are frequently observed in various clinical pain populations (Lewis et al., 2007; Lotze and Moseley, 2007), including in FM (Valenzuela-Moguillansky, 2012), would not necessarily imply alterations in motor function. In the FM group, the increased sensitivity to sensory-motor (compared to sensory-sensory conflict) occurred for almost every item of the sensory disturbances questionnaire, suggesting that this increased conflict sensitivity is related to various aspects of sensory perception (e.g. body image, somatosensory perception). In other clinical conditions, a dissociation has been shown between the alterations of the perception and control of action (Frith et al., 2000), but this has not been previously assessed in FM. For example, it would be interesting to test whether motor learning during visuomotor adaptation is preserved in FM, which would confirm that the update of controllers is not altered.

We demonstrated that proprioceptive inputs (in conflict with visual feedback) do not seem to explain the greater sensitivity to conflicts in FM compared to Controls. Indeed, sensory-sensory conflict did not induce higher sensory disturbances in FM compared to Controls. Moreover, sensory disturbances were not related to proprioceptive accuracy. It is noteworthy that proprioception was not found to be altered in the present study, while proprioceptive deficits have been described in other chronic pain conditions (Gelecek et al., 2006; Lee et al., 2010; Lewis et al., 2010; Brun et al., 2018b). EEG studies in healthy individuals showed that the visual and somatosensory gains are modified during exposure to conflicts (Bernier et al., 2009; Lebar et al., 2015, 2017). Even if there is no difference between FM and Controls in proprioception, it cannot be excluded that somatosensory and visual gains differed between groups during sensory-motor conflicts, but our protocol was not designed to test this hypothesis.

Several limitations need to be highlighted. First, the sensorimotor task was very easy to perform (slow movement of flexion and extension) and a higher complexity could lead to differences between FM and Controls in motor disturbances. Moreover, only two trials per condition were performed and therefore it was not possible to study learning effects. The difference explained between Controls and FM might be interpret as better ability for Controls to update sensory prediction. Secondly, electromyography was not recorded to ensure that participants were effectively relaxed during the Passive movements. Finally, the significant correlation between sensory and motor disturbances in FM need to be interpreted cautiously since we did not find such significant correlation in Controls. It is important to note that previous studies did not find significant associations between sensory and motor disturbances (Brun et al., 2017; Katayama et al., 2018; Osumi et al., 2018), which could be due to lower variability in sensory disturbances since only healthy individuals were tested.

In conclusion, our results confirm previous reports that people with FM are more sensitive to sensorimotor conflicts than pain-free healthy individuals (McCabe et al., 2007; Brun et al., 2018c). This increased sensitivity is mainly explained by a sensory-motor conflict rather by a sensory-sensory conflict. We suggest this arises due to a deficit in updating predicted sensory feedback rather than in selecting appropriate motor commands. Finally, our results suggest that even if FM impacts on conflict-induced sensory disturbances, it does not impact motor disturbances. Further studies are needed to better characterize sensorimotor dysfunctions in fibromyalgia in relation to clinical profile.

CONFLICT OF INTEREST

None of the authors have any conflicts of interest.

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AUTHOR CONTRIBUTIONS

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

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuroscience.2020.03.017.

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