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ORIGINAL RESEARCH

# Emotional and Attentional Bias in Fibromyalgia: A Pilot ERP Study of the Dot-Probe Task

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## ABSTRACT

***Introduction***: The present research investigates the neural correlates of attentional bias in fibromyalgia (FM) with a dot-probe task performed during an electroencephalogram (EEG) recording.

***Methods***: For this purpose, 30 female participants were recruited, divided into two groups: a group of patients with FM (FM, $n = 15$, $M_{age} = 51.87$) and a healthy control group (HC) (HC, $n = 15$, $M_{age} = 46.13$).

***Results***: The results did not show behavioral differences between groups, but the EEG results showed that healthy controls had larger P300 amplitudes than patients with FM. Regarding late positive potentials (LPP), we found that patients with FM had larger amplitudes than healthy controls in a later time window.

***Conclusion***: In summary, while the P300 results suggest that patients allocate less attentional resources to the task, the increased amplitudes of their LPP suggest augmented emotional processing of the target stimuli. Altogether, our results seem to support the thesis of generalized attentional deficits in FM.

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## PLAIN LANGUAGE SUMMARY

Fibromyalgia (FM) is a chronic musculoskeletal pain condition. There has been discussion in the scientific literature as to whether patients with FM suffer from a generalized attentional deficit or an attentional bias—preferentially selecting pain-related information. Attentional bias in FM patients has been studied as hypervigilance, which refers to early detection of pain-related information or innocuous information. Thus, the aim of this study was to test whether there is a generalized attentional deficit or attentional bias in relation to pain in patients with FM, by studying the neural activity underlying cognitive processes, specifically with evoked potentials (P300 and late positive potential—LPP). The P300 has been related to the use of attentional resources and the LPP to affective modulation. For this purpose, we studied two groups: a group of patients with FM and a healthy control group. Our hypotheses considered that FM patients, compared to healthy controls, would show an attentional bias for pain-related words (1) reflected in higher hits and shorter reaction time when detecting the target of a cognitive task (dot-probe), and (2) manifested by increased amplitudes of P300 and LPP evoked potentials while performing the task. The electrophysiological results suggest that FM patients may have a generalized attentional deficit and, despite this being the case, FM patients are more emotionally involved in the task.

**Keywords:** Attention bias; Attentional deficits; Chronic pain; Dot-probe; EEG; Fibromyalgia

**Key Summary Points**

**Why carry out this study?**

Fibromyalgia (FM) is a chronic musculoskeletal pain condition. It is estimated to affect between 2% and 4% of the general population. It represents a burden on the health system and has repercussions at the family and social level.

The aim of this study was to test whether attentional bias or generalized attentional deficit exists in patients with FM.

The following hypotheses were tested: Patients with FM, compared to healthy controls, would show an attentional bias for pain-related words (1) reflected in higher hits and shorter reaction time when detecting the target of a cognitive task (dot-probe), and (2) manifested by increased mean amplitudes of P300 and late positive potential (LPP).

**What was learned from the study?**

The first hypothesis (behavioral data) was not confirmed by our results, probably because the stimuli may be irrelevant in capturing the attention of patients and controls, thus making it difficult to reveal behavioral differences.

The second hypothesis (electrophysiological data): Electrophysiological results suggest that FM patients present a generalized attentional deficit, thus not supporting the hypervigilance hypothesis (attentional bias). This demonstrates the importance of assessing and treating cognitive symptoms in FM.

Fibromyalgia is characterized by higher levels of depression and pain-related thoughts, but does not influence the results of the dot-probe task.

## INTRODUCTION

Several studies have investigated attentional bias in fibromyalgia (FM), due to its potential role in hypervigilance and chronicity [1]. Attentional bias is regarded as selective attention towards specific information, occurring when a response to stimuli is consistently facilitated or disrupted [2]. As a result, it may modulate patients' attention towards pain-related information, and this excessive vigilance may be associated with avoidance of situations considered threatening by patients, along with isolation, pain persistence, and lower functionality [3]. Moreover, attentional bias appears to predict future health care engagement, increased pain, and relapse [2], thus representing an important target for treatment [4, 5].

The dot-probe paradigm has been used extensively to study attentional bias [6]. It involves the presentation of two stimuli (e.g., an emotional stimulus paired with a neutral one). Afterward, the pair of stimuli disappear, and one of them is replaced by a dot (dot-probe). Participants are instructed to indicate the location of this dot as quickly as possible, through a response button [7]. Faster responses when the dot is placed on the location of the pain-related stimulus represent a bias to this stimulus.

Although widely used in cognitive science, this research is scarce in FM [8, 9]. One study used the dot-probe paradigm to explore the efficiency of a mindfulness meditation on attentional bias to pain-related threat in FM patients, after stimuli presented for durations of 100 and 500 ms. The results showed that the mindfulness meditation reduced avoidance of pain-related threat at early levels of processing and facilitated disengagement from threat at later stages of processing [9]. A second study used a modified dot-probe task to improve patients' attentional bias through the training of attentional shift from threatening to neutral stimuli [8].

The present study aims to explore the neural correlates of the attentional bias in FM, using a dot-probe task comprising neutral and pain-related verbal stimuli. Besides behavioral data

(accuracy and reaction times), we analyzed the P300 and the late positive potential (LPP) time-locked to the probes. The P300 is a positive component that emerges after 300 ms at centro-parietal electrodes. Its amplitude is modulated by the probability of an event [10], by the personal relevance attributed to the stimuli, intentional engagement, and selective attention. The LPP is subsequent to the P300 and emerges at the same electrodes. It is strongly correlated with memory encoding [11–14], and is larger after those rated as emotionally meaningful and arousing. Both P300 and LPP are considered signatures of salience and threat [15], providing neural measures of attentional bias in FM towards neutral and pain-related words.

We hypothesized that, in comparison with controls, patients would demonstrate an attentional bias towards pain-related words, manifested in higher accuracy and lower reaction times for emotional than for neutral words. Regarding the electrophysiological results, we hypothesized that patients would show increased P300 and LPP amplitudes for pain-related stimuli, while healthy controls would show similar amplitudes in both conditions. Moreover, we controlled the effects of affective states and clinical aspects of pain, such as depression, level of functionality, and pain catastrophizing.

# METHODS

## Participants

Thirty female participants were recruited for the present study, subdivided into two groups: a group of patients with fibromyalgia (FM, $n = 15$) and a control group of healthy participants (HC, $n = 15$). The sociodemographic results are presented in Table 1. Healthy participants were recruited from the community, while patients were recruited from the National Association against Fibromyalgia and Chronic Fatigue Syndrome (MYOS).

FM patients were included if they (1) had a formal diagnosis of FM based on criteria of the American College of Rheumatology (ACR), (2) were between the ages of 25 and 65 years, and (3) had more than four years of formal education. Healthy participants were included if they reported no history of chronic pain and complied with the remaining criteria. Participants of both groups were excluded for the following: (1) left hand as dominant; (2) reported use of narcotic analgesics medication; (3) history of brain injury, neurological or psychiatric diagnosis; (4) non-compensated sensory or motor deficits; and (5) nationality other than Portuguese. Both groups were statistically matched regarding sex, education, and age.

Data from one FM participant were not included in the event-related potentials (ERP) analysis due to a computer error in saving the electroencephalogram (EEG) data. Five participants (two HC and three FM) were excluded from the ERP analysis due to excessive noise in the morphology of the ERPs.

## Instruments and Tasks

*Semi-structured interview*. A semi-structured interview was conducted to collect individual and clinical data. This interview was conducted to gather data concerning the characterization of the samples and to confirm inclusion/exclusion criteria.

*Beck Depression Inventory* (BDI-II) [16]. The BDI-II is a self-report inventory to assess current depressive symptoms. It comprises 21 items, and answers are given on a four-point Likert scale (0 = non-depressive state; 3 = severe depression). It presents good psychometric qualities (for main sample $\alpha = 0.91$; for student sample $\alpha = 0.895$; for clinical sample $\alpha = 0.925$).

*Fibromyalgia Impact Questionnaire, Portuguese Version* (FIQ-P) [17, 18]. The FIQ-P provides measures of the health-related status and functional capacity of patients with FM. It comprises 20 questions that explore the patient's functional ability to perform daily tasks (cooking, cleaning, walking, mobility, among others). Responses are distributed on a Likert scale of 0 (always able to) to 3 (unable to do). Answers are given on a four-point Likert scale (0 = can always perform; 3 = unable to perform). It presents good psychometric qualities ($\alpha = 0.814$).

**Table 1** Clinical and sociodemographic characteristics of fibromyalgia patients ($n$ = 15) and healthy controls ($n$ = 15)

| | Fibromyalgia patients | Healthy controls | Statistical test | Effect size |
|---|---|---|---|---|
| Age (years) | | | | |
| Mean (SD) | 51.87 (7.12) | 46.13 (8.41) | $t$ = 2.02 | $d$ = 0.74 |
| Age range | 38–64 | 33–58 | | |
| Education % ($n$) | | | | |
| Primary | 20 (3) | 7 (1) | $\chi^2$ = 0.73 | Cramer's $V$ = 0.73 |
| Basic cycle | 20 (3) | 27 (4) | | |
| High school | 40 (6) | 40 (6) | | |
| Higher education | 20 (3) | 27 (4) | | |
| Civil status % ($n$)* | | | | |
| Married | 93 (14) | 53 (8) | $\chi^2$ = 0.03 | Cramer's $V$ = 0.03 |
| Single | 0 (0) | 33 (5) | | |
| Widowed | 0 (0) | 0 (0) | | |
| Separated/divorced | 6.70 (1) | 13 (2) | | |
| Employment status % ($n$) | | | | |
| Active | 47 (7) | 80 (12) | $\chi^2$ = 0.23 | Cramer's $V$ = 0.23 |
| Never active | 7 (1) | 7 (1) | | |
| Inactive for more than 1 year | 40 (6) | 13 (2) | | |
| Inactive less than 1 year | 7 (1) | 0 (0) | | |
| Salary (monthly) % ($n$) | | | | |
| More than €1800 | 7 (1) | 0 (0) | $\chi^2$ = 0.06 | Cramer's $V$ = 0.06 |
| €1200–1800 | 7 (1) | 20 (3) | | |
| €600–1200 | 33 (5) | 67 (10) | | |
| Less than €600 | 53 (8) | 13 (2) | | |
| Pain duration (years) | | | | |
| Mean (SD) | 26.13 (14.75) | – | – | – |
| Range | 8–50 | – | – | |
| Diagnosis time (years) | | | | |
| Mean (SD) | 10.67 (5.84) | – | – | – |
| Range | 5–27 | – | | |
| Time elapsed since the diagnosis (years) | | | | |
| Mean (SD) | 15.47 (13.10) | – | – | – |
| Range | 0–40 | – | | |

**Table 1** continued

| | Fibromyalgia patients | Healthy controls | Statistical test | Effect size |
|---|---|---|---|---|
| Pain intensity (10 cm VAS)* | | | | |
| Mean (SD) | 4.35 (2.14) | 0.41 (1.10) | $t = 6.35$ | $d = 2.32$ |
| Range | 0.70–8 | 0–4 | | |
| Fatigue level (10 cm VAS)* | | | | |
| Mean (SD) | 5.15 (2.38) | 1.70 (1.60) | $t = 4.65$ | $d = 1.70$ |
| Range | 1–9.1 | 0–3.9 | | |
| Sleep quality (10 cm VAS)* | | | | |
| Mean (SD) | 5.99 (2.40) | 2.46 (2.61) | $t = 3.85$ | $d = 1.41$ |
| Range | 0.90–10 | 0–7.1 | | |
| Medications % (*n*) | | | | |
| Analgesics* | 53 (8) | 0 (0) | $\chi^2 = 0.001$ | Cramer's $V = 0.001$ |
| NSAIDs | 13 (2) | 0 (0) | $\chi^2 = 0.14$ | Cramer's $V = 0.14$ |
| Anxiolytic* | 47 (7) | 0 (0) | $\chi^2 = 0.003$ | Cramer's $V = 0.003$ |
| Antidepressants* | 67 (10) | 7 (1) | $\chi^2 = 0.001$ | Cramer's $V = 0.001$ |
| Antiepileptics | 7 (1) | 0 (0) | $\chi^2 = 0.31$ | Cramer's $V = 0.31$ |
| Antipsychotics | 0 (0) | 7 (1) | $\chi^2 = 0.31$ | Cramer's $V = 0.31$ |

*NSAIDs* nonsteroidal anti-inflammatory drugs, *SD* standard deviation, *VAS* visual analogue scale
*$p < 0.05$

*Pain Catastrophizing Scale* (PCS) [19, 20]. The PCS is a self-report questionnaire regarding thoughts, perceptions, and feelings related to pain. It comprises 13 items, and participants are instructed to indicate the frequency of the described symptoms on a five-point Likert scale (0 = never; 4 = always). It presents good psychometric qualities (for rumination scale $\alpha = 0.796$; for magnification scale $\alpha = 0.789$; for discouragement scale $\alpha = 0.897$).

*Dot-probe task*. The experimental task was presented in E-Prime 2.0 (2011, Psychology Software Tools, Inc., Pittsburgh, PA, USA). This task comprised four blocks of 20 trials, preceded by a training block. Each trial was composed of a fixation cross (500 ms), followed by pairs of words presented for 500 ms (one word on the left and the other on the right side of the central fixation cross). The pain-related verbal stimuli appeared with equal probability on the left and right sides. Another fixation cross was presented during a variable interval between 100 and 300 ms, followed by the dot-probe. The dot-probes were presented for 150 ms and randomly positioned on the location of one of the words. In half of the trials, they appeared in the

position of the pain-related word, and in the other half they appeared in the position of the neutral word. Participants were instructed to answer after the dot-probe, on a black screen presented for 1750 ms. Participants indicated the position in which the dot-probe had appeared by pressing buttons 1 or 2 of a response box with their index finger of the dominant hand. An example of a trial sequence is presented in Fig. 1.

The stimuli comprised 20 neutral and 20 pain-related words, selected from a previous validation study [21]. Participants were instructed to respond as quickly and accurately as possible, avoid eye movement during the EEG recordings, and stare at the fixation cross during each trial. A pause was included after each experimental block. Behaviorally, we assessed the number of correct answers (hits), the number of incorrect answers (errors), the number of trials with no responses (omissions), and the reaction times during hits and errors.

## Procedures

The current study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. Ethical approval was provided by the scientific committee of the Faculty of Psychology and Education Sciences of the University of Porto, by the ethics committee of Centro Hospitalar de Vila Nova de Gaia/ Espinho, and by the National Association against Fibromyalgia and Chronic Fatigue Syndrome (MYOS in Portuguese). All of the subjects provided written informed consent prior to their participation in this study.

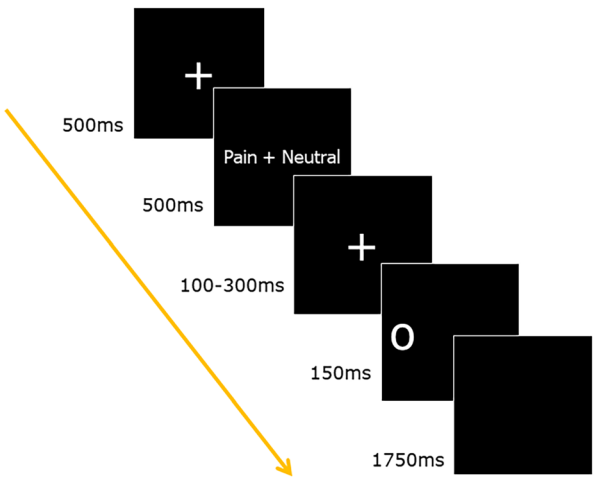


**Fig. 1** Schematic representation of dot-probe task

Participants were tested individually in one experimental session conducted in a laboratory setting. After informed consent was obtained, a semi-structured interview was conducted. The BDI-II, FIQ-P, and PCS were then administered in a balanced order.

Participants who fulfilled the inclusion criteria were recruited for the dot-probe task, which was performed inside an EEG chamber. After the placement of the EEG cap (see details below), participants sat comfortably at 115 cm from a 17-inch screen, read the instructions, and completed five practice trials.

## EEG Recording and Processing

The EEG data were recorded using a 128-electrode HydroCel Geodesic Sensor Net, with a Net Amps 300 amplifier (both from Electrical Geodesics Inc., Eugene, OR, USA) at a digitizing rate of 500 Hz. Impedance was kept below 50 kOhm for all electrodes (as this is a high-impedance system). The electrodes were referenced to Cz during recording, and re-referenced offline to the average of all electrodes. The EEG data were preprocessed in EEGLAB (version 13.6.5b) [22]. The data were downsampled to 250 Hz and band-pass-filtered at 0.3–30 Hz. Bad channels were interpolated (up to a maximum of 10% of the sensors), and data were decomposed through independent component analysis. Eyeblink, saccade, and heart rate artifacts were corrected by subtracting the respective component activity from the signal. The EEG records were segmented into epochs ranging from −200 to 800 ms, time-locked to the dot-probe onset. All segments were visually inspected after baseline correction (200 ms pre-stimulus), and the remaining artifactual epochs were manually rejected. Epochs were averaged by condition (pain-related, neutral). After this inspection, the number of valid trials for pain-related condition ($M$ = 34.79 SD = 6.05) and for neutral condition ($M$ = 34.93 SD = 6.10) did not differ

significantly between groups ($p = 0.677$) or conditions ($p = 0.907$).

Two ERP components were analyzed for each participant: P300 and LPP. Three time windows and one region of interest (ROI)[1] were selected for statistical analysis, based on previous studies, visual inspection of grand-average waveforms, and topographical maps (Fig. 2). For the P300 component, its higher amplitude occurs at centro-parietal regions, specifically at Pz. The visual inspection of our topographical maps showed a maximum amplitude over this region, leading us to select a ROI including Pz and a cluster of the surrounding electrodes, in order to increase the signal-to-noise ratio. Thus, the P300 mean amplitude was calculated between 300 and 400 ms after dot-probe onset, at the centro-parietal ROI (electrodes: 54, 55 [CPz], 61, 62 [Pz], 78, 79). Similarly, the LPP reaches its largest amplitude over centro-parietal sites. As our topographical maps were consistent with this evidence (Fig. 2), we measured the mean LPP amplitudes in the same ROI of the P300, but in a later time window. As the LPP shows a temporally broad distribution (e.g. [23]), we divided its corresponding time window into an early (LPPe; 400–600 ms) and late component (LPPl; 600–800 ms).

### Statistical Analysis

The effects of *condition* (pain-related, neutral) and *group* (FM, HC) were investigated through a mixed factors analysis of variance (ANOVA), with *group* as a between-subjects factor and *condition* as a within-subjects factor. This same model was used to analyze reaction times, accuracy rates, and electrophysiological results. Analysis of covariance (ANCOVA) was also performed to explore the effect of depression, anxiety, and pain catastrophizing on behavioral results for the dot-probe task. Pearson's $r$ was computed to explore the correlations between behavioral and electrophysiological results. The threshold for statistical significance was set at $\alpha = 0.05$ for all analyses. Violations of sphericity were corrected via the Greenhouse–Geisser method. Significant ANOVA main effects were quantified using Sidak-corrected post hoc comparisons. Statistical analysis was performed using SPSS version 24 software (IBM Corp., Armonk, NY, USA).

[1] Electrode notation included in the ROIs corresponds to the 128-channel geodesic sensor net (EGI). Electrodes described in brackets are their 10–10 International System equivalents.

## RESULTS

### Behavioral Results

Significant differences were observed between groups in depression (BDI-II), $t(28) = 5.50$, $p < 0.001$, $d = 2.01$, impact of fibromyalgia (FIQ-P), $t(28) = 13.3$, $p < 0.001$, $d = 4.85$, and pain catastrophizing (PCS), $t(28) = 26.2$, $p < 0.001$, $d = 1.26$. The results showed that the FM group had higher values in all of the self-reported measures, as shown in Table 2. Covariance analyses were performed to explore the effect of the above variables on the results of the dot-probe task, but no significant effects were found (all $p > 0.05$).

Regarding the results obtained for the dot-probe task (Table 3), we did not find a main effect for *group* $F(1,28) = 1.17$, $p = 0.289$, $\eta^2 = 0.040$ or *condition* ($F < 1$) for the hits. Despite of a significant group*condition interaction, $F(1,28) = 4.27$, $p = 0.048$, $\eta^2 = 0.132$, the post hoc analyses did not reveal a significant difference between groups in the emotional ($p = 0.151$) or the neutral stimuli ($p = 0.499$). The analyses performed for errors did not reveal a main effect for either *group* or *condition* (both $F < 1$), or a significant group*condition interaction, $F(1,28) = 2.00$, $p = 0.168$, $\eta^2 = 0.067$. The analysis of omissions revealed the same pattern of results: we did not find a main effect of *group*, $F(1,28) = 1.13$, $p = 0.297$, $\eta^2 = 0.039$ or *condition* ($F < 1$), or a significant group*condition interaction, $F(1,28) = 1.98$, $p = 0.170$, $\eta^2 = 0.066$. However, considering our hypothesis, we explored this interaction in the post hoc analyses, which revealed a significant difference between *groups* in the pain-related condition ($p = 0.045$), with patients showing more omissions than healthy participants in this condition.

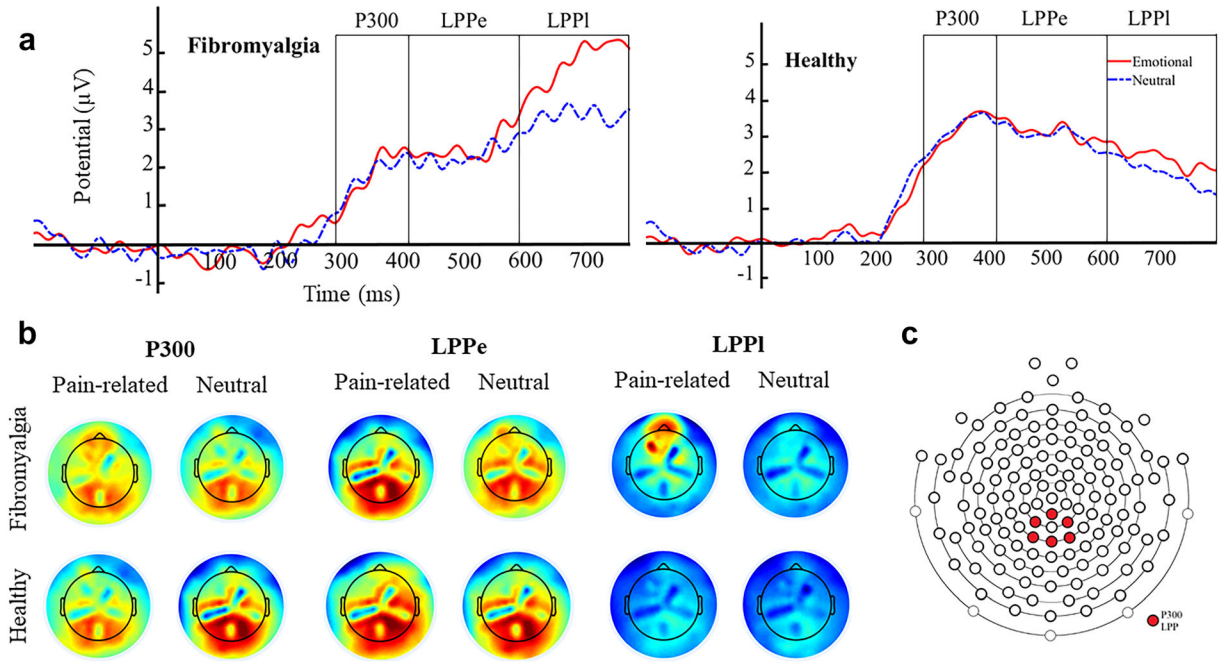


**Fig. 2** **a** Grand average of P300 (300–400 ms) and LPP (400–800 ms) for patients with fibromyalgia and healthy controls. **b** Topographical maps for event-related potentials elicited by pain-related and neutral words. **c** Electrode locations in the 128-channel HydroCel Geodesic Sensor Net (EGI) where event-related-potential components were measured

**Table 2** Means (and standard deviations) of self-reported measures of depression, fibromyalgia impact, and pain catastrophizing for fibromyalgia ($n$ = 15) and healthy control groups ($n$ = 15)

| | Fibromyalgia | Healthy controls |
|---|---|---|
| Depression (BDI, total)* | 20.9 (9.87) | 5.20 (5.05) |
| Fibromyalgia impact (FIQ, total)* | 62.4 (12.7) | 17.6 (2.99) |
| Pain catastrophizing (PCS, total)* | 31.8 (16.5) | 13.4 (12.5) |

*$p < 0.001$

Regarding reaction times to the hits (see Table 3), no main effects were found for *group* or *condition*, or for the interaction between the two variables (all $F < 1$). Similarly, no main effect or significant interaction was found for reaction times errors (all $F < 1$).

## Electrophysiological Results

Regarding the mean amplitude of the P300, we found a main effect of *group*, $F(1,22) = 5.27$, $p = 0.032$ $\eta^2 = 0.193$, revealing that heathy controls had higher amplitudes than patients with FM (Table 4 and Fig. 2). The main effect of *condition* as well as the group*condition interaction were nonsignificant (both $F < 1$).

Regarding the LPPe, we did not find a main effect of *group*, $F(1,22) = 1.78$, $p = 0.196$, $\eta^2 = 0.075$ or c*condition*, or a significant group*condition interaction (both $F < 1$). Finally, regarding LPPl, we found a main effect of *group*, $F(1,22) = 4.83$, $p = 0.039$, $\eta^2 = 0.187$,

**Table 3** Behavioral results [means (and standard deviations)] in the dot-probe task for fibromyalgia ($n$ = 15) and healthy control groups ($n$ = 15)

| | Fibromyalgia | | Healthy controls | |
|---|---|---|---|---|
| | Pain-related stimuli | Neutral stimuli | Pain-related stimuli | Neutral stimuli |
| Hits | 37.5 (5.08) | 37.9 (5.06) | 39.5 (1.30) | 38.9 (2.52) |
| Errors | 2.07 (5.12) | 1.80 (5.07) | 0.47 (1.30) | 0.73 (2.05) |
| Omissions | 0.40 (0.74) | 0.27 (0.79) | 0.00 (.00) | 0.33 (0.62) |
| Reaction times hits (ms) | 290 (101) | 290 (93.8) | 256 (116) | 257 (109) |
| Reaction times errors (ms) | 102 (146) | 84.0 (146) | 112 (328) | 80.5 (172) |

*M* mean, *SD* standard deviation
*$p < 0.05$

**Table 4** Means (and standard deviations) of the P300, LPPe, and LPPl mean amplitudes (μv) in function of group and condition for fibromyalgia ($n$ = 15) and healthy control groups ($n$ = 15)

| | Fibromyalgia | | Healthy controls | |
|---|---|---|---|---|
| | Pain-related stimuli | Neutral stimuli | Pain-related stimuli | Neutral stimuli |
| P300* | 2.05 (1.52) | 2.02 (1.93) | 3.47 (2.03) | 3.66 (1.54) |
| LPPe | 2.71 (1.54) | 2.62 (2.09) | 3.39 (1.55) | 3.49 (0.95) |
| LPPl* | 4.39 (3.25) | 3.58 (2.23) | 2.39 (1.52) | 2.26 (1.71) |

*$p < 0.05$

revealing that patients with FM had higher mean amplitudes than healthy controls. The main effect of *condition* and the group*condition interaction were nonsignificant (both $F < 1$).

## DISCUSSION

Negative bias in information processing may initiate, exacerbate, and perpetuate characteristics of a certain disease. This hypothesis has motivated the study of patients with chronic pain, mainly regarding the processing of information related to pain. Previous studies have shown that people with chronic pain selectively process information related to their clinical condition to the detriment of neutral information [23, 24]. However, other studies have failed to find evidence of possible attentional biases [25, 26]. Several studies, conducted with different methodologies, presented participants with stimuli related to pain and stimuli of different emotional valence, in order to compare the response pattern given to each category of stimuli. The task most commonly used to study attentional bias is the dot-probe task, which aims to investigate whether the occurrence of attentional bias is caused by the antecedence of a pair of stimuli irrelevant to the goal of the task. The results of previous studies conducted with this method have been mixed [24, 25, 27].

In the present study, we used the dot-probe task to assess the existence of attentional bias for neutral and pain-related verbal stimuli. Through an ERP methodology, we aimed to extend the knowledge regarding attentional bias in FM, investigating for the first time the

possible neural correlates of the behavioral results of this task. The following hypotheses were tested: (1) patients with FM would show attentional bias for pain-related words, which would be manifested by higher hits and lower reaction times for dots preceded by pain-related words than for dots preceded by neutral words, in comparison with healthy controls; (2) the increasing processing of the pain-related condition would be manifested in increased P300 and LPP mean amplitudes in patients with FM in comparison with healthy controls.

The first hypothesis was not confirmed by our results. In fact, we did not find a main effect of group, condition, or a significant group*-condition interaction, revealing that both patients and controls had a similar number of hits for pain-related and neutral conditions. We found the same pattern of results in reaction times, which are in accord with previous results [3, 25, 28, 29]. We may interpret such findings in reaction times as a lack of ecological validity of the experimental stimuli, which may be irrelevant for capturing the attention of patients and controls.

The stimuli exposure time in the dot-probe task may have been insufficient to capture the attention of the FM group. In fact, a previous study [30] suggested that the time during which the pair of words is exposed might influence attention, considering that the authors only found an attentional bias when the stimuli exposition was longer (1250 ms). As the stimuli exposure in our study was 500 ms, it is likely that this duration was not sufficient to induce an attentional bias.

Interestingly, patients had higher omission rates in the pain-related condition in comparison with healthy controls, which may be suggestive of attentional bias, but in the opposite direction of our prediction. Indeed, when confronted with affectively relevant words, individuals with FM may have difficulties in averting attention from the stimuli, losing focus on the task goal, and failing more often in the localization of the dot-probe. This type of explanation is compatible with the thesis of attentional bias for relevant stimuli.

The use of electroencephalography in this research allowed us to study the P300 and LPP amplitudes elicited by the dot-probe, which are respectively regarded as correlates of selective attention and affective assessment of the stimuli. The results showed differences between groups, but not dependent on the condition. A lower mean amplitude of the P300 was found in participants with FM for both conditions—pain-related and neutral—suggesting that patients with FM may have generalized attentional deficits. Therefore, the electrophysiological results do not support the hypothesis of hypervigilance in patients with FM, suggesting instead reduced attentional resources for the processing of general information. Conversely, the allocation of attentional resources for the processing of any type of information seems to be generally decreased in these patients. This explanation is consistent with the results of other studies that have demonstrated a relation between P300 amplitudes and attentional resources, showing that the amplitude of the P300 is proportional to the amount of attentional resource employed [31]. Augmented amplitudes may be associated with the evaluation of stimuli, context updating, and memory storage [32], indicating lower attentional resources available for secondary tasks in dual-task paradigms [33].

Later stages of attentional processing have been associated with late positive ERP components, which have been related to the elaborative emotional process after the conceptual identification of the stimulus [34, 35]. For example, Montoya and colleagues [36, 37] found that late ERP components (300 ms after the presentation of the stimulus) were significantly influenced by emotional valence and elaborative processing.

In this study, we analyzed a late positive component, in the 600–800 ms time window. We found a main effect of group, with the FM group presenting higher amplitudes than controls in both conditions. Previous findings showed that words that are emotionally relevant to participants, even with a negative valence such as unpleasant words, elicited more positive amplitudes than neutral/pleasant stimuli [38–41]. This effect may indicate that participants with chronic pain might have been more emotionally involved in the experiment than healthy controls [41], despite a reduced

allocation of attentional resources to the probes. In this sense, our study seems to support the thesis that people with FM are more emotionally involved in the task, despite a reduced allocation of attentional resources to the probes. Thus, this ERP result is congruent with the behavioral results found with omissions, suggesting that people with FM have an attentional bias to pain-related words, which may increase the affective influence of these words on cognitive processing, negatively interfering with the attentional resources allocated to the probes.

We also investigated the effects of affective variables, such as depression, impact of FM, and pain catastrophizing, on participants' performance in the dot-probe task. As expected, people with FM reported higher depression symptoms, as well as higher scores on pain-related scales. While certain studies based on neuropsychological tests of attention demonstrate that anxiety and depression do not contribute to attentional deficits (e.g. [42]), other studies, for example using the Stroop task, have shown that anxiety and depression modulate attentional bias [24, 43].

In the present study, although patients had higher levels of depression than controls, as well as thoughts, perceptions, and feelings related to pain, these variables did not influence the results of the dot-probe task, in accord with previous findings [24, 25, 28, 29, 42, 43]. The results showed that these variables did not appear to influence the results of the dot-probe task. Thus we can infer that FM is associated with higher levels of depression, as well as thoughts, perceptions, and feelings related to pain.

Despite the novelty of the results, several limitations must be considered in interpreting our findings. The small sample size may have impacted the statistical power of the results. Moreover, the lack of a clinical control group with chronic pain (e.g., back pain, neck pain, among others) prevents us from concluding that the attentional deficits suggested by our results are pathognomonic of FM, rather than simply any pathology that is associated with chronic pain. Furthermore, the use of verbal stimuli may induce motor artifacts, and the exposure time of the dot-probe may have been too short to induce the effects of interest, as discussed above. Therefore, in future studies, authors should consider including a block of nonverbal stimuli in the task, including verbal stimuli with direct descriptions of pain-related stimuli, and collecting physiological data to increase the comprehension of the behavioral results. For future studies, we also suggest the validation and use of the revised version of the FIQ, and the use of the Symptom Impact Questionnaire instead of the FIQ for the healthy control patients [44].

Despite these limitations, this study is a further step in the direction of a better understanding of the cognitive alterations associated with FM, unearthing new clues for future research in this area. Likewise, the neurophysiological functioning associated with attentional processing seems to be generally altered in FM patients. Our results suggest that people with FM may be more emotionally engaged with the task, despite a decrease in the allocation of attentional resources to the stimuli.

Behavioral results may be insufficient to assess attentional bias in people with FM, and previous studies have identified significant neural differences between individuals with FM and healthy participants. For instance, a recent study found that female patients with FM showed the same electrical brain activity pattern during single task and dual task conditions, whereas healthy controls seemed to adapt their brain activity to task commitment [45]. In this sense, pain-related stimuli may be used in dual-task conditions, as they seem to interfere with the detection of probes. Moreover, these neural changes related to FM appear to be modulated by pain intensity [46] and depressive symptoms [47], reinforcing the need to control these variables in future studies.

## CONCLUSION

To the best of our knowledge, this is the first study providing data on the neural correlates of the attentional processing of patients with FM, as assessed with a dot-probe task. The decreased P300 amplitude suggests that patients allocate

less attentional resources to the task, and the increased amplitude of their LPP appears to suggest an augmented emotional processing of the target stimuli. Interestingly, such neural changes emerged despite similar behavioral results. In conclusion, our results support the thesis of generalized attentional deficits in FM, which is in accord with previous findings and is considered during diagnosis.

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***Authors' Contributions.*** Susana Cardoso developed concept and study design, formulating the questions, acquisition data, performed the treatment, statistical analysis and interpretation of data, prepared, drafting and revising the manuscript. Carina Fernandes provided substantial contributions to acquisition data, treatment and interpretation of data for this analysis and participated in revising manuscript. Fernando Barbosa provided substantial contributions to developed concept and study design and interpretation of data for this analysis and participated in revising manuscript. All authors approved the final version for publication. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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***Compliance with Ethics Guidelines.*** The present study was conducted in accordance with the Declaration of Helsinki of 1964 and its later amendments. The current study was part of a larger research project of Doctoral Programme in Psychology of Faculty of Psychology and Education Sciences of the University of Porto (FPCEUP), where the project received ethics approval by the scientific committee. The project was also approved by the ethics committee of Centro Hospitalar de Vila Nova de Gaia/Espinho, and by the National Association Against Fibromyalgia and Chronic Fatigue Syndrome (MYOS). All of the subjects provided written informed consent prior to their participation in this study.

***Data Availability.*** Data cannot be provided because their availability was not written consented by the participants. However, the data can be provided to the reviewers if requested.

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