ORIGINAL ARTICLE

Brain Electrical Activity Associated With Visual Attention and Reactive Motor Inhibition in Patients With Fibromyalgia

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ABSTRACT

Objective: Fibromyalgia (FM) is a generalized chronic pain condition associated with multiple cognitive impairments, including altered inhibitory processes. Inhibition is a key component of human executive functions and shares neural substrate with pain processing, which may explain the inhibitory deficits in FM. Here, we investigated the integrity of brain inhibitory mechanisms in these patients.

Methods: We recorded the electroencephalographic activity of 27 patients with FM and 27 healthy controls (HCs) (all women) while they performed a reactive motor inhibition task (the stop-signal paradigm). We analyzed task-induced modulations in electrophysiological markers related to inhibition (N2, P3, and midfrontal theta oscillations) and visual attention (posterior alpha oscillations).

Results: The FM group performed the task correctly, with no differences relative to HCs at the behavioral level. We did not find any between-group differences in N2 amplitude ($F(1,52) = 0.01$, $p = .93$), P3 amplitude ($F(1,52) = 3.46$; $p = .068$), or theta power ($F(1,52) = 0.05$; $p = .82$). However, modulation of posterior alpha power after presentation of either the *go* or *stop* stimuli was lower in patients than in HCs ($F(1,52) = 7.98$; $p = .007$).

Conclusions: N2, P3, theta power, and behavioral results indicate that the mechanisms of motor inhibition are sufficiently preserved to enable correct performance of the stop-signal task in patients with FM. Nevertheless, the lower modulation of alpha suggests greater difficulty in mobilizing and maintaining visual attentional resources, a result that may explain the cognitive dysfunction observed in FM.

Key words: cognitive dysfunction, electroencephalography, fibromyalgia, motor inhibition.

INTRODUCTION

Fibromyalgia (FM) is a chronic syndrome involving widespread pain, fatigue, sleep disorders, and cognitive dysfunction. Cognitive dysfunction complaints are approximately 2.5 times more frequent in patients with FM than in chronic pain patients affected by different rheumatic conditions and have a major impact on the patients' quality of life (1–3). Cognitive alterations in patients with FM have been found in different dimensions such as attention, executive function, as well as working, semantic, and episodic memory (4,5).

Execution of an organized cognitive or behavioral response requires well-preserved inhibitory mechanisms (6). Inhibition, a type of executive function, allows humans to stop unwanted behavior and to eliminate undesired mental representations (7). Previous studies have reported alterations in behavioral indices or neuroimaging data associated with motor response inhibition, suggesting changes in frontal networks related to executive functioning in FM (8–11). Nevertheless, evidence for motor inhibition deficits in patients with FM remains scarce and sometimes contradictory, because abnormalities are not always observed at the behavioral level (10,11). Furthermore, although alterations in motor inhibition have been detected using proactive motor inhibition tasks (go/no-go), there is no previous research concerning the brain activity of patients with FM while they perform reactive inhibition tasks (such as the stop-signal task).

The stop-signal task requires the immediate cancellation of an already initiated motion plan after the presentation of a stop signal. Although the mechanisms involved in emotional-motivational control of pain-related information are different from those involved in motor inhibition, the simplicity in operationalizing the latter makes the stop-signal task a useful tool for studying inhibition processes in FM (12). In this line, recent reports have suggested a direct relationship between the capacity to tolerate induced pain and the ability to perform tasks that require motor

BDI = Beck Depression Inventory, **BMI** = body mass index, **EEG** = electroencephalogram, **ERP** = event-related potentials, **FM** = fibromyalgia, **FSQ** = fibromyalgia survey questionnaire, **HC** = healthy control, **MAOI** = monoamine oxidase inhibitor, **MFE-30** = Memory Failures of Everyday Questionnaire, **NSAID** = nonsteroidal anti-inflammatory drug, **PCA** = principal components analysis, **PCS** = Pain Catastrophizing Scale, **SARIs** = serotonin antagonist and reuptake inhibitor, **SSD** = stop-signal delay, **SNRI** = serotonin-norepinephrine reuptake inhibitor, **SSRI** = selective serotonin reuptake inhibitor, **SSRT** = stop-signal reaction time, **SSS** = Symptom Severity Score, **TCA** = tricyclic antidepressant, **TF** = temporal factor, **VAS** = visual analogue scale, **WPI** = Widespread Pain Index

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inhibition (13,14). Conversely, people with a lower inhibitory capacity may show increasing and sustained pain avoidance responses, which may contribute to the pain becoming chronic (15). Thus, although the existing evidence suggests that the presence of chronic pain may be related to alterations in inhibition processes, this relationship has not been yet explored using a reactive motor inhibition task in FM.

At the electroencephalographic level, the stop-signal tasks evoke the appearance of event-related potential (ERP) components such as N2 and P3. These components have their neural origin in medial and fronto-central cortical areas, and they are related to conflict detection and inhibition evaluation, respectively (16–18). In the frequency domain, inhibition is associated with an increase in midfrontal theta power, oscillatory activity that is also associated with the N2 and P3 components (19). Moreover, performance of the stop-signal task requires adequate involvement of visual attention mechanisms, which is associated with a reduction in posterior alpha power (20,21).

To further investigate the possible alterations in motor inhibition mechanisms, we recorded the brain electrical activity of patients with FM while they performed the stop-signal task. We hypothesized that patients have slower reaction times and make more inhibition errors than healthy controls (HCs). We also expected to find differences in the amplitude of N2 and P3 ERP components, both associated with motor inhibition. Given the difficulty in interpreting these components because of the overlapping activity related to the go and stop signals (22), we applied temporal principal component analysis (PCA) to the ERP data to better differentiate between the activity evoked by each of the signals. We also included an electroencephalogram (EEG) index obtained by time-frequency decomposition (midfrontal theta), which has been related to cognitive control and motor inhibition. Finally, we investigated modulation of the posterior alpha power after stimulus presentation to explore the integrity of visual attention processes during the performance of the stop-signal task and its relationship with clinical variables.

METHODS

Participants

Twenty-seven patients with FM and 27 HCs (all women in both groups) participated in the study. The patients were recruited from a local hospital (Complexo Hospitalario Universitario de Santiago) and from patients' associations in Santiago de Compostela (Spain) and surrounding areas. All patients were diagnosed by a physician and fulfilled the 1990 and 2010 American College of Rheumatology criteria for diagnosis of FM (23,24). HCs were recruited through advertisements placed in community centers. From the initial sample (35 FMs and 35 HCs), three patients with FM and three controls were excluded from the analysis for having extreme proportions (<0.1 to >0.9) of correct inhibitions during the stop-signal task. Five patients with FM and four HCs were excluded because of insufficient quality of the EEG recordings. One additional control participant was excluded because of self-reported high levels of pain. See Table 1 for sociodemographic and clinical data. The initial sample used in this study is the same as that described in a previous article (25). Registration sessions were conducted between June 2014 and May 2015. The study was approved by the ethics committee of the University of Santiago in accordance with the Declaration of Helsinki. All healthy volunteers and patients were informed about the experimental procedures and gave written informed consent before participation.

All participants were interviewed about their health status and assessed for pain levels and other symptoms of FM. They completed visual analogue scales (VAS) to assess pain level and mood state during the last month. Participants also completed the *Pain Catastrophizing Scale* (PCS) (26,27) and the *Beck Depression Inventory* (BDI) (28,29), with cut-off scores as follows: 0–9 minimal depression; 10–18 mild depression; 19–29 moderate depression; and 30–63 severe depression. The Widespread Pain Index (WPI) and the Symptom Severity Score (SSS) were also obtained using the Spanish version of the *Fibromyalgia Survey Questionnaire* (FSQ) (23,30). Item 2 of the FSQ scale was used to assess the presence of cognitive complaints (scored from 0, no problems, to 3, severe problems). Cognitive complaints were also assessed using the total score of the *Memory Failures of Everyday Questionnaire* (MFE-30) (31). The MFE-30 is composed of 30 items to evaluate subjective memory complaints. Each item is rated on a five-point Likert-type scale ranging from 0 to 4, making a total score between 0 and 120. Cut-off scores are as follows: 0–7 optimal performance; 8–35 normal performance; 36–50 mild deterioration; and >50 moderate or severe mnesic deterioration. The MFE-30 was only applied to 24 patients with FM and 19 HCs, and therefore, the statistical analyses including this questionnaire were done with fewer participants.

TABLE 1. Sociodemographic and Clinical Variables for Patients With FM and HCs

	FM	HC	Statistics
Age, y	49.9 (9.6)	50.0 (10.5)	$t_{(52)} = -0.76$; $p = .45$
Years of education	10.7 (3.4)	10.6 (3.1)	$t_{(52)} = -0.13$; $p = .90$
BMI	24.2 (4.2)	25.8 (5.6)	$t_{(52)} = -1.14$; $p = .26$
PCS	23.0 (14.7)	12.0 (8.9)	$t_{(52)} = 3.2$; $p = .002$
BDI	21.5 (11.7)	8.6 (4.6)	$t_{(52)} = 5.2$; $p < .001$
VAS pain	6.3 (1.6)	2.2 (2.3)	$t_{(52)} = 7.4$; $p < .001$
VAS mood	5.4 (2.8)	2.9 (2.4)	$t_{(52)} = 3.8$; $p < .001$
FSQ2	1.96 (0.76)	0.85 (.67)	$t_{(52)} = 5.7$; $p < .001$
SSS	9.2 (1.9)	3.8 (2.2)	$t_{(52)} = 9.37$; $p < .001$
WPI	12.1 (4.1)	2.0 (2.0)	$t_{(52)} = 11.6$; $p < .001$
MFE-30	52.7 (26.4)	24.6 (9.5)	$t_{(41)} = 4.4$; $p < .001$
Medication			
Antidepressants			
SSRIs	5	0	
TCAs	4	0	
SNRIs	3	0	
SARIs	1	0	
MAOIs	1	1	
Anxiolytics	13	1	
NSAIDs	17	1	
Pregabalin/ Gabapentin	6	0	
Opioids	5	0	

FM = fibromyalgia; HC = healthy control; BMI = body mass index; PCS = Pain Catastrophizing Scale; BDI = Beck Depression Inventory; VAS = visual analogue scale; FSQ2 = Item 2 of the Fibromyalgia Survey Questionnaire; SSS = Symptom Severity Score; WPI = Widespread Pain Index; MFE-30 = Memory Failures of Everyday Questionnaire; SSRIs = selective serotonin reuptake inhibitors; TCAs = tricyclic antidepressants; SNRIs = serotonin-norepinephrine reuptake inhibitors; SARIs = serotonin antagonist and reuptake inhibitors; MAOIs = monoamine oxidase inhibitors; NSAIDs = nonsteroidal anti-inflammatory drugs.

Mean (SD) values for each measured variable are provided.

Task and Procedure

The participants were fitted with an electrode cap for EEG recording and were seated facing a 17-in monitor (viewing distance, 80 cm) on which the stimuli were presented. The participants were asked to fix their sight

in the center of the screen and to avoid moving their heads during the task. The recording sessions were conducted in an electrically isolated room with low light and noise levels.

The stop-signal task involved presentation of arrows pointing right or left (Figure 1). All arrows were first blue and then changed to green, yellow, or red (all colors with the same level of luminance). The first arrow was presented for 500 milliseconds and the color change occurred at an interval (also called Stop-Signal Delay [SSD]) of between 150 and 350 milliseconds, with 50-millisecond steps. The SSD interval was determined using the staircase-tracking algorithm, which increased by 50 milliseconds if the previous stop trial was correctly inhibited and decreased the SSD by 50 milliseconds if the previous stop trial was not inhibited. This algorithm causes a distribution approximately 1/2 of successful and 1/2 of unsuccessful inhibited trials. The participants were asked to respond quickly with the index finger of the hand on the side to which the arrow was pointing. If the arrow changed to red, they had to immediately stop their response, but if the arrow changed to green or yellow, they had to continue responding. A fixation cross with a random duration between 1.8 and 2 seconds was shown during the interstimulus interval.

The task consisted of 240 trials, 80 of which were stop trials (red arrow). Participants had five breaks of undetermined duration and were able to resume the task whenever they wished. All participants completed 10 practice trials to ensure that they understood the instructions. The task was designed and presented using PsychoPy software (32).

EEG Recording and Data Analysis

EEG activity was recorded via 32 active electrodes inserted in an electrode cap (following the 10–20 international system). Vertical and horizontal eye movements were registered using four additional surface electrodes. The FP1 electrode was used as reference and FPz as ground. Impedances were kept less than 10 KΩ. The signal was recorded at a sampling rate of 500 Hz and filtered with an on-line band-pass filter (0.1–100 Hz) and a notch filter (50 Hz). A Brain Vision actiCHamp amplifier was used for recording.

The EEG data were analyzed using EEGlab 13.3 software (33). Channels with low-quality recordings were removed and replaced by spherical spline interpolation (with less than 0.01% interpolated electrodes in each group). The segments with prominent ocular artefacts were removed after visual inspection. The EEG was resampled and filtered using a high-pass FIR filter at 0.5 Hz and low-pass FIR filter at 30 Hz. Epochs were extracted from −800 to 1800 milliseconds, time locked to the color change of the arrow. The periods analyzed were therefore not based on the initial arrow but rather on the moment when the color changes, and the trial is confirmed as go or stop. For FM participants, the M (SD) number of epochs retained was 147.6 (10.6) in the go condition and 78.3 (2.1) in the stop condition, whereas for HCs, the M (SD) was 148.8 (12.4) and 78.1 (7.6), respectively, with no difference between the two groups ($F(1,52) = 0.07$; $p = .8$). An extended version of the independent component analysis was applied, and the components associated with eye movements or muscular activity were manually removed. The EEG was re-referenced using the reference electrode standardization technique method (34). This method allows the EEG to be transformed from an initial reference in any location to a virtual point located at infinity, which is an ideal location for a neutral reference, because it is far from the influence of neural or noisy electrical activity. For the ERPs, the baseline was corrected using an interval between −450 and − 350 milliseconds before the stop or go signals were displayed. This interval was chosen because there may be activity after −350 milliseconds evoked by the presentation of the first arrow.

After the ERPs were averaged, we performed a temporal PCA (tPCA) using the ERP PCA toolkit (35). tPCA enables separation of temporarily overlapping components, thus simplifying the analysis and description of complex multidimensional data. This technique produces a series of temporal factors (TFs) free from the influence of nearby components, and it enables elimination of subjective influences in the identification of ERP peaks. A scree test was used to select the number of factors to be retained (36). The results of the scree test indicated that six factors, together accounting for 93% of the variance, should be retained. Factors were extracted on the basis of the covariance matrix (Promax rotation). The components were then reconstructed to microvolt units by multiplying the factor loads by the factor scores for each electrode, participant, and condition. The peak amplitude (measured in the electrode that showed the largest amplitude of each component) was used for statistical comparisons. Of the six components

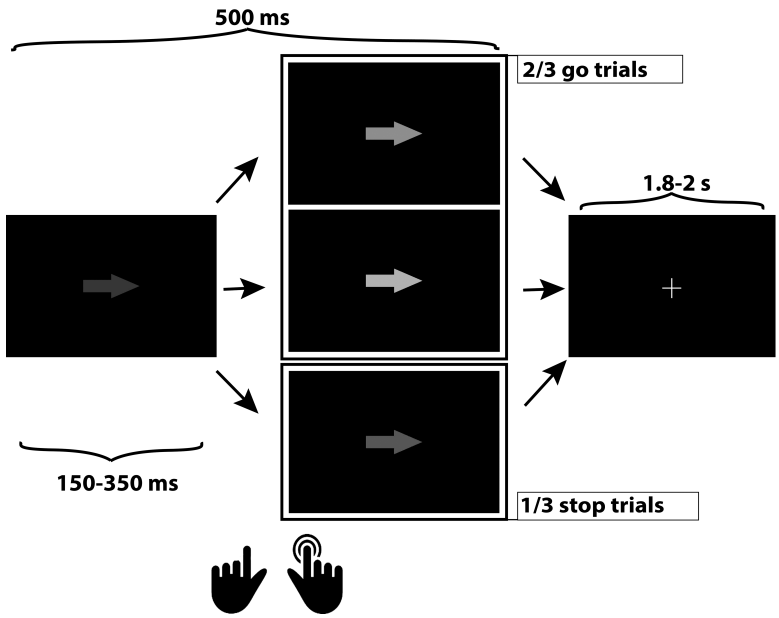

FIGURE 1. Design of the stop-signal task. Each trial began with a blue arrow pointing to the right or left. The arrow then changed to green or yellow in the go trials (2/3) or red in the stop trials (1/3). The participants were required to respond as quickly as possible to the direction of the arrow and to stop their response if the arrow changed to red. The interval between stimuli was of variable duration between 1.8 and 2 seconds. Color image is available only in online version (www.psychosomaticmedicine.org).

extracted, we did not analyze TF4, because the latency was very late (852 milliseconds) and was not associated with any of the expected factors. The remaining factors are described in the results section.

Time-frequency decomposition of the EEG was performed by computing the inverse fast Fourier transform of the multiplication of the power spectrum of the EEG data by the power spectrum of different complex Morlet wavelets. Wavelets were created in 25 logarithmically frequency spaced steps (3–35 Hz), with 3 cycles at the lowest frequency up to 8 at the highest frequency, also in logarithmically increasing steps. Event-related spectral perturbation was normalized by transforming the power change of each time-frequency pixel to decibel, relative to the mean power in the baseline interval (−600 to −400 milliseconds) for each frequency. We selected electrodes FC1 and FC2 for analysis of the theta band as well as electrodes O1 and O2 for analysis of alpha activity, i.e., the locations where these oscillations usually show maximum power modulation (37). We carried out statistical analysis of the mean power in the time-frequency window where the modulation was greatest.

With regard to behavioral data, we computed the mean reaction time, the percentage of successfully stopped trials, and the stop-signal reaction time (SSRT). SSRT is an index of the speed of the stopping process, and here, we calculated it by subtracting the mean SSD from the mean go reaction time for each participant (38).

Statistical Analysis

Differences between groups in sociodemographic variables, measures of FM symptoms, and behavioral data (reaction times, the percentage of successfully stopped trials and SSRT) were analyzed using *t* tests for independent samples. Repeated-measures analyses of variance were applied to the electrophysiological data (factors obtained by tPCA and theta and alpha power) with the factors group (FM or HC) and condition (go or stop trials). The Greenhouse-Geisser correction was applied to adjust the degrees of freedom of the *F* values when the assumption of sphericity was not fulfilled. Effect sizes are reported using Hedges's g_s for independent samples *t* test and η_p^2 for repeated-measures analyses of variance. The Spearman's rank correlation coefficients were computed to assess the relationship between alpha power modulation and sociodemographic and symptomatic variables. Correlations were corrected for multiple comparisons using the false discovery rate procedure. All statistical analyses were performed using SPSS 20.

RESULTS

Behavioral Data

Both groups performed similarly at the behavioral level, with no differences in RTs for either the go trials (FM: 590 ± 79 milliseconds; HC: 584 ± 72 milliseconds; $t_{(52)} = 0.3$; $p = .76$; Hedges's $g_s = .078$) or the unsuccessfully inhibited stop trials (FM: 502 ± 63 milliseconds; HC: 503 ± 58 milliseconds; $t_{(52)} = -0.08$; $p = .94$; Hedges's $g_s = .016$).

There were also no between-group differences in the percentage of successfully stopped trials (FM = 56 ± 22%; HC = 55 ± 21%; $t_{(52)} = 0.28$; $p = .78$; Hedges's $g_s = .072$) or in the complementary unsuccessfully stopped trials (same nonsignificant results). No differences were observed either for the SSRT (FM = 334 ± 81 milliseconds; HC = 328 ± 73%; $t_{(52)} = 0.35$; $p = .73$; Hedges's $g_s = .090$).

Electrophysiological Data

We obtained the following results for the TFs extracted after the tPCA.

TF1: The first TF peak measured via the CP2 electrode (the location where it showed its maximum value) occurred at 504 milliseconds and was thus related to the P3 component (Figure 2). Although patients showed less amplitude in this factor, there were no significant between-group differences (FM: 2.5 ± 2.5 μV; HC: 3.7 ± 2.9 μV; $F(1,52) = 3.46$; $p = .068$; $\eta_p^2 = .062$). Condition had a main effect on TF1 ($F(1,52) = 18.9$; $p < .001$; $\eta_p^2 = .267$) with a higher amplitude in stop than in go trials (go: 2.5±2.6 μV; stop: 3.7±2.8 μV). The group by condition interaction was not significant ($F(1,52) = 1.04$; $p = .31$; $\eta_p^2 = .02$).

TF2: The peak activity of this factor—with positive polarity—was measured via the F8 electrode at 116 milliseconds. Given its negative polarity at central electrodes and its latency, TF2 seems to be related to the ERP component N2. No between-group differences were observed for this factor (FM: 1.7 ± 2.3 μV; HC: 1.6 ± 2.1 μV; $F(1,52) = 0.01$; $p = .93$; $\eta_p^2 < .001$), whereas condition had a significant main effect ($F(1,52) = 40.9$; $p < .001$; $\eta_p^2 = .441$), with higher amplitude in stop than go trials (go: 1.3 ± 2.2 μV; stop: 2.0 ± 2.2 μV). The group by condition interaction was not significant ($F(1,52) = 2.2$; $p = .14$; $\eta_p^2 = .041$).

TF3: The peak activity was recorded via the P8 electrode at 364 milliseconds. Given that the peak activity is detected by posterior electrodes, this component seems to be related to the visual processing of the stimulus. No between-group differences were observed for this factor (FM: −2.5 ± 2.9 μV; HC: −2.5 ± 2.4 μV; $F(1,52) = 0.0$; $p = .99$; $\eta_p^2 < .001$). Condition had a significant main effect ($F(1,52) = 67.8$; $p < .001$; $\eta_p^2 = .566$), with higher amplitude in stop trials (go: −1.7 ± 2.3 μV; stop: −3.3 ± 2.7 μV). The group by condition interaction was not significant ($F(1,52) = 0.05$; $p = .82$; $\eta_p^2 = .001$).

TF5: The peak activity was recorded via the FT10 electrode at −36 milliseconds. Because of its negative latency, this factor seemed to be related to the brain activity evoked by presentation of the first arrow. There were no between-group differences in the amplitude of TF5 (FM: 1.2 ± 0.9 μV; HC: 1.5 ± 1.0 μV; $F(1,52) = 0.66$; $p = .42$; $\eta_p^2 = .013$). Condition did not have a significant effect (go: 1.3 ± 1.0 μV; stop: 1.4 ± 0.9 μV; $F(1,52) = 1.8$; $p = .18$; $\eta_p^2 = .034$), and the group by condition interaction was not significant either ($F(1,52) = 2.3$; $p = .13$; $\eta_p^2 = .043$).

TF6: The maximum amplitude of this factor was recorded via the O2 electrode at 184 milliseconds, and it therefore seems to be related to the visual processing of the second stimulus. No between-group differences were observed (FM: −2.0 ± 1.6 μV; HC: −2.5 ± 2.6 μV; $F(1,52) = 0.58$; $p = .45$; $\eta_p^2 = .011$). However, the amplitude was higher in the stop trials than in the go trials (go: −2.1 ± 1.9 μV; stop: −2.4 ± 2.4 μV; $F(1,52) = 5.32$; $p = .025$; $\eta_p^2 = .093$). The group by condition interaction was not significant ($F(1,52) = 0.6$; $p = .44$; $\eta_p^2 = .011$).

Regarding the time-frequency data, an increase in midfrontal theta power (FC1 and FC2 electrodes; from 200 to 500 milliseconds and 3 to 6 Hz) was observed in both groups, with no significant difference between them (FM: 3.6 ± 1.4 dB; HC: 3.7 ± 1.1 dB; $F(1,52) = 0.05$; $p = .82$; $\eta_p^2 = .001$). Theta power modulation was higher in stop than in go trials (go: 3.2 ± 1.4 dB; stop: 4.1 ± 1.4 dB; $F(1,52) = 43.87$; $p < .001$; $\eta_p^2 = .458$). The group by condition interaction was not significant ($F(1,52) = 0.85$; $p = .36$; $\eta_p^2 = .016$). See Figure 3.

Finally, modulation of posterior alpha power (O1 and O2 electrodes; from 300 to 600 milliseconds and 9 to 13 Hz) was significantly lower in patients with FM than in controls (FM: −0.4 ± 1.6 dB; HC: −1.6 ± 1.8 dB; $F(1,52) = 7.98$; $p = .006$; $\eta_p^2 = .133$). In addition, alpha modulation was higher in stop than in go trials (go: −0.8 ± 1.6; stop: −1.3 ± 1.8; $F(1,52) = 9.65$; $p = .003$; $\eta_p^2 = .157$). The group

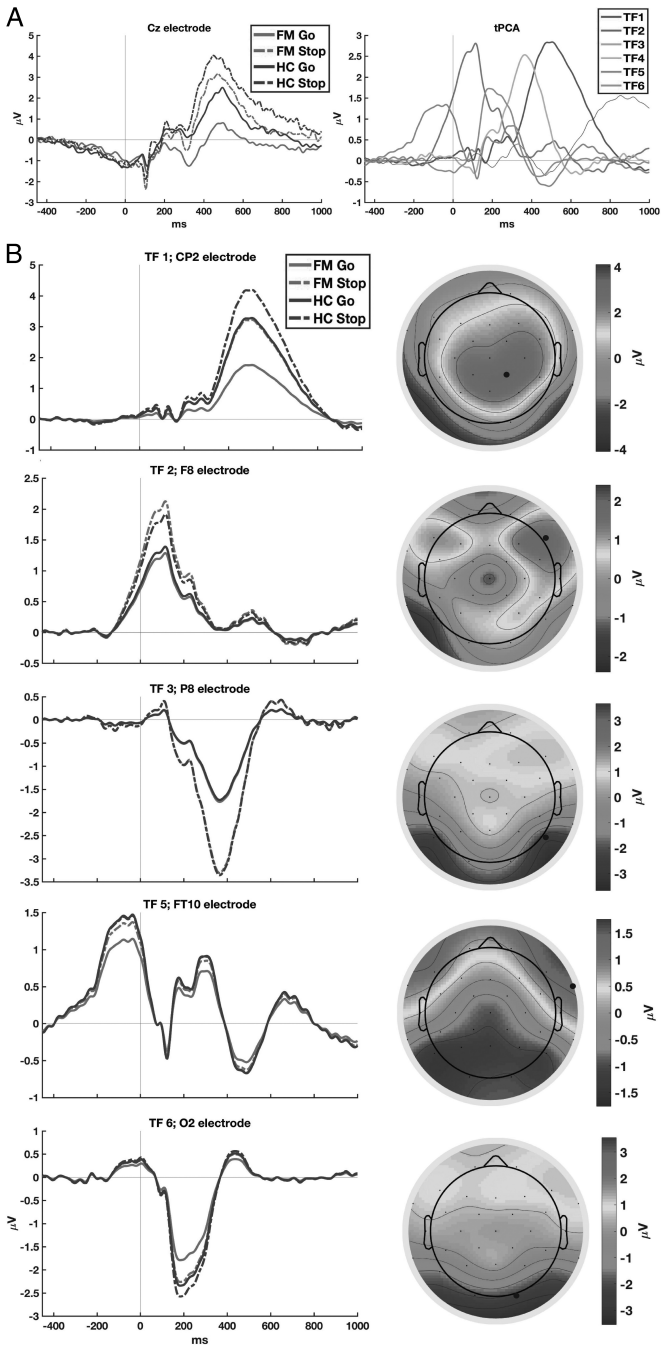

FIGURE 2. Event-related potentials and temporal principal component analyses. A left, Averaged ERPs obtained from patients with FM and HCs in go and stop trials recorded in the Cz electrode. A right, Time course of the factors extracted after tPCA. B, Time course and topography of each TF analyzed. FM = fibromyalgia; HC = healthy controls; TF = temporal factor. Color image is available only in online version (www.psychosomaticmedicine.org).

by condition interaction was not significant ($F(1,52) = 0.01$; $p = .93$; $\eta_p^2 < .001$).

Given that the power of alpha was sensitive to between-group differences, we verified the extent to which this index was related to sociodemographic and clinical variables by computing the Spearman's rank correlations (Table 2 and Figure 4). Alpha power was positively correlated with variables such as pain catastrophizing, depression, both VAS (measuring level of pain and mood), the level of cognitive dysfunction, the SSS, and the widespread pain index. Lower modulation of alpha power (lower power reduction) was therefore associated with more severity in these clinical variables. Note that these correlations were calculated using both groups together. When calculating the correlations using the FM group alone, only a marginally significant correlation

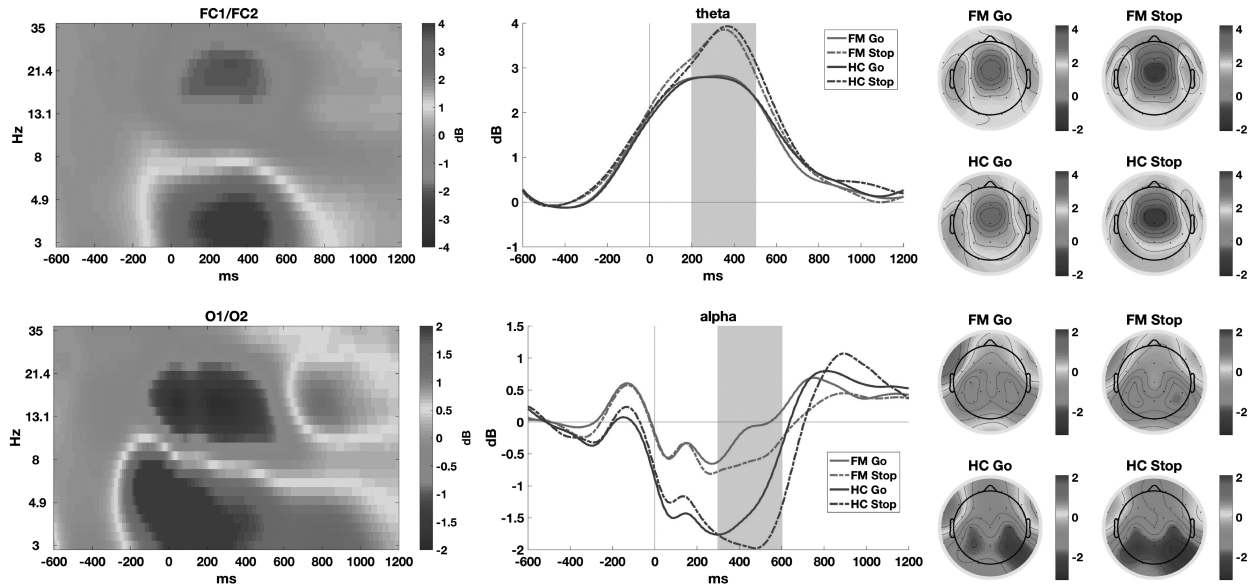

FIGURE 3. Time-frequency analyses. Left, Spectrograms of the evoked activity in the electrodes FC1/FC2 (top) and O1/O2 (bottom). Middle, Time course of the theta power (3–6 Hz) and alpha power (9–13 Hz) bands obtained from patients with FM and HCs. Right, Topographies of the theta activity between 200 and 500 milliseconds (top box) and the alpha activity between 300 and 600 milliseconds (bottom box) for each group and condition. FM = fibromyalgia; HC = healthy controls. Color image is available only in online version (www.psychosomaticmedicine.org).

appears (alpha power for Go trials and SSS; $r = .385$; $p = .047$), which did not survive the false discovery rate correction.

DISCUSSION

Little is known about possible motor inhibition alterations in patients experiencing chronic pain. Because inhibitory control is crucial for correcting inappropriate behavior and has been related to pain tolerance, we investigated whether FM patients show dysfunction in motor inhibition processes. We found that patients with FM did not show any behavioral alteration in reactive motor inhibition during performance of a stop-signal task. In addition, the brain electrical activity related to inhibition processes (N2, P3, and midfrontal theta) was not different in FM and in HCs. However, we found that modulation of posterior alpha power during the stimuli processing was lower in the patients with FM than in the controls. These findings suggest that patients with FM preserve sufficient cognitive capacity to correctly perform a reactive motor inhibition task, although they show alterations during the initiation of mechanisms related to visual attention.

Patients Maintain Their Ability to Inhibit Initiated Motor Responses

FM patients frequently complain of emotional and cognitive problems, alterations that can even be physiologically manifested and induce somatic symptoms (39,40). The bulk of the evidence supports the presence of deficiencies in different processes, such as attention, executive functioning, and working memory (41,42). However, some contradictory results have been reported (43,44). Moreover, despite the various arguments suggesting a link between chronic pain and inhibitory deficits, there is a lack of knowledge about the integrity of inhibitory circuits in those patients and particularly in FM. People with better inhibitory control can tolerate higher levels of pain, suggesting a relationship between inhibition and pain perception (45). Nevertheless, no studies have explored processes of reactive motor inhibition in FM using the stop-signal task.

In the present study, the results did not confirm any behavioral difference between patients and HCs in the stop-signal task and thus indicate that the inhibitory mechanisms during the execution of simple tasks that require response cancellation to an external stimulus are not altered in FM. This result is consistent with some

TABLE 2. Correlations Between Posterior Alpha Power and Clinical Variables

	Age	BMI	Years of Education	PCS	BDI	VAS Pain	VAS Mood	FSQ2	SSS	WPI	MFE-30
Alpha (go trials)	−.10 (.5)	−.01 (.9)	−.10 (.5)	.28 (.039)	.33 (.017)*	.31 (.023)*	.34 (.013)*	.39 (.004)*	.36 (.008)*	.22 (.11)	.40 (.008)*
Alpha (stop trials)	−.06 (.6)	−.08 (.5)	−.19 (.2)	.30 (.029)	.41 (.003)*	.28 (.044)	.32 (.017)*	.39 (.004)*	.40 (.003)*	.26 (.056)	.35 (.020)*

BMI = body mass index; PCS = Pain Catastrophizing Scale; BDI = Beck Depression Inventory; VAS = visual analogue scale; FSQ2 = Item 2 of the Fibromyalgia Survey Questionnaire; SSS = Symptom Severity Score.

Spearman's rank correlations were calculated by merging both groups of participants. The p values are shown between parentheses. The p values with an asterisk remained significant after false discovery rate correction (p value used for threshold = .023).

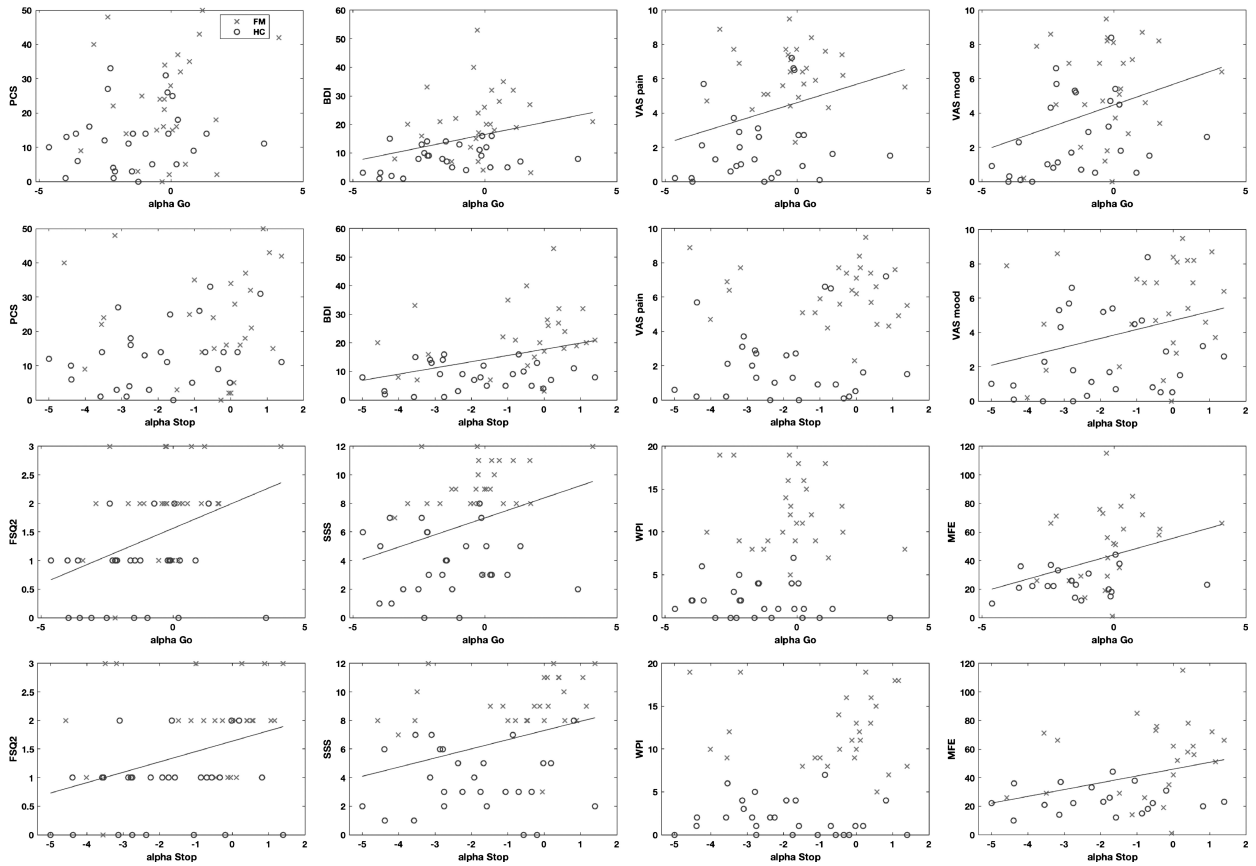

FIGURE 4. Scatter plots for correlations between alpha power and clinical variables. Regression lines (computed using least-squares method) are only shown in significant correlations. PCS = Pain Catastrophizing Scale; BDI = Beck Depression Inventory; VAS = visual analogue scale; FSQ2 = Item 2 of the Fibromyalgia Survey Questionnaire; SSS = Symptom Severity Score; WPI = Widespread Pain Index; MFE = Memory Failures of Everyday Questionnaire; FM = Fibromyalgia Group; HC = Healthy Controls Group. Color image is available only in online version (www.psychosomaticmedicine.org).

of the previous research findings observed using proactive motor inhibition tasks (go/no-go) in patients with FM (10,11).

We applied temporal principal components analysis to the ERP data to better differentiate between the brain activity related to inhibitory processes and that related to the perceptual processing of stimuli. We also performed time-frequency analysis, which provides information on the power modulation of oscillatory activity and enables better characterization of brain functioning. The N2 and midfrontal theta indexes both presumably reflect the detection of conflict during motor inhibition (46). They seem to be originated in fronto-central brain locations (47,48), which play a significant role in both nociceptive processing and motor inhibition (49). No between-group differences were found in either the TF identified as N2 nor the theta power. The P3 component is another characteristic ERP elicited during stop-signal tasks. The neural origin of this component seems to be located in areas such as the midcingulate cortex and the inferior frontal cortex (17,50,51), and it is interpreted as the cognitive evaluation of the motor inhibition (16). Again, although the mean P3 amplitude was smaller in patients, the difference relative to HCs was not significant. Similarly, no between-group differences were observed for any of the remaining TFs extracted. Altogether, the results show no alterations in reactive motor inhibition—at either behavioral or electrophysiological level—in the patients, suggesting adequate functioning of frontal inhibitory neural networks in FM.

The ERP findings contrast with the alterations in neuroimaging data observed in patients with FM during motor inhibition (10,11). Rather than the stop-signal paradigm, these studies used a proactive inhibition task (go/no-go). Both tasks probably involve overlapping but distinct neural networks, given that the stop-signal task implies cancellation of an already prepared response and creates greater inhibitory pressure than the go/no-go task (12,52). The present findings also differ from those we have previously obtained, i.e., alterations of midfrontal theta activity during the execution of tasks that require cognitive control and the maintenance of top-down attention, such as the Multi-Source Interference Task and the n-back working memory task (25,53). A possible explanation, as other studies have stressed, is that the differences between patients and controls are more evident during tasks with a higher cognitive load (54) or with an added source of distraction (55). As already mentioned, the lack of differences at both behavioral and electrophysiological levels may be due to the simplicity of the stop-signal task, and thus, the alterations may be more evident in tasks that require higher and sustained top-down attentional control.

Patients Show Impaired Modulation of Posterior Alpha Oscillations

The only electrophysiological marker that indicated significant between-group differences was posterior alpha power. The lower

modulation of alpha power in the FM group occurred in both stop and go trials, suggesting that this alteration is not exclusively related to motor inhibition, but to the deployment of visual-spatial attention during the task. Numerous studies have reported a relationship between the reduction in alpha power and visual information perception and task execution (56,57). This finding supports the hypothesis that the cognitive dysfunction reported in FM may be related to difficulties in maintaining the levels of visual attention required for correct task performance. These patients seem to be more vulnerable to distraction and have difficulty managing different sources of simultaneous information or coping with complex and unstable environments (38,58). Attention-related problems have previously been described in FM (54,59) and explained by the competition with pain, which is thought to capture attentional resources and make such resources less available for performance of other tasks (60).

The alpha power data apparently contrast with the lack of differences in TF 6, which also seem to be related to the activation of visual areas. Nevertheless, they are different measures, because ERPs provide information on phase-locked activity linked to the processing of the stimuli, whereas time-frequency data show power modulation in both phase-locked and nonphase-locked activity. Thus, given that time-frequency analyses provide information on power changes sustained over time, our findings suggest that patients with FM do not have deficits in the perceptual processing of the stimuli, but rather experience difficulty in maintaining sustained visual cortical activation.

As expected, patients reported higher disturbance in the usual symptoms of FM, such as pain, depression, catastrophizing, and cognitive dysfunction. Interestingly, these variables were correlated with the alpha power. Thus, higher scores for depression, catastrophizing, cognitive dysfunction, or pain were associated with lower modulation of alpha power. This finding suggests that the ability to deploy visual attentional resources is affected by the severity of symptoms frequently reported in FM and indicates that alpha power modulation may be used as an index of FM symptom and used for monitoring therapy interventions.

Limitations

One limitation of this study stems from the confounding effects of the medication consumed by patients with FM (mainly nonsteroidal anti-inflammatory drugs, antidepressants, anxiolytics, and pregabalin/gabapentin). Although some of these drugs affect the central nervous system, it is not known how they influence the results (61). Although medication can reduce the level of attention and thus worsen task performance, it can also restore sleep and reduce pain levels, thus possibly improving task execution. On the other hand, selection of patients who do not consume medication or the temporary withdrawal of medication would cause limitations because of selection bias and the effects of the temporary restriction, respectively.

Another limitation is that the results obtained with a simple reactive motor inhibition task cannot be applied to other inhibition processes in FM. Nevertheless, because reactive motor inhibition may use overlapping circuits with other types of inhibition, such as emotional and motivational control (12), the study findings may contribute to our understanding of possible alterations in FM. Furthermore, as we have already mentioned, there seems to be a relationship between the ability to inhibit motor responses and the capacity to cope with pain (13). Use of this task thus represents a first step in the study of altered inhibition of patients with FM, providing a simple measure to assess the integrity of inhibitory processes.

CONCLUSIONS

We demonstrated that patients with FM maintain the capacity to perform a reactive motor inhibition task. The brain activity associated with inhibitory mechanisms was also similar in patients and controls, suggesting that motor inhibition mechanisms are conserved, or at least at a sufficient degree for correct performance of this type of task. However, modulation of posterior alpha power was lower in the FM group after stimulus presentation; this index was significantly correlated with the severity of FM symptoms. These results suggest that patients with FM show a deficit in the initiation and maintenance of attentional resources associated with the processing of visual stimuli and that the cognitive dysfunction may be explained by relatively weaker organization of visual cortical processing. Treatments capable of modulating posterior alpha activity (e.g., medication, noninvasive brain stimulation, or psychological treatment) may be useful for improving cognitive deficits and thus the quality of life of patients with FM.

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