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Limb Laterality Discrimination, Evoked Sensations and Somatosensory Behavior in Fibromyalgia Syndrome: A Cross-Sectional Study

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Abstract: The main objective of this study was to assess the status of body schema using limb laterality discrimination tasks and pain measurement variables of patients with FMS compared to healthy subjects. The secondary aim was to analyze the relationships between laterality discrimination with respect to somatosensory variables. Thirty female patients with FMS (with a mean age of 52.43 ± 11.82 years) and thirty healthy women (with a mean age of 47.93 ± 5.92 years) were recruited. The main outcome measures were laterality discrimination, referral of evoked sensations, pressure pain threshold and conditioned pain modulation. The main analysis showed that patients with FMS have a longer reaction time for laterality discrimination in hands (hands—20 images, t = 4.044, $p < 0.0001$, $d = 1.04$; hands—50 images t = 4.012, $p < 0.0001$, $d = 1.31$; feet—20 images t = 2.982, $p < 0.01$, $d = 0.76$; feet—50 images, t = 2.159, $p < 0.05$, $d = 0.55$). With regard the secondary analysis, patients with FM have higher mechanical hyperalgesia (t = −9.550; $p < 0.0001$, d = 2.51) and decreased response to conditioned pain modulation compared with healthy subjects (t = 15.519; $p < 0.0001$, d = 4.17). A positive correlation was found in patients with FMS between greater laterality discrimination ability and better function of conditioned pain modulation (hands r = 0.676, $p < 0.0001$; feet r = 0.485, $p < 0.01$). In conclusion, patients with FMS have a longer reaction time and lower accuracy for laterality discrimination, increased mechanical hyperalgesia and decreased conditioned pain modulation compared to healthy subjects. Finally, it seems that there is a positive correlation between greater laterality discrimination ability and better conditioned pain modulation function.

Keywords: fibromyalgia; limb laterality recognition; conditioned pain modulation; mechanical hyperalgesia

1. Introduction

Fibromyalgia syndrome (FMS) is a highly prevalent chronic pain condition, characterized by chronic widespread musculoskeletal pain as the main symptom, associated with the presence of tender points in multiple locations. FMS patients can have other concomitant symptoms such as fatigue, unrefreshing sleep, stiffness, depression, anxiety, or cognitive dysfunction [1–6].

Pain has been extensively investigated in patients with FMS using different methods. At the peripheral level, findings have been found that type C fibers suffer alterations in function, presenting characteristics of a fine fiber neuropathy [7].

At the spinal cord level, findings of hyperexcitability have been found in pain transmission, demonstrated by temporal summation phenomena [8]. In several studies in patients with FMS, functional magnetic resonance imaging has been used to measure brain activity. They found activation of regions involved in pain processing to potentially harmless stimuli including S1 and S2 cortices, anterior cingulate cortex, caudate nucleus, putamen, cerebellum, and medial frontal gyrus in FMS patients [9]. This also occurs in basal resting situations without the presence of nociceptive stimuli. In individuals with FMS, there is a predominance in the activation of the insula, the S1 cortex, the primary motor cortex, the supplementary motor area and the superior temporal area, while in healthy individuals, frontoparietal and visual areas were activated [10]. In addition, there is also evidence of alterations in pain modulation in patients with FMS presenting dysfunctions of different pain inhibitory mechanisms [11–13]. The different alterations cause an imbalance between excitation-inhibition of pain in favor of the facilitation of nociceptive transmission, which translates into a state of central sensitization.

Body schema is defined as the way a person feels about their own body. It is influenced by the proprioception system (kinesthesia, sense of force, sense of effort, and sense of balance), exteroception (tactile, visual, auditory, olfactory, and taste stimuli), and interoception (sense of the physiological condition of the entire body) [14]. One of the methods to evaluate the interoception of the body schema is laterality discrimination, i.e., whether a part of the body corresponds to the left or right. This judgment of laterality is a process that requires the participant to perform a mental rotation of the internal representation of the body part to be identified [15]. Complex pain mechanisms at both the peripheral and central levels can influence the state of the body schema in populations suffering from chronic pain [16–18]. Sensory information via the thalamus is made redundant, in part by information from the posterior cord of the medial lemniscus in movement planning. It is suggested that this information may be contaminated by pain, such that planning will be different [19]. Motor output will be modified by this incoming information, which may lead to alterations in pain processing [20]. It is also known that the reorganization of S1 can lead to dysfunctions in motor output and motor learning [21]. Studies show that patients suffering from chronic pain disorders like complex regional pain syndrome or phantom limb pain perform worse in laterality discrimination tests compared to healthy subject [13,22–25]. Although published data regarding FMS are scarce, there are indications of difficulty in performing laterality discrimination [22]. Additionally, many studies have found that patients with chronic pain show aberrant alterations in sensitivity to mechanical stimuli such as pain threshold to pressure [8,23,24] and dysfunctions of descending pain inhibitory pathways measured by the conditioned pain modulation test [13,25]. These biomarkers may be useful in assessing pain sensitivity in patients with FMS [26].

Despite the available evidence, the underlying mechanisms of pain in FMS remain poorly understood. To the authors' knowledge, no previous research has specifically investigated the relationship between laterality discrimination and conditioned modulation of pain in FMS patients or other chronic pain conditions. The main objective of this study was to assess the status of body schema using limb laterality discrimination tasks and pain measurement variables of patients with FMS compared to healthy subjects. The secondary aim was to analyze the relationships between laterality discrimination with respect to somatosensory variables.

2. Materials and Methods

This was a cross-sectional study conducted according to the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement.

2.1. Participants

The study sample comprised 30 women with a prior formal diagnosis of FMS, recruited from the fibromyalgia association "AFINSYFACRO" in Mostoles, Spain, and 30 healthy female subjects who served as controls, recruited from a local support group through advertisements and informative presentations. Data were collected from February 2021 to December 2021. The study protocol was approved by the Ethical Review Board of the Rey Juan Carlos University (2605202012920) in accordance with the Declaration of Helsinki, and all participants provided written informed consent before participating. Inclusion criteria in FMS patients for this study were: (1) Medical diagnosis of fibromyalgia; (2) Pain of more than 12 weeks' duration; and (3) Speaking and understanding Spanish correctly. We excluded FMS patients with: (1) Cognitive inability to understand and correctly complete any of the measurement variables; (2) Previous experience with treatments or other investigations in which the recognition of the laterality of different parts of the human body had been used. Inclusion criteria for control participants were: (1) No pain (NPRS = 0); and (2) Speak and understand Spanish correctly. We excluded participants with: (1) Previous episode of musculoskeletal pain in the last week; or (2) Presence of rheumatologic disease. A flowchart is shown in Figure 1.

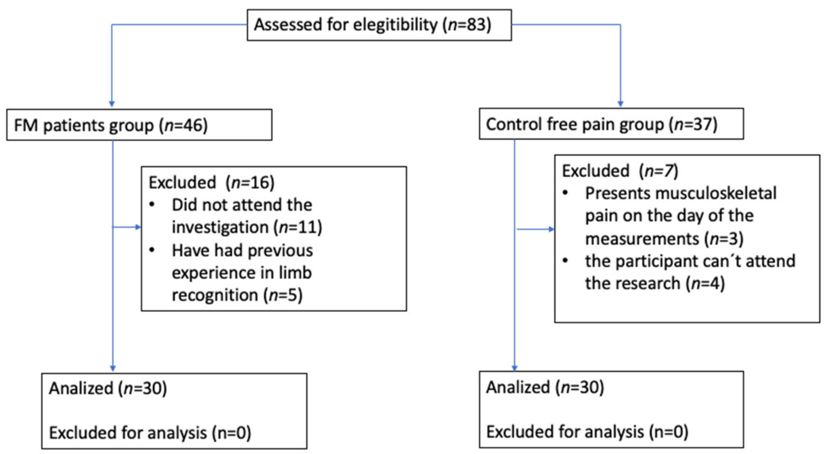

Figure 1. Study design. The following flowchart shows how the participants were distributed in the FMS study and control groups. The cases that were discarded because they did not meet the selection criteria or abandoned the investigation are shown.

2.2. Pain and Clinical Status

Pain and clinical status were assessed by using self-administered questionnaires. FMS patients provided an overall measure of pain severity on a numeric pain rating scale (NPRS), and the impact of ongoing pain and daily function was evaluated by the Spanish Version of Fibromyalgia Impact Questionnaire (FIQ). This questionnaire has been validated and adapted to the Spanish population with a sensitivity of 85.6% (95% CI: 83.1–88.1) and a specificity of 73.2% (95% CI: 68.4–78) [27,28].

2.3. Left/Right Judgment Test (LRJT)

A series of 20 and 50 images representing left or right hands and a series of 20 and 50 images representing left and right feet with different rotations and seen from palmar or dorsal views were shown on the screen of an electronic device via an installed application. The order of appearance was random. The images were shown for a maximum of 10 s or until an answer was made. Patients were instructed to indicate hand or foot side as quickly and accurately as possible by pressing the appropriate key on the screen of the electronic device, "Left" for the left and "Right" for the right. Participants were shown an example image to familiarize themselves with the test and were asked to not move their limbs during the test. The reaction time (s) and number of correct hits (%) were recorded as the result measurements. The reliability of the Recognise online application was previously established in populations with and without pain [29]. The intraclass correlation coefficient (ICC) response time for "feet" was ICC = 0.63–0.75 and for "trunk" ICC = 0.51–0.91. For the accuracy of the answers, ICC = 0.61–0.77 for "feet" and ICC = 0.69–0.71 for "trunk" [30]. Internal and external validity were established before the application was activated. Trials were conducted using a panel of images tested with the letters "L" for "left" and "R" for "right". The application was tested three times, and the internal validity was 100% [31]. "Left" and "right" were included as a factor in the analysis because a study conducted by Saimpont et al. [32] performed a similar separation in their research based on the hands.

2.4. Referral of Evoked Sensations

We asked FMS participants to describe if they had felt any type of pain, any type of strange sensation such as tingling or any type of vasovagal symptom such as an increase in temperature during the laterality discrimination. In the case of having experienced pain or a strange sensation, we also ask the location of these.

2.5. Pressure Pain Threshold (PPT)

A handheld pressure algometer (Model FDIX, Wagner InstrumentMark, Greenwich, CT, USA) with a 1-cm diameter flat rubber probe was used to evaluate the PPT before and during the conditioning stimulus. With a pressure algometer, we measured pressure pain on the upper muscle fibers of the trapezius of each participant. To improve accuracy, the researcher in charge of taking this measurement precisely marked the area of pain with a marker. Each measurement was performed three times. This form of measurement has shown very high intra-examiner reliability values, with ICC = 0.97, and high inter-examiner reliability values, with ICC = 0.79, in the upper trapezius muscle of healthy subjects [33].

2.6. Conditioned Pain Modulation (CPM)

The CPM value is the result of the subtraction of the value of the PPT during the conditioning stimulus from the value of the PPT without stimulus. The cold pressor test was used to establish the paradigm of conditioned pain modulation. The patient had to immerse the opposite hand to that which the PPT was measuring for one minute in a water bath with a temperature of 12 °C, maintained at a constant temperature. If during the procedure, the patients did not tolerate this test, they had to immediately remove their hand from the water. Cold test as a conditioning stimulus has shown good intra-session reliability in healthy volunteers (ICC = 0.64) and patients with chronic pain (ICC = 0.77) [34].

2.7. Data Analysis

We performed the data analysis with the Statistics Package for Social Science (SPSS 25.00, IBM Chicago, IL, USA), employing a 95% (95% CI) confidence interval and considering all values with a p-value inferior to 0.05 to be statistically significant. The Chi-square test was used to compare the difference between nominal variables (such as sex). Each group consisted of 30 participants, normality tests were performed, and no statistical differences were found that indicated abnormal distribution. Student's t-test for independent samples was used as a statistical test to compare continuous variables between groups. The effect size (Cohen's d) was then calculated to compare the study variables. According to Cohen's method, the effect was considered small (0.20–0.49), medium (0.50–0.79) or large (>0.8). The relationship between LRJT and pain processing variables (CPM and mechanical hyperalgesia, referral of evoked sensations, pain intensity and disability (FIQ)) was analyzed using Pearson's correlation coefficient. A Pearson correlation coefficient >0.60 indicated a strong correlation, a coefficient between 0.30 and 0.60 indicated a moderate correlation and a coefficient <0.30 indicated a low correlation. For statistical analyses, the significance level for all tests was set at $p < 0.05$.

3. Results

3.1. Baseline Clinical Status of FMS Patients

Thirty participants were healthy female controls (with a mean age of 47.93 ± 5.92 years) and 30 were female patients diagnosed with FMS (with a mean age of 52.43 ± 11.82 years), Table 1). According to the Fibromylagia Impact questionnaire (FIQ), patients had, on average, mild to moderate symptoms and moderate to severe function deficits with 88.04 ± 3.71. The mean pain intensity was 6.23/10 (SD ± 1.99).

Table 1. Descriptive statistics of demographic variables (*n* = 60).

Measures	FMS (*n* = 30)	Pain Free-Controls (*n* = 30)	*p* Value Independent Samples Student *t*-Test
Age	52.43 ± 11.28	47.93 ± 5.92	0.68
Pain (NPRS)	6.23 ± 1.99	-	
FIQ	88.04 ± 3.71	-	

[1] Data are presented as mean (SD). Patients in the FMS sample present high intensities of clinical pain intensity on the numeric pain rating scale (NPRS), high levels of impact of the disease measured with the Fibromyalgia Impact Questionnaire (FIQ), lower tolerance to pressure pain threshold (PPT) and a dysfunction in the descending inhibitory capacity, as measured with conditioned pain modulation (CPM). Healthy subjects tolerate higher PTT and present good inhibitory system function. The FIQ and NPRS was administered only to FMS participants.

In relation to the sociodemographic variables shown in Table 1, there were no statisically significant differences between healthy subjects and patients.

3.2. Impairment of Right/Left Judgment

FM patients have a longer reaction time (hands—20 images, t = 4.044, $p < 0.0001$, d = 1.04; hands—50 images t = 4.012, $p < 0.0001$, d = 1.31; feet—20 images t = 2.982, $p < 0.01$, d = 0.76; feet—50 images, t = 2.159, $p < 0.05$, d = 0.55) and lower accuracy for both hand and foot images (hands—20 images, t = −3.104, $p < 0.01$, d = 0.80; hands—50 images t = −3.455, $p < 0.01$, d = 0.89; feet—20 images t = −2.272, $p < 0.05$, d = 0.58; feet—50 images, t = −2.407, $p < 0.05$, d = 0.62). The Student's *t*-test showed statistical significance for all variables judging laterality with a moderate to high effect size; see Table 2.

Table 2. Group comparison of right/left judgment performance between FM and pain free controls.

Measures	FMS	Pain Free-Controls	*p* Value Samples Student *t*-Test
ACC hands (20 images)	81.25 ± 11.95	89.08 ± 6.93	0.003
ACC hands (50 images)	81.63 ± 7.98	88.26 ± 6.84	0.001
RT hands (20 images)	2.79 ± 0.95	2.01 ± 0.45	0.000
RT hands (50 images)	3.02 ± 0.81	2.35 ± 0.43	0.000
ACC feets (20 images)	85.50 ± 13.69	91.66 ± 5.77	0.027
ACC feets (50 images)	84.03 ± 9.50	89.13 ± 6.65	0.001
RT feets (20 images)	2.54 ± 1.05	1.94 ± 0.34	0.004
RT feets (50 images)	2.63 ± 0.90	2.23 ± 0.46	0.035

Group comparison of right/left judgment performance. ACC = accuracy in %, RT = reaction time in seconds, FM fibromyalgia. Results displayed as mean ± SD.

The recording of the right/left laterality judgment task measurements counted the right/left recognition hit scores (% successes) and the reaction time required for the response. The successes rates for the feet and hand images when 20 of each were used with healthy volunteers were 89.08% and 91.66%, respectively (SD: 6.93% and 5.77%, respectively). However, in the group of fibromyalgia patients, the correct rate was slightly lower, i.e., 81.25% (SD: 11.95%) for the hands and 85.59% (SD: 13.69%) for 20 images of feet, with statistically significant differences for the two tasks (hands t = −3.104; $p < 0.001$; Feet: t = −2.272; $p < 0.05$).

3.3. Pressure Pain Thresold

Patients with FM had reduced PPT, indicative of mechanical hyperalgesia compared to healthy controls. The independent sample student's *t*-test revealed significant inter-group differences (t = −9.550; $p < 0.0001$, d = 2.51) with a high effect size. Data are shown in Table 3.

Table 3. Between group comparison of psychophysiological measures.

Measures	FMS (*n* = 30)	Pain Free-Controls (*n* = 30)	*p* Value Independent Samples Student *t*-Test
PPT	2.03 ± 0.36	3.38 ± 0.67	0.000
CPM	0.14 ± 0.14	1.53 ± 0.45	0.000

Differences between groups in psychophysiological measures of PPT (pressure pain thresholds) and CPM (conditioned pain modulation). The FM group had reduced PPT, indicative of mechanical hyperalgesia and decreased activation of the descending inhibitory pain system.

3.4. Conditioned Pain Modulation

Patients with FM have decreased response to conditioned pain modulation. There were statistically significant differences between patients and healthy subjects in conditioned pain modulation processing (t = 15.519; $p < 0.0001$, d = 4.17) with a high effect size, meaning that they had decreased activation of the descending inhibitory pain system. Data are shown in Table 3 and for CPM.

3.5. Referral of Evoked Sensations

None of the patients reported any type of painful or strange sensation during the laterality recognition task. Regarding vasovagal symptoms, seven subjects experienced an increase in temperature during this procedure.

3.6. Correlation Analysis

In examining the bivariate relationships between psychophysiological variables (PPT and CPM) and the reaction time and laterality recognition ability of the patients, we found a single strong correlation in our analysis of the FM group, i.e., a positive association was found between the ability to correctly identify the 50 images of the hands and CPM (r = 0.676, $p < 0.0001$). There was also a positive correlation between the ability to correctly identify the 50 images of the feet and CPM (r = 0.485, $p < 0.01$). No statistically significant correlations were found between the other psychophysiological variables and the reaction time and the percentage of correct hand and foot image. The results can be seen in Table 4.

Table 4. Correlation coefficients between performance on the lateral recognition and psychophysiological variables.

Measures	PPT	PPT Post	CPM	FIQ	Pain Intensity
ACC hands (20 images)	0.28	0.25	0.15	0.10	0.02
ACC hands (50 images)	0.10	0.32	**0.67 ***	−0.34	−0.16

Table 4. *Cont.*

Measures	PPT	PPT Post	CPM	FIQ	Pain Intensity
RT hands (20 images)	0.06	0.02	−0.08	0.07	−0.01
RT hands (50 images)	0.04	−0.04	−0.26	0.30	0.28
ACC feets (20 images)	0.09	0.18	0.29	−0.05	−0.16
ACC feets (50 images)	0.02	0.19	**0.48 ***	−0.17	0.24
RT feets (20 images)	0.04	0.00	−0.11	0.07	0.17
RT feets (50 images)	0.07	0.03	−0.06	0.07	0.16

Correlation coefficients between performance regarding the lateral recognition and psychophysiological variables. * Indicates correlation is significant at the level $p < 0.05$. PPT = pressure pain thresholds, CPM = conditioned pain modulation, Acc = accuracy, RT = reaction time. A strong correlation was found between ACC hands (50 images) and CPM in the FM group. A positive correlation was found between AAC feet (50 images) and CPM in the FM group.

4. Discussion

The main objective of this study was to compare upper and lower limb laterality discrimination tasks, the evoked sensations, pressure pain threshold and conditioned pain modulation between patients with FMS and healthy subjects. The secondary aim was to analyze the relationships between laterality discrimination with respect to somatosensory variables. This study showed that the ability to discriminate hands and feet as left and right, as well as reaction time, was impaired in patients with FMS. We also found that patients had mechanical hyperalgesia and decreased conditioned modulation compared to the group of healthy subjects. Finally, we found that a greater ability to recognize laterality was related to a greater amount of conditioned pain modulation.

4.1. Limb Laterality Discrimination and Pain in Fibromyalgia Pain Syndrome

To the best of our knowledge, only one previous study has evaluated laterality discrimination in patients with FMS, although in this study, the authors found that patients with FMS had impaired ability to discriminate laterality. They also found impaired ability to discriminate two-point discrimination but did not measure the somatosensory variables which were applied in this study [22]. In the present investigation, the study of aspects related to pain and laterality discrimination in patients with FMS was deepened. Regarding somatosensory variables, our results are consistent with the results of other investigations in which PTT [8,35] and CPM [13,25] were measured in patients with FMS, showing alterations in pain processing and pain modulation in this population. Our results are in line with those obtained in this other research group [22] and expand current knowledge by including the judgment of laterality of the feet, performing the test with 20 or 50 images and delving into the study of pain by including measurements of PTT, CPM and strange sensations during the laterality discrimination. Our results suggest that the laterality discrimination task in patients with FMS not only presents difficulties for images of the hands but also of the feet, as is reflected both in the number of correct answers and the reaction times. At first, because the results were very similar, it seemed that there was no difference between identifying 20 or 50 images of hands or feet and the relationship between the LRJT and the PTT and CPM measurements. However, in a more in-depth statistical analysis, we found that there was a strong correlation between the ACC of 50 images of the hands and the CPM and a positive association between the ACC of 50 images of the feet and the CPM. These findings are novel for patients with FMS and open the possibility that the LRJT is a task with potential utility in the field of pain assessments in the FMS population. On the other hand, in our study, we found no correlation between the LRJT and mechanical hyperalgesia, as measured with PPT. The qualitative data collected regarding sensations evoked during the LRJT were consistent with the nature of the task, since these patients did not suffer any type of pain symptomatology or unusual sensations, as the mental rotation movement occurred implicitly. In addition, seven patients with FMS reported feeling an increase in body temperature.

The results of this study are also in line with those of another study in which Schmid et al. evaluated the ability to recognize laterality, but in patients with carpal tunnel syndrome [36]. Those authors found impaired accuracy in judging the right and left sides of hand images and proposed that the performance of these tasks occurs in brain areas similar to the imagined or realized movements [37,38]. In contrast, in a population of patients with chronic whiplash-associated disorders, they did not find that the accuracy of imagery judgements was different from controls in terms of reaction time, but they did find a correlation between mechanical hyperalgesia and laterality judgements of the cervical spine and feet [39]. In another study of patients with lower back pain, no differences were found in the accuracy of judgement of laterality and reaction time compared to healthy controls [30].

One possible explanation for these findings is that CPM is a pain assessment tool that highlights the malfunction of descending inhibitory pain systems, which have been seen in previous research to be altered in patients with FMS [11–13]. The cortical and subcortical somatosensory and motor areas appear to be responsible for accuracy in laterality discrimination [40].

4.2. Neurophysiological Implications of Laterality Discrimination and Fibromyalgia

In the neurophysiological processing of laterality discrimination, neuroimaging studies using positron emission tomography have shown that this process involves the activation of different brain areas [15]. Immediately after the presentation of the visual stimulus, the attentional process involves activation of the anterior cingulate cortex and attentional parietal areas contralateral to the stimulated hemisphere, as well as occipital areas contralateral to the stimulated hemisphere. During the process of implicit motor imagery, blood flow increases to primary motor and primary somatosensory areas, similar to those activated during actual movement or explicit motor imagery, such as the supplementary motor area, the superior premotor cortex and the inferior parietal and inferior occipitotemporal premotor cortex. In image representation techniques, laterality discrimination tasks consist of the internal simulation of a movement that involves imagining a motor action without performing it [15]. The recognition of images in different positions and contexts performed during laterality discrimination tasks requires the integration and processing of proprioceptive information in relation to the position of the hands and feet, and this provides relevant input to the sensorimotor cortex to modify activity and produce an improvement in pain-conditioned modulation [41].

On the other hand, it has been observed that suffering from chronic pain does not only produce both peripheral and central changes. Neuroplastic reorganization of the body representation in the primary somatosensory area occurs due to altered input in chronic pain patients [42], and that amount of maladaptive neuroplasticity increases when pain is of longer duration and intensity [43].

Patients with FMS after stimulation with thermal stimuli showed greater brain activity at lower stimulus intensity than healthy subjects in multiple brain regions such as the posterior insula, posterior cingulate cortex and dorsolateral prefrontal cortex. Some experts believe that this is due to interactions in brain regions that are associated with the summation of responses evoked by posterior horn neurons, such as the thalamus, posterior insula, S1, IBS and anterior medial cortex [44–47]. These alterations may explain in part why women with fibromyalgia may be less able to discriminate laterality or why they need more time to do so.

4.3. Applications for Clinical Practice

In only one previous study, carried out in another population with phantom limb pain [48], was the possibility of using LRJT assessed not only as a therapeutic tool for the initial phases of chronic pain treatment, but also as a diagnostic tool that could help identify cases in which there are indications that such people could suffer from some chronic pain condition in the absence of physical injuries. In 2011, the criteria of the American College of Rheumatology for the diagnosis of FMS were updated [49]. According to the scientific literature, this method correctly classifies 88.1% of patients with FMS [50]. However, the continuous progress in the knowledge of chronic pain and neuroscience could allow tasks such as the LRJT to be used to evaluate patients with FMS, allow a chronological follow-up of this aspect or serve as a prognostic tool for individuals suffering from chronic pain.

4.4. Limitations

The first limitation in this study is that the evaluators who carried out the measurements were not blinded and knew the groups to which the participants belonged. The second limitation is that the patients were not assessed for the medication they were taking, because this could have influenced the results when judging laterality. The third limitation is that no measures related to physical activity were carried out to determine whether they might be associated with the ability to recognize laterality. Previous studies have found that patients who engage in some form of physical activity have a greater ability to recognize laterality. Finally, an important limitation to take into account is that it was not possible to record the psychological and cognitive state of the patients by means of validated questionnaires, and this produces a bias in the interpretation of the results, since these variables influence both the pain and the image representation techniques such as the one we used. Finally, the evoked sensations were described by the research team but are not validated; this should be considered an important limitation.

4.5. Future Research Lines

In the future, we intend to pursue research on laterality discrimination to be able to infer neuroplastic changes in cortical activity. Laterality discrimination could even be used as a biomarker to evaluate the activity of the cerebral cortex in relation to movement planning and its relationship with other areas such as pain processing and somatosensory reception areas.

5. Conclusions

This study showed that patients with FMS have selective impairment of left/right judgment compared to healthy subjects. No correlation was found between PTT and hands and feet laterality discrimination in FMS patients. The altered left/right judgment in hands and feet was related to altered CPM. The results are in line with previous reports, which suggested the presence of central mechanisms in patients with FMS.

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References

1. Wolfe, F.; Smythe, H.A.; Yunus, M.B.; Bennett, R.M.; Bombardier, C.; Goldenberg, D.L.; Tugwell, P.; Campbell, S.M.; Abeles, M.; Clark, P.; et al. The american college of rheumatology 1990 Criteria for the classification of fibromyalgia. *Arthritis Rheum.* **1990**, *33*, 160–172. [CrossRef]
2. Wolfe, F.; Ross, K.; Anderson, J.; Russell, I.J.; Hebert, L. The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Care Res.* **1995**, *38*, 19–28. [CrossRef] [PubMed]
3. Sarzi-Puttini, P.; Buskila, D.; Carrabba, M.; Doria, A.; Atzeni, F. Treatment Strategy in Fibromyalgia Syndrome: Where Are We Now? *Semin. Arthritis Rheum.* **2008**, *37*, 353–365. [CrossRef] [PubMed]
4. Staud, R.; Domingo, M. Evidence for Abnormal Pain Processing in Fibromyalgia Syndrome. *Pain Med.* **2001**, *2*, 208–215. [CrossRef] [PubMed]
5. Wolfe, F.; Brähler, E.; Hinz, A.; Häuser, W. Fibromyalgia Prevalence, Somatic Symptom Reporting, and the Dimensionality of Polysymptomatic Distress: Results from a Survey of the General Population. *Arthritis Care Res.* **2013**, *65*, 777–785. [CrossRef]
6. Silverman, S.L.; Harnett, J.; Zlateva, G.; Mardekian, J. Identifying Fibromyalgia-Associated Symptoms and Conditions from a Clinical Perspective: A Step Toward Evaluating Healthcare Resource Utilization in Fibromyalgia. *Pain Pract.* **2010**, *10*, 520–529. [CrossRef]
7. Serra, J.; Collado, A.; Solà, R.; Antonelli, F.; Torres, X.; Salgueiro, M.; Quiles, C.; Bostock, H. Hyperexcitable C Nociceptors in Fibromyalgia. *Ann. Neurol.* **2014**, *75*, 196–208. [CrossRef]
8. Desmeules, J.A.; Cedraschi, C.; Rapiti, E.; Baumgartner, E.; Finckh, A.; Cohen, P.; Dayer, P.; Vischer, T.L. Neurophysiologic evidence for a central sensitization in patients with fibromyalgia. *Arthritis Rheum.* **2003**, *48*, 1420–1429. [CrossRef]
9. Gracely, R.H.; Ambrose, K.R. Neuroimaging of Fibromyalgia. *Best Pract. Res. Clin. Rheumatol.* **2011**, *25*, 271–284. [CrossRef]
10. Kaplan, C.M.; Schrepf, A.; Vatansever, D.; Larkin, T.E.; Mawla, I.; Ichesco, E.; Kochlefl, L.; Harte, S.E.; Clauw, D.J.; Mashour, G.A.; et al. Functional and neurochemical disruptions of brain hub topology in chronic pain. *Pain* **2019**, *160*, 973–983. [CrossRef] [PubMed]
11. Staud, R.; Robinson, M.E.; Vierck, C.J., Jr.; Price, D.D. Diffuse Noxious Inhibitory Controls (DNIC) Attenuate Temporal Summation of Second Pain in Normal Males but Not in Normal Females or Fibromyalgia Patients. *Pain* **2003**, *101*, 167–174. [CrossRef]
12. Harris, R.E.; Clauw, D.J.; Scott, D.J.; McLean, S.A.; Gracely, R.H.; Zubieta, J.-K. Decreased Central μ-Opioid Receptor Availability in Fibromyalgia. *J. Neurosci.* **2007**, *27*, 10000–10006. [CrossRef] [PubMed]
13. O'Brien, A.T.; Deitos, A.; Pego, Y.T.; Fregni, F.; Carrillo-de-la-Peña, M.T. Defective Endogenous Pain Modulation in Fibromyalgia: A Meta-Analysis of Temporal Summation and Conditioned Pain Modulation Paradigms. *J. Pain* **2018**, *19*, 819–836. [CrossRef] [PubMed]
14. Lotze, M.; Moseley, G.L. Role of distorted body image in pain. *Curr. Rheumatol. Rep.* **2007**, *9*, 488–496. [CrossRef] [PubMed]
15. Parsons, L.M. Integrating cognitive psychology, neurology and neuroimaging. *Acta Psychol.* **2001**, *107*, 155–181. [CrossRef]
16. Haggard, P.; Iannetti, G.D.; Longo, M.R. Spatial Sensory Organization and Body Representation in Pain Perception. *Curr. Biol.* **2013**, *23*, R164–R176. [CrossRef]
17. Tsay, A.; Allen, T.J.; Proske, U.; Giummarra, M.J. Sensing the Body in Chronic Pain: A Review of Psychophysical Studies Implicating Altered Body Representation. *Neurosci. Biobehav. Rev.* **2015**, *52*, 221–232. [CrossRef]
18. Wand, B.M.; Parkitny, L.; O'Connell, N.E.; Luomajoki, H.; McAuley, J.H.; Thacker, M.; Moseley, G.L. Cortical changes in chronic low back pain: Current state of the art and implications for clinical practice. *Man. Ther.* **2011**, *16*, 15–20. [CrossRef]
19. Anderson, W.S.; Weiss, N.; Lawson, H.C.; Ohara, S.; Rowland, L.; Lenz, F.A. Demonstration of motor imagery movement and phantom movement-related neuronal activity in human thalamus. *NeuroReport* **2011**, *22*, 88–92. [CrossRef]
20. Nijs, J.; Daenen, L.; Cras, P.; Struyf, F.; Roussel, N.; Oostendorp, R.A.B. Nociception Affects Motor Output: A Review on Sensory-Motor Interaction with Focus on Clinical Implications. *Clin. J. Pain* **2012**, *28*, 175–181. [CrossRef]
21. Meier, M.L.; Vrana, A.; Schweinhardt, P. Low Back Pain: The Potential Contribution of Supraspinal Motor Control and Proprioception. *Neuroscientist* **2019**, *25*, 583–596. [CrossRef] [PubMed]
22. Martínez, E.; Guillen, V.; Buesa, I.; Azkue, J.J. A Distorted Body Schema and Susceptibility to Experiencing Anomalous Somatosensory Sensations in Fibromyalgia Syndrome. *Clin. J. Pain* **2019**, *35*, 887–893. [CrossRef] [PubMed]
23. Scott, D.; Jull, G.; Sterling, M. Widespread Sensory Hypersensitivity Is a Feature of Chronic Whiplash-Associated Disorder but not Chronic Idiopathic Neck Pain. *Clin. J. Pain* **2005**, *21*, 175–181. [CrossRef] [PubMed]
24. Fernández-de-Las-Peñas, C.; Coppieters, M.W.; Cuadrado, M.L.; Pareja, J.A. Patients with Chronic Tension-Type Headache Demonstrate Increased Mechano-Sensitivity of the Supra-Orbital Nerve. *Headache* **2008**, *48*, 570–577. [CrossRef] [PubMed]
25. Potvin, S.; Marchand, S. Pain Facilitation and Pain Inhibition during Conditioned Pain Modulation in Fibromyalgia and in Healthy Controls. *Pain* **2016**, *157*, 1704–1710. [CrossRef]
26. Arroyo-Fernández, R.; Bravo-Esteban, E.; Doménech-García, V.; Ferri-Morales, A. Pressure-Induced Referred Pain as a Biomarker of Pain Sensitivity in Fibromyalgia. *Pain Physician* **2020**, *23*, E353–E362.

27. Rivera, J.; González, T. The Fibromyalgia Impact Questionnaire: A validated Spanish version to assess the health status in women with fibromyalgia. *Clin. Exp. Rheumatol.* **2004**, *22*, 554–560. [PubMed]
28. Casanueva, B.; García-Fructuoso, F.; Belenguer, R.; Alegre, C.; Moreno-Muelas, J.V.; Hernandez, J.L.; Pina, T.; González-Gay, M. The Spanish version of the 2010 American College of Rheumatology Preliminary Diagnostic Criteria for fibromyalgia: Reliability and validity assessment. *Clin. Exp. Rheumatol.* **2016**, *34*, S55–S58.
29. Bray, H.; Moseley, G.L. Disrupted working body schema of the trunk in people with back pain. *Br. J. Sports Med.* **2011**, *45*, 168–173. [CrossRef]
30. Linder, M.; Michaelson, P.; Röijezon, U. Laterality judgments in people with low back pain–A cross-sectional observational and test–retest reliability study. *Man. Ther.* **2016**, *21*, 128–133. [CrossRef]
31. Wallwork, S.B.; Butler, D.S.; Fulton, I.; Stewart, H.; Darmawan, I.; Moseley, G.L. Left/right neck rotation judgments are affected by age, gender, handedness and image rotation. *Man. Ther.* **2013**, *18*, 225–230. [CrossRef] [PubMed]
32. Saimpont, A.; Pozzo, T.; Papaxanthis, C. Aging Affects the Mental Rotation of Left and Right Hands. *PLoS ONE* **2009**, *4*, e6714. [CrossRef] [PubMed]
33. Walton, D.M.; Macdermid, J.C.; Nielson, W.; Teasell, R.W.; Chiasson, M.; Brown, L. Reliability, Standard Error, and Minimum Detectable Change of Clinical Pressure Pain Threshold Testing in People with and without Acute Neck Pain. *J. Orthop. Sports Phys. Ther.* **2011**, *41*, 644–650. [CrossRef]
34. Nuwailati, R.; Bobos, P.; Drangsholt, M.; Curatolo, M. Reliability of conditioned pain modulation in healthy individuals and chronic pain patients: A systematic review and meta-analysis. *Scand. J. Pain* **2022**, *22*, 262–278. [CrossRef] [PubMed]
35. Terzi, H.; Terzi, R.; Kale, A. The Relationship between Fibromyalgia and Pressure Pain Threshold in Patients with Dyspareunia. *Pain Res. Manag.* **2015**, *20*, 137–140. [CrossRef] [PubMed]
36. Schmid, A.B.; Coppieters, M.W. Left/Right Judgment of Body Parts Is Selectively Impaired in Patients with Unilateral Carpal Tunnel Syndrome. *Clin. J. Pain* **2012**, *28*, 615–622. [CrossRef] [PubMed]
37. Szameitat, A.J.; Shen, S.; Sterr, A. Motor imagery of complex everyday movements. An fMRI study. *NeuroImage* **2007**, *34*, 702–713. [CrossRef]
38. Michelon, P.; Vettel, J.M.; Zacks, J. Lateral Somatotopic Organization during Imagined and Prepared Movements. *J. Neurophysiol.* **2006**, *95*, 811–822. [CrossRef]
39. Pedler, A.; Motlagh, H.; Sterling, M. Laterality judgments are not impaired in patients with chronic whiplash associated disorders. *Man. Ther.* **2013**, *18*, 72–76. [CrossRef]
40. Schwoebel, J.; Coslett, H.B.; Bradt, J.; Friedman, R.; Dileo, C. Pain and the Body Schema: Effects of Pain Severity on Mental Representations of Movement. *Neurology* **2002**, *59*, 775–777. [CrossRef]
41. Jongsma, M.L.A.; Meulenbroek, R.G.J.; Okely, J.; Baas, C.M.; Van Der Lubbe, R.H.J.; Steenbergen, B. Effects of Hand Orientation on Motor Imagery-Event Related Potentials Suggest Kinesthetic Motor Imagery to Solve the Hand Laterality Judgment Task. *PLoS ONE* **2013**, *8*, e76515. [CrossRef] [PubMed]
42. Krigolson, O.; van Gyn, G.; Tremblay, L.; Heath, M. Is There "Feedback" during Visual Imagery? Evidence from a Specificity of Practice Paradigm. *Can. J. Exp. Psychol./Rev. Can. Psychol. Exp.* **2006**, *60*, 24–32. [CrossRef] [PubMed]
43. Kim, W.; Kim, S.K.; Nabekura, J. Functional and structural plasticity in the primary somatosensory cortex associated with chronic pain. *J. Neurochem.* **2017**, *141*, 499–506. [CrossRef]
44. Lim, M.; Roosink, M.; Kim, J.S.; Kim, H.W.; Lee, E.B.; Son, K.M.; Kim, H.A.; Chung, C.K. Augmented Pain Processing in Primary and Secondary Somatosensory Cortex in Fibromyalgia: A Magnetoencephalography Study Using Intra-Epidermal Electrical Stimulation. *PLoS ONE* **2016**, *11*, e0151776. [CrossRef] [PubMed]
45. Ellingson, L.D.; Shields, M.R.; Stegner, A.J.; Cook, D.B. Physical Activity, Sustained Sedentary Behavior, and Pain Modulation in Women with Fibromyalgia. *J. Pain* **2012**, *13*, 195–206. [CrossRef] [PubMed]
46. Craggs, J.G.; Staud, R.; Robinson, M.E.; Perlstein, W.M.; Price, D. Effective Connectivity Among Brain Regions Associated with Slow Temporal Summation of C-Fiber-Evoked Pain in Fibromyalgia Patients and Healthy Controls. *J. Pain* **2012**, *13*, 390–400. [CrossRef]
47. McLoughlin, M.J.; Stegner, A.J.; Cook, D.B. The Relationship Between Physical Activity and Brain Responses to Pain in Fibromyalgia. *J. Pain* **2011**, *12*, 640–651. [CrossRef] [PubMed]
48. Wong, C.K.; Wong, C.K. Limb Laterality Recognition Score: A Reliable Clinical Measure Related to Phantom Limb Pain. *Pain Med.* **2018**, *19*, 753–756. [CrossRef]
49. Wolfe, F.; Clauw, D.J.; Fitzcharles, M.-A.; Goldenberg, D.L.; Katz, R.S.; Mease, P.; Russell, A.S.; Russell, I.J.; Winfield, J.B.; Yunus, M.B. The American College of Rheumatology Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity. *Arthritis Care Res.* **2010**, *62*, 600–610. [CrossRef]
50. Moyano, S.; Kilstein, J.G.; de Miguel, C.A. New Diagnostic Criteria for Fibromyalgia: Here to Stay? *Reumatol. Clin.* **2015**, *11*, 210–214. [CrossRef]