Title

Sensory disturbances induced by sensorimotor conflicts are higher in complex regional pain syndrome and fibromyalgia compared to arthritis and healthy people, and positively relate to pain intensity

Running head

Sensorimotor conflicts: chronic pain & healthy people

Authors

C. Brun[1,2]*, C. Mercier[1,2], S. Grieve[3,4], S. Palmer [4], J. Bailey[5], C.S. McCabe[3,4,6]

Affiliations

1. Center for interdisciplinary research in rehabilitation and social integration, Québec, QC, Canada.
2. Department of Rehabilitation, Laval University, Québec, QC, Canada.
3. Royal United Hospitals NHS Foundation Trust, Bath, UK.
4. University of the West of England, Bristol, UK.
5. Resolve your Pain, Rachael's Retreat, Potts Close, Batheaston, BA1 7NG, UK
6. The Florence Nightingale Foundation, London, UK

* **Corresponding author**

Clémentine Brun

Center for interdisciplinary research in rehabilitation and social integration

525 boulevard Wilfrid Hamel

Québec, G1N 2H9

+1 418 529 9141 # 6578

E-mail: clementine.brun.1@ulaval.ca

Original article

Funding sources

C. Brun was supported by fellowships from the Centre interdisciplinaire de recherche en réadaptation et en intégration sociale (CIRRIS), from the Centre thématique de recherche en neurosciences (CTRN), from the Faculté de médecine de l'Université Laval, from

Fonds de recherche Nature et Technologies (FRQNT), from the Réseau provincial en adaptation et réadaptation (REPAR) and from the Quebec pain research network (QPRN). C. Mercier is supported by a salary award from Fonds de recherche Québec-Santé (FRQS, grant number: 29251). C. McCabe was funded by a National Institute for Health Research Career Development Fellowship (CDF/2009/02/) and J. Bailey was employed on this award. This paper presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. The authors have declared no conflicts of interest.

Conflicts of interest

None of the authors have any conflicts of interest.

Significance

Individuals with complex regional pain syndrome and fibromyalgia were more sensitive to sensorimotor conflicts than arthritis patients and controls. Moreover, conflict-induced sensory disturbances were specific to higher pain intensity and higher sensory abnormalities in all groups, suggesting that pain lowers the threshold for the detection of sensorimotor conflicts.

ABSTRACT

Background: Sensorimotor conflicts are well-known to induce sensory disturbances. However, explanations as to why patients with chronic pain are more sensitive to sensorimotor conflicts remain elusive. The main objectives of this study were 1) to assess and compare the sensory disturbances induced by sensorimotor conflict in complex regional pain syndrome (n=38), fibromyalgia (n=36), arthritis (n=34) as well as in healthy volunteers (n=32); 2) to assess whether these disturbances were related to the intensity and duration of pain, or to other clinical variables assessed using questionnaires (abnormalities in sensory perception, depression and anxiety); and 3) to categorize different subgroups of conflict-induced sensory disturbances. **Methods:** 140 participants performed in phase or anti-phase movements with their arms while viewing a reflection of one arm in a mirror (and the other arm obscured). They were asked to report changes in sensory disturbances using a questionnaire. **Results:** First, results showed that patients with complex regional pain syndrome and fibromyalgia were more prone to report sensory disturbances than arthritis patients and healthy volunteers in response to conflicts (small effect size). Secondly, conflict-induced sensory disturbances were correlated to pain intensity (large effect size) and abnormalities in sensory perception (only in the CRPS group), but were not related to the duration of the disease or psychological factors. Finally, we identified two distinct subgroups of conflict-induced sensory disturbances. **Conclusions:** Our results suggest that pain lowers the threshold for the detection of sensorimotor conflicts, a phenomenon that could contribute to the maintenance of pain in clinical populations.

1. INTRODUCTION

Incongruence between motor intentions and sensory feedback arising from actions (i.e. sensorimotor conflict) might contribute to pain and other sensory disturbances in chronic pain pathologies, phantom limb pain being the most cited example (Harris, 1999; McCabe et al., 2000; McCabe and Blake, 2008). Sensorimotor conflicts can also occur in other chronic pain conditions associated with altered body perception. Individuals with complex regional pain syndrome (CRPS) report pain disproportionate to the original injury, perceive alterations in the size and shape of their painful limb (Moseley, 2008; Peltz et al., 2011), and overestimate the force exerted in observed hand actions (Hotta et al., 2015). Individuals with fibromyalgia (FM) and arthritis report sensations of excessive swelling (McCabe et al., 2000). These alterations of body perception are positively related to pain intensity (Lewis and Schweinhardt, 2012; Valenzuela-Moguillansky, 2013). As motor deficits are also often observed in chronic pain conditions (Burgunder, 1998; Schilder et al., 2012), both sensory and motor deficits could contribute to a greater mismatch between motor intentions and sensory feedback.

Harris' theory (Harris, 1999) suggesting that sensorimotor conflict could be the origin of pain in some pathologies has been challenged by recent reviews failing to show that sensorimotor conflicts induce pain in healthy volunteers (HV) (Boesch et al., 2016; Don et al., 2016). However, various sensory disturbances are being evoked, and those appear to be more intense in people with pain (Don et al., 2016). Therefore, rather than conflicts being the primary cause of pain, it could be hypothesized that the presence of pain makes people more vulnerable to conflicts, which in turn contribute to the presence of sensory disturbances and the maintenance of pain.

However, the reasons why chronic pain patients are more sensitive to conflicts remains elusive. A number of factors may contribute, including the intensity and duration of pain, or co-morbidities such as anxiety or depression. FM patients self-report increased sensitivities to somatosensory and non-somatosensory stimuli (Wilbarger and Cook, 2011), supporting the idea of a generalized hypervigilance (McDermid et al., 1996). Moreover, chronic pain is well-known to be positively associated with mood and anxiety disorders (McWilliams et al., 2003). Body perception disturbances in CRPS are related to higher anxiety (Michal et al., 2016) and in FM patients higher pain intensity is related to lower mood (Scheidt et al., 2014). Therefore, higher vulnerability to sensorimotor conflicts in chronic pain conditions compared to HV might be explained by several clinical characteristics as the origin of the pathology, intensity and duration of pain, altered sensory perception, and anxiety and mood disorders.

Thus, the objectives of this study were (a) to assess and compare the sensory disturbances induced by sensorimotor conflict in different chronic pain populations (CRPS, FM, Arthritis) and in HV, (b) to assess whether these disturbances were related to the intensity and duration of pain or other clinical variables (sensory perception abnormalities, depression, anxiety), (c) to explore data for different subgroups of sensory disturbances induced by sensorimotor conflict, which could lead to a simpler assessment of sensory disturbances, and potentially explain underlying mechanisms.

2. METHODS

2.1. Study design

This study formed part of a larger multi-centre cross-sectional observational study which investigated sensorimotor conflict and its relationship to behavioural and neurophysiological variables, including data collection via electroencephalography (EEG). The sample size for the whole study was determined by the pragmatic practical constraints of collecting EEG data, and the primary outcome measure was motor response times, as measured by EEG to innocuous and noxious stimuli.

The participants attended the Royal National Hospital for Rheumatic Diseases, Bath, UK or Salford Hospital, Manchester, UK on a single occasion. Data were collected by the same researcher at both sites. This research study protocol was devised in 2013 as part of a larger study. It was not preregistered as it was submitted for ethical approval prior to the current recommendations. However, the authors acknowledge that protocol preregistration is now recognised as best practice in order to promote transparency and prevent selective reporting (Keefe et al., 2018; Lee et al., 2018). The study protocol was peer reviewed by members of the NHS and University Ethics committees and the hospital's Research and Development committee.

2.2. Ethical approval

Ethical approval was granted by the National Research Ethics Service Committee South West – Frenchay (11/SW/0246). The University of the West of England, Bristol, UK, sponsored the study and collaborated with the University of Manchester, UK. Written informed consent was provided by all participants.

2.3. Recruitment

A convenience sample of 140 adult participants (≥ 18 years) were recruited, comprising healthy volunteers (HV) (n=32) and those living with one of the following three chronic pain conditions. Inclusion criteria for the latter were defined as;

- Fibromyalgia (FMS) (n=36): meeting the ACR criteria (Wolfe et al., 2010)
- Complex Regional Pain Syndrome Type 1 (CRPS) (n=38): meeting the Budapest clinical criteria for unilateral CRPS in an upper or lower limb (Harden et al., 2010)
- Osteoarthritis / Rheumatoid Arthritis (n=34): meeting the American College of Rheumatology (ACR) clinical criteria for Rheumatoid Arthritis (Aletaha et al., 2010) or the UK National Institute for Health and Care Excellence clinical criteria for Osteoarthritis (National Clinical Guideline Centre (UK)., 2014).

Exclusion criteria for all groups were co-morbidities that affected sensory processing or any asymmetrical disfigurement on their upper limbs which was unrelated to their chronic pain condition (patients only). For example, co-morbidities that could potentially influence sensory processing would include diabetic neuropathy or stroke. The total study sample size was calculated to answer the overarching study questions of the larger cross-sectional study and the overall patient group was matched with the HV by gender and age (≤ 10 years). In the HV group, participants who reported brief acute pain episodes (e.g. headache) were excluded from the study.

Participants were recruited from the outpatient department and wards at the Royal National Hospital for Rheumatic Diseases, Bath, UK and the musculoskeletal pain clinic at Salford Royal Hospital, Salford, UK. Healthy volunteers were recruited from hospital staff, family members of patient participants and other professional contacts known to the researchers. Participants were informed that the study was being undertaken to investigate the commonalities and differences between people living with chronic pain and those who do not have pain; for example if the brain reacts to tests in similar ways. They were informed that some of the testing may cause brief discomfort, but that this would settle back to normal very quickly. This information was provided as part of a requirement of informed consent for ethical approval as the majority of participants had chronic pain, which commonly is exacerbated by movement. No further information was provided regarding possible sensory perceptions.

2.4. Experimental conditions and procedure

Two conditions of mirror Visual feedback (VF) were investigated; Congruent or Incongruent VF. Participants were required to perform in phase or anti-phase bilateral arm movements. These active arm movements, performed when participants were asked to flex and extend both arms at the elbow, assessed visual sensorimotor conflict. When viewing their moving arms via the mirror, the anti-phase movements were perceived by the participant as if they were moving their limbs in the same direction (Incongruent VF condition).

Prior to the study visit, the baseline documentation (see 2.5.1 and 2.5.2) was posted to each participant and it was requested that this was completed either the night before, or the morning of the assessment (preferably the latter).

At the visit, and following completion of written consent, they were asked to remove watches and jewellery prior to the start of the study procedures. There were four experimental conditions (in phase and anti-phase movements with the left and right arms), and each was undertaken for a timed 20 seconds. Participants were seated at a table with a mirror in front of them, positioned vertically at waist height and at right angles to their body. An arm was placed either side of the mirror, so that one arm was hidden. Participants were asked to flex and extend both arms at the elbow in phase, either side of the mirror (Fig. 1A). The participant viewed the mirror side. This exercise was repeated with the arms moving in an anti-phase manner (Fig 1B). On completion of the experiment, the mirror was turned and the other arm viewed in the same manner.

The researcher alternated, between participants, as to whether the first condition was conducted by the left or right arm. In phase movements were conducted before anti-phase movements.

« Insert Fig. 1 approximately here»

2.5. Outcome measures

Demographic measures included age, gender, as well as a brief medical history including disease duration (patient groups only). Participants were asked to complete the following questionnaires:

2.5.1. *Psychological Measures*

2.5.1.1. The Hospital and Anxiety and Depression Scale (**HADS**) (Zigmond and Snaith, 1983): This is a self-report measure used to screen for anxiety and depression in non-psychiatric patients. It consists of 14 items on 2 sub-scales and the participant is asked to assess their emotional state over the past week using a 4-point Likert scale. It excludes items referring to somatic manifestations of mood disorders as these may be present in patients as a result of their illness.

2.5.1.2. **The Cardiff Anomalous Perceptions Scale (CAPS)** (Bell et al., 2006) is a measure which asks questions about a broad range of sensations and perceptions, some of which are unusual and some of which are everyday. It is not condition specific and is appropriate for use across a wide population.

2.5.2. Assessment of pain

Participants completed a 0-10 Visual Analogue Score (VAS) to report the mean pain during the last 24H.

2.5.2.1. The Brief Pain Inventory (BPI) – short form (Cleeland and Ryan, 1994): a self-report questionnaire which measures current pain intensity over the previous week and the extent to which pain has interfered with physical, social and psychological aspects of functioning.

2.5.3. *Sensory disturbances*

After each experimental condition, the participant completed a 9 item scale designed to assess sensory disturbances and were required to rate the intensity of each item from 0 to 6 (0=not at all and 6=very strong): a perceived change in weight or temperature of the limb, pain, discomfort, a perceived lost limb, a sense of gaining an extra limb or a report of peculiarity of the limb. This scale is based on previous studies assessing the impact of sensorimotor conflict on sensory disturbances in healthy volunteers (Foell et al., 2013; McCabe et al., 2005) and in chronic pain populations (McCabe et al., 2007).

2.6 Statistical analyses

2.6.1. Population

For the demographic and clinical characteristics, a one-way analysis of variance (ANOVA) was performed to assess whether groups differed. When a significant difference was found, multiple comparisons were performed with Tukey correction.

2.6.2. Effect of Group, Pain intensity and Visual Feedback on the Total score of sensory disturbances

As there was no statistical difference between the left and right arm for all groups (see Table 1S in Supplementary Material) in sensory disturbances, statistical analyses were performed on the mean of both arms. Sensory disturbances were assessed with a 9-item scale (see section 2.5.3), the average of the 9 items was computed as a Total score of sensory disturbances. To test the effect of Group and Visual feedback on the Total score a 2x4 analysis of covariance (ANCOVA) with pain intensity as a covariate was used: 2[Visual feedback (Congruent *or* Incongruent)] x 4[Group (CRPS, FM, HV *or* Arthritis)]. The Pain intensity was included as a covariate as it was differed according to the Group (see Table 2). When applicable, multiple comparisons were performed with Tukey correction.

2.6.3. Correlations analyses

Correlation analyses were performed for each group to test the association between the Total score of sensory disturbances during the Incongruent VF condition and clinical outcomes. For the pain groups (CRPS, FM and Arthritis), Pearson's partial correlations were performed to control the Pain intensity. For the HV group, Pearson's correlations were performed.

2.6.4. Subgroups of sensory disturbances

We had previously observed that some sensory disturbance items seemed to be more frequent in response to visual incongruence than others, and some appeared to occur predominantly in the presence of pain in an acute pain model (Brun et al., 2017). A principal component analysis (PCA) was performed on the 9 items of the sensory disturbances questionnaire measured during the Incongruent Visual feedback condition to determine whether it was possible to identify subgroups of related items. All the experimental groups were pooled together to do the PCA in order to have larger variability. First, analyses with Bartlett's test and Kaiser Maier-Olkin (KMO) index were performed in order to test whether the correlation matrix was adapted to perform a PCA. Bartlett's test has to be significant and KMO index superior or equal to 0.60 to perform the PCA. Secondly, a scree-plot, displaying the eigenvalues as a factor of each component, was used to determine which components explained most of the variability in the data. Third, items were related to one specific component if the absolute value of the loadings factors was superior or equal to 0.45. Finally, internal consistency for each component was measured with Cronbach's alpha.

PCA can convert a large set of sensory disturbances that are possibly correlated into (smaller) subgroups of disturbance that are distinct from each other. Because the subgroups obtained are independent from each other, they could vary differently according to the Group and the Visual Feedback conditions. Therefore, the effect of Group and Visual feedback was tested on each Subgroup of sensory disturbances using the same design as used for the Total score. Therefore, the effect of Group and Visual feedback was performed on each Subgroup of sensory disturbances in the same design used for the Total score: a 2x4 analysis of covariance (ANCOVA) with pain intensity as a covariate was used: 2[Visual feedback (Congruent *or* Incongruent)] x 4[Group (CRPS, FM, HV *or* Arthritis)]. The Pain intensity was included as a covariate as it was different according to the group (see Table 2). When applicable multiple comparisons were performed with Tukey correction.

Data analyses were performed with R 3.4.4 and IBM SPSS Statistics 24 (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp). Normality of the data were assessed with Komolgorov-Smirnov test for the eight experimental conditions (Congruent_CRPS ($p>0.22$), Incongruent_CRPS ($p>0.70$), Congruent_FM ($p>0.35$), Incongruent_FM ($p>0.87$), Congruent_Arthritis ($p>0.19$, Incongruent_Arthritis ($p>0.65$), Congruent_HV ($p<0.05$), Incongruent_HV ($p>0.29$)). When necessary, p-values were Greenhouse-Geisser corrected for sphericity. Moreover, all analyses of variance were assessed with a Type II model designed for unequal sample sizes. The statistical significance was set at $p<0.05$.

3. RESULTS

3.1 Population

Table 1 presents the demographic and clinical characteristics for each group. Table 2 presents the results of the ANOVA. For most variables, CRPS and FM participants were different from HV and Arthritis participants, but never different from each other (but see Table 2 for details for each variable).

« Insert Table 1 approximately here»

« Insert Table 2 approximately here»

3.2. Effect of Group, Pain intensity and Visual Feedback on the <u>Total score</u> of sensory disturbances

Table 1S in Supplementary Material reports mean and SD for each experimental condition in each group. Fig. 2 displays intensity of sensory disturbances for each group and each item and Fig. 3 displays the Total score of the sensory disturbances questionnaire according to the Visual feedback conditions and the Pain intensity. Table 3 displays the ANCOVA results (F and p-values). As shown in Fig. 2 and Fig. 3, and consistent with previous observations (for a review, see Don et al. 2016 (Don et al., 2016)), all participants reported more sensory disturbances during the Incongruent VF than the Congruent VF condition (Table 3). Moreover, the Pain intensity (the covariate) was positively associated with the intensity of sensory disturbances. After controlling for Pain intensity, there was no significant main effect of Group. However, there was a significant interaction between the Group and the Visual feedback conditions, meaning that CRPS and FM were more sensitive to sensorimotor conflicts that HV and OA. Finally, a significant interaction between Visual Feedback and Pain intensity was observed, meaning that more severe pain was associated with a larger increase in sensory disturbances during the Incongruent VF condition relative to the Congruent VF condition.

« Insert Table 3 approximately here»

« Insert Fig. 2 approximately here»

« Insert Fig. 3 approximately here»

3.3. Correlations analyses

Table 4 displays partial correlation analyses for each pain group (CRPS, FM and Arthritis). After controlling for Pain intensity for the pain groups, sensory disturbances evoked by the sensorimotor conflict were not significantly related to the duration of the disease, the level of depressive symptoms and anxiety. However, a positive relationship was found with the amount of anomalous sensations and perceptions for the CRPS group.

« Insert Table 4 approximately here»

3.4. Subgroups of sensory disturbances

The type and the intensity of sensory disturbances induced by the VF incongruence appears to differ across groups. Indeed, as shown on Fig. 2, during the Incongruent VF condition HV reported mainly feelings of peculiarity and a perceived extra-limb, while the three pain groups reported other additional disturbances such as pain, discomfort, changes in weight and temperature and a perceived lost limb. Therefore, a PCA was performed in order to identify different subgroups of sensory disturbances.

Bartlett's test and ($p<10^{-16}$) and KMO index (0.85) authorized the realisation of the PCA. Based on the Kaiser criteria, two components were retained (component 1: eigenvalue of 5.1; component 2: eigenvalue of 0.97 and all others eigenvalues <0.70). The first and the second components explained respectively 41% and 19% of the variance, with a very good internal consistency for the first component (Cronbach's alpha 0.90) and good for the second component (Cronbach's alpha 0.72). For each component, the average score of the items was computed and used for further analysis. Subgroup 1 of items (component 1) includes the items 'pain', 'discomfort', 'losing a limb', 'heavier', 'lighter', 'hotter' and 'colder', and Subgroup 2 (component 2) included 'having an extra limb' and 'feelings of peculiarity'.

3.4. Effect of Group, Pain intensity and Visual Feedback on each <u>Subgroup</u> of sensory disturbances

Table 3 displays the ANCOVA results (F and p-values) for the Subgroup 1 and Subgroup 2 in comparison to the Total score of the sensory disturbances questionnaire. Fig 1S in supplementary material depicts the intensity of sensory disturbances according to the Visual feedback conditions and pain intensity for each Subgroup.

<u>Subgroup 1</u>. The results were similar to the Total score of the sensory disturbances questionnaire.

<u>Subgroup 2</u>. While higher Pain intensity was associated with more report of Subgroup 2 sensations, it did not make participants more prone to report Subgroup 2 sensations specifically in the condition of Incongruent VF. This effect was contrary to what was

observed in the Total score and Subgroup 1 sensations. However, similar to what was observed for the Total Score and Subgroup 1, participants reported more Subgroup 2 sensations during Incongruent VF compared to Congruent VF.

4. DISCUSSION

The first objective of this study was to assess and compare the sensory disturbances induced by sensorimotor conflicts in three chronic pain populations as well as in HV. In accordance with previous studies (Brun et al., 2017; Daenen et al., 2010; Foell et al., 2013; Katayama et al., 2016; McCabe et al., 2005, 2007; Roussel et al., 2015), Incongruent VF induced more sensory disturbances than the Congruent VF condition in all groups. This effect was stronger in the CRPS and FM groups compared to the Arthritis group, which might be explained by the different origin of these pathologies and by the fact that they differ on several clinical characteristics. However, the effect size of the Group was very small (η^2_p<0.10) suggesting that higher sensitivity to sensorimotor conflict in the presence of pain is not mainly explained by the origin of the pathology.

The second objective of the study was to assess whether sensory disturbances induced by sensorimotor conflict are related to the intensity and duration of pain or to other clinical variables such as sensory perception abnormalities, depression and anxiety. Our results show that the extent of sensory disturbances is strongly related to the intensity of pain, regardless of the pathology. This result extends previous results showing that in the presence of acute (Brun et al., 2017; Daenen et al., 2012a) and chronic pain (Daenen et al., 2010, 2012b; McCabe et al., 2007), people are more prone to report changes in sensory perception in response to sensorimotor conflicts compared to pain-free individuals (for a systematic review see Don et al., 2016). Moreover, conflict-induced sensory disturbances were related to sensory perception abnormalities (assessed with the CAPS) in the CRPS group, but not to the duration of the disease or the psychological factors of anxiety and depression. The CAPS assesses the perceptual anomalies for the five senses, for example a perceived change in sensory intensity, a distorted sensory perception and a distorted perception of one's own body (Bell et al., 2006). Inaccurate sensory perception, inducing a greater mismatch between sensory feedback and motor intentions, could explain why people with pain are more vulnerable to sensorimotor conflict. Indeed, proprioceptive deficits are observed in CRPS (Bank et al., 2013; Lewis et al., 2010; Peltz et al., 2011) and women with fibromyalgia self-report an increase in sensory sensitivities in somatosensory and non-somatosensory stimuli (Wilbarger and Cook, 2011). Altogether, our results suggest that sensory disturbances induced by sensorimotor conflicts are specific to pain and sensory perception abnormalities.

A third objective, focusing more on methodological aspects, was to categorize conflict-induced sensory disturbances in to different subgroups. Two subgroups were identified. This suggests that sensory disturbances are potentially related to two different processes, the corollary being that they should be considered separately. This result is consistent with recent findings showing that the presence of acute pain influences the nature of sensory disturbances evoked by sensorimotor conflicts (Brun et al., 2017). In the absence of acute pain, participants mainly reported conflict-induced disturbances such as feelings of peculiarity, perception of an extra limb and perception of losing control, and these sensations were not influenced by the presence of acute pain. However, in the presence of acute pain, participants reported changes in pain, discomfort, temperature and a perceived lost limb (Brun et al., 2017). Interestingly, two electroencephalography (EEG) studies in pain-free individuals (Katayama et al., 2016; Nishigami et al., 2014) also support the presence of two distinct mechanisms in response to sensorimotor conflicts. Nishigami and collaborators (Nishigami et al., 2014) found that the effect of sensorimotor conflict was related to an increased activity of the right posterior parietal cortex compared to the congruent visual feedback condition. Using functional imaging, a previous study found similar activation in the parietal cortex and activation in the dorsolateral prefrontal cortex during exposure to sensorimotor conflicts (Fink et al., 1999). Moreover, the specific sensation “feelings of peculiarity” evoked during sensorimotor conflict was also related to activation of the parietal cortex (Katayama et al., 2016). However, the activity of two pain related areas – the anterior cingulate and the posterior cingulate cortex – was more pronounced in participants who reported higher discomfort during sensorimotor conflict (Nishigami et al., 2014). Thus, it could hypothesized that Subgroup 1 sensations are related to activation of the cingulate cortex while the Subgroup 2 sensations are related to activation of the parietal cortex.

Moreover, our results suggest that sensorimotor conflicts induce feelings of peculiarity and the perception of having an extra limb (Subgroup 2 sensations), no matter whether individuals have pain or not. However, the presence of pain appears to lower the threshold for the detection of sensorimotor conflicts. Indeed for the Subgroup 2 sensations, people with pain reported higher sensory disturbances even in the Congruent VF condition, suggesting that the Congruent VF can be interpreted as a sensorimotor conflict for individuals with pain, consistent with previous observations (Brun et al., 2017; McCabe et al., 2007). This inaccurate perception of a sensorimotor conflict might be explained by the fact that in the presence of acute (Gandevia and Phegan, 1999) and chronic pain (Bultitude and Rafal, 2010; Lewis et al., 2007; Valenzuela-Moguillansky, 2013) alterations of body perception are frequently observed. As pain did not make people more prone to report higher Subgroup 2 sensations (feelings of peculiarity and the perception of having an extra limb) during sensorimotor conflict, we suggest that these two items could be removed from the sensory disturbances questionnaire.

Finally, we showed that in the presence of pain, people report new conflict-induced sensory disturbances (Subgroup 1 sensations), including an increase in painful and discomfort sensations, changes in weight and temperature of the limb and having the impression of a lost limb. In contrast with the theory suggesting that sensorimotor conflicts trigger painful sensations (Harris, 1999), the present results rather suggest that sensorimotor conflicts would contribute to the manifestation of sensory disturbances and pain maintenance. Recent systematic reviews and meta-analyses (Boesch et al., 2016; Don et al., 2016) showed that there is no clear evidence that sensorimotor conflicts trigger painful sensations in both clinical and healthy populations. Our results rather suggest that sensorimotor conflicts might influence painful sensations and other sensory abnormalities in chronic pain populations. These results can be interpreted in line with the body matrix model (Moseley et al., 2012), defined as a body-centred representation depending on multisensory integration in order to maintain the integrity of the body. This model suggests that the body matrix might be altered in consequence to abnormal feedback (e.g. altered sensory inputs, brain damage (Moseley et al., 2012), or brain adaptation (Tabor et al., 2017)) and such alterations might impact on the homeostasis and thermoregulation of the body (Moseley et al., 2012). For example, using the rubber hand illusion, a study showed that participants in whom the illusion of ownership of the rubber hand was stronger were those with a higher drop in temperature in their hand (Moseley et al., 2008). Moreover, a previous study showed that sensorimotor conflicts also altered body ownership in healthy people (Salomon et al., 2016). Therefore, in our study we could hypothesize that sensorimotor incongruence disrupts the body matrix due to altered visual feedback about limb movement and induces changes in ownership (having the impression of losing a limb), thermoregulation (changes in temperature of the limb) and sensory perception (pain and discomfort sensation). Furthermore, having pain makes people more vulnerable to the consequences of a disrupted body matrix induced by sensorimotor conflict.

Some limitations of this study need to be highlighted. Firstly, visual conditions (Congruent VF and Incongruent VF) were presented in a fixed order, rather than randomized (confounder) and a convenience sample was used. However, the results of our study are in line with previous studies showing that Incongruent VF induced more sensory disturbances than Congruent VF (Brun et al., 2017; Daenen et al., 2010; Foell et al., 2013; Katayama et al., 2016; McCabe et al., 2005, 2007; Roussel et al., 2015) suggesting that these potential methodological biases had a minimal impact on our results. Secondly, in order to provide an informed consent, participants were informed that the experimental manipulations might cause brief discomfort and therefore it could have an impact on the results. However, participants were not told about what experimental conditions (Congruent or Incongruent VF) could lead to greater discomfort. Thirdly, for the third aim two factors were extracted from the principal components analysis, although the eigenvalue of the second factor was slightly inferior to 1 (0.97). This suggests that the Subgroup 2 sensations could be removed from the sensory disturbances questionnaire, which is also supported by the fact that pain did not make people more prone to report Subgroup 2 sensations during sensorimotor conflict.

In conclusion, sensory disturbances induced by sensorimotor conflicts are higher in the CRPS and FM groups compared to Arthritis and HV, but the effect size was very small. Regardless of the pathology, conflict-induced sensory disturbances are mainly specific to pain (large effect size). Indeed, the other clinical characteristics were not related to sensory disturbances in each pain group, except for the sensory perception abnormalities in the CRPS group. Moreover, sensory disturbances induced by sensorimotor conflict can be categorized into two subgroups, suggesting they are potentially related to two different processes. Finally, our results contrast with the theory suggesting that sensorimotor conflicts trigger painful sensations and rather suggest that sensorimotor conflicts would contribute to pain maintenance.

ACKNOWLEDGMENTS

We wish to sincerely thank the patients who kindly participated in this study.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to either the study design and methodology, data acquisition or data analysis and interpretation. All authors discussed the study findings, have been consulted in the drafting of the final article, and have given their approval for publication.

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Figure Captions

Fig. 1: Mirror Visual Feedback (VF) depicting (A) Congruent VF and (B) Incongruent VF. The arrows denote direction of limb movement.

Fig. 2: Type and intensity of sensory disturbances for the Congruent and Incongruent Visual Feedback (VF) conditions for each group and each item of the questionnaire. From left to right: 1:new pain, 2:discomfort, 3:losing a limb, 4:hotter, 5:colder, 6:heavier, 7:lighter, 8:having an extra limb and 9: feelings of peculiarity. Mean ± SEM are reported. Score of 0 = no change in sensory perception, score of 6 = maximal change in sensory perception. Grey and checkerboard bars correspond respectively to the Subgroup 1 and 2 of sensory disturbances identified by the principal component analysis.

Fig. 3: Total score of sensory disturbances for each participant (all groups) according to the Visual Feedback (VF) conditions and the pain intensity