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Review

Measurement of event-related potentials from electroencephalography to evaluate emotional processing in Fibromyalgia Syndrome: A systematic review and meta-analysis

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ABSTRACT

Objective: The present systematic review and meta-analysis intended to: 1) determine the extent of abnormalities in emotional processing linked to emotional event-related potentials (ERPs) in Fibromyalgia Syndrome (FMS) and 2) integrate data from similar emotional tasks into a meta-analysis to clearly demonstrate the scientific and clinical value of measuring emotional ERPs by electroencephalography (EEG) in FMS.
Methods: A systematic review and meta-analysis of studies comparing emotional processing indicated by ERPs in FMS patients and healthy controls was conducted. Fifteen articles were included in the systematic review after applying the eligibility criteria.
Results: Nine articles demonstrated disturbances in emotional processing in FMS. These emotional disturbances were distributed over the whole range of ERP latencies, mainly over central, parietal, temporal and occipital areas. Despite of this, quantitative analysis revealed only significant differences in N250 and LPP/LPC between FMS patients and healthy controls, with smaller LPP/LPC and greater N250 seen in FMS.
Discussion: N250 and LPP/LPC seem to be the ERPs with the greatest potential to determine emotional alterations in FMS. These ERPs are related to complex cognitive processes such as decoding features relevant to affect recognition (N250) as well differentiation between emotions, persistent engagement, conflict resolution or evaluation of emotional intensity (LPC/LPP). However, differences in task setup had an important impact on the variation of ERP outcomes. Systematization of protocols and tasks is indispensable for future studies.

1. Introduction

1.1. Symptoms and characteristics of Fibromyalgia Syndrome

Fibromyalgia Syndrome (FMS) is a chronic pain condition characterized by widespread pain and symptoms such as depression, anxiety, fatigue, sleep disturbances (insomnia) and cognitive impairments (Duschek et al., 2022; Montoro et al., 2015; Maffei, 2020; Muñoz Ladrón et al., 2022; Reyes del Paso et al., 2015; Sarzi-Puttini et al., 2021; Wolfe et al., 2010). The symptoms have a significant impact on the patient's quality of life, well-being and psychosocial functioning (Arnold et al., 2008; Galvez-Sánchez et al., 2019; Penrod et al., 2004). The prevalence rate of FMS is about 2–4 % in the general population (Cabo-Meseguera et al., 2017; Schilling and Weidner, 2021; Wolfe et al., 1995), and women are more predisposed to FMS than men (Srinivasan et al., 2019). FMS is a complex disease diagnosed by exclusion and fulfillment of the following criteria: chronic pain (>3 months) in several regions of the body, unrefreshing sleep or sleep disturbances, and physical and/or mental fatigue/exhaustion (Wolfe, 2010; Wolfe et al., 2010). Despite the existence of diagnostic criteria, the diagnosis of Fibromyalgia Syndrome (FMS) frequently relies on negotiations between the physician and the affected individual to address psychosocial considerations (Galvez-Sánchez and Reyes Del Paso, 2020; Srinivasan et al., 2019; Wolfe et al., 2018). Moreover, there is a noted inclination towards overdiagnosing FMS in women, as suggested by studies (Galvez-Sánchez and Reyes Del Paso, 2020; Srinivasan et al., 2019).

The etiology of FMS remains elusive. Coupled with the substantial impact of FMS symptoms, and the absence of a moderately effective

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treatment, FMS places a significant health-economic burden (Arnold et al., 2008; D'Onghia et al., 2022; Galvez-Sánchez et al., 2019; Penrod et al., 2004). Several theories have attempted to understand FMS. These have considered various factors, including the neurological, psychological, and genetic (Gyorfi et al., 2022). One of the most widely supported theories regarding FMS etiology posits it as a condition characterized by Central Sensitization wherein the central nervous (CN) system becomes more responsive to stimuli (Cook et al., 2004; Burgmer et al., 2009; Gracely et al., 2002; Pujol et al., 2009; Gracely and Ambrose, 2011; López-Ruiz et al., 2019; Montoro et al., 2016a; Rhudy et al., 2013), including emotional stimuli, leading to heightened emotional experiences and responses in individuals with FMS (Pinto et al., 2023). Consistently, emotional distress is highly prevalent in FMS (Kleykamp et al., 2021). Emotional distress can likewise instigate the conventional stress response, thereby influencing the modulation of sensory input to the brain (Littlejohn and Guymer, 2018; Montoro et al., 2018). Certainly, many of the brain areas exhibiting heightened responsiveness to painful stimulation in individuals with FMS-i.e., prefrontal and supplementary motor cortices, the insula, anterior cingulate, sensory-motor cortex, right thalamus, and basal ganglia (Cook et al., 2004; Burgmer et al., 2009; Gracely et al., 2002; Pujol et al., 2009) are associated with emotion regulation and processing (Balducci et al., 2024; Kohn et al., 2014; Levy and Wagner, 2011; Morawetz et al., 2017; Ochsner and Gross, 2008; Zhang et al., 2020). Additionally, alterations in neurotransmitter levels, such as serotonin, norepinephrine, and substance P, may also contribute to disturbances in mood in FMS (Becker and Schweinhardt, 2012).

Consequently, within the framework of behavioral observations, FMS patients have exhibited greater subjective reactions to aversive stimuli and blunted reactions to positive emotional stimuli during affective picture viewing paradigms (Bartley et al., 2009; Rhudy et al., 2013). Broadly, an emotion-driven selective attention in FMS has been documented (see Amaro-Diaz et al., 2022 systematic review). Pain augmentation caused by negative affect (sadness, disgust, fear) has also been observed comparing FMS patients with controls by using mood induction and language decision tasks (Davis et al., 2001; Montoya et al., 2005a). Further, greater catastrophizing, emotional avoidance, alexithymia, disturbed affect (i.e., greater negative affect and less positive affect) through self-reported questionnaires, along with challenges in emotion-based decision making (e.g., Iowa Gambling Task), a bias towards negative information (e.g., emotional modification of the Stroop task) and diminished interoceptive awareness (Schandry mental tracking task) have been reported in FMS patients (Davis et al., 2001; Duschek et al., 2014, 2017; Geisser et al., 2003; Hassett et al., 2008; Montoro et al., 2016b; Montoro and del Paso, 2015; Rogers and Farris, 2022; Van Middendorp et al., 2008; Walteros et al., 2011; Weiß et al., 2013). These affective states have been related to functional impairments and diminished quality of life of FMS patients (Galvez-Sánchez et al., 2020a, 2020b; Montoro and Galvez-Sánchez, 2022). They have also been shown to exert a substantial influence on the pain experience of those with FMS (Davis et al., 2001; Montoya et al., 2005a; Plazier et al., 2015).

It should be noted that the emotional peculiarities documented in Fibromyalgia Syndrome (FMS) manifest shared characteristics with various pathologies, such as anxiety and depressive disorders, as evidenced by traits like catastrophizing, and a bias towards negative information (Cetingok et al., 2022; Henao-Pérez et al., 2022; Kaviani et al., 2004; Løge-Hagen et al., 2019). Similarly, these features extend to diverse psychological traits, notably intolerance of uncertainty, exemplified by behaviors like emotional avoidance (Del Popolo Cristaldi et al., 2021), rather than indicating exclusive abnormalities specific to FMS. Nonetheless, though not exclusive, these emotional peculiarities exert a distinctively influence in individuals with FMS. As an illustration, catastrophizing is postulated to serve as a predisposing factor for depression among individuals experiencing chronic pain. By contrast, its influence is notably absent in individuals without chronic pain (Trudel and Cormier, 2023). Conversely, intolerance of uncertainty exhibits an inverse pattern (Trudel and Cormier, 2023), and has been recognized as a significant factor influencing psychological adjustment in non-chronic pain patients, as demonstrated in studies conducted by Árbol et al. (2021), Carleton (2012), Hong and Cheung (2015), Miranda et al. (2008), Trudel and Cormier (2023). The co-occurrence of anxiety and depressive disorders in FMS patients (Cetingok et al., 2022; Henao-Pérez et al., 2022) complicates the delineation between these conditions. However, it is noteworthy that the aforementioned emotional peculiarities and the associated altered emotional processing persist in FMS patients even in the absence of comorbid depression or anxiety disorders, underscoring their significance in FMS pathology (Goldway et al., 2022; Fischer-Jbali et al., 2022a, 2022b). Further, the brain alterations associated with FMS emotional factors are evident not only under pain processing but also in resting state what implies that, even at rest, the brain reserves a certain activity for these factors (Malfliet et al., 2017). Consequently, these emotional idiosyncrasies cannot be solely attributed to comorbidities or shared features among different psychological traits. In light of these findings, the research focused on emotional processing in FMS has surged in recent years, prompting efforts to optimize and tailor psychological treatments, to effectively address the specific emotional challenges associated with FMS.

1.2. *Emotional event-related potentials (ERPs) and associated emotional/cognitive processes*

Research related to CN emotional alterations has mainly combined several classical tasks from cognitive psychology such as stroop, dot probe, Go/No-Go and picture frame tasks. These tasks have been manipulated by incorporating additional emotional elements, such as emotional faces, words, or pictures—referred to hereinafter as "emotional tasks." These tasks are commonly coupled with the recording of event-related potentials (ERPs) through electroencephalography (EEG). The emotional processing of words, pictures, or faces is associated with a cascade of ERPs, wherein each component indexes a specific emotional and/or cognitive processing stage. Emotional processing of words, pictures or faces is related to a cascade of ERPs wherein each component indexes a particular emotional and/or cognitive processing stage (Frühholz et al., 2011). Short-latency ERPs are mainly involved in initial automatic processing such as basic visual processes, visuospatial orienting, stimulus detection [P100, 80–130 ms] (Carretié et al., 2004; Schindler et al., 2019), perceptual encoding of structural features of the face [N170, 150–180 ms] (Ding et al., 2017; Hinojosa et al., 2015), and automatic attentional allocation and semantic processes, i.e., automatic selective processing of emotionally relevant words [early posterior negativity (EPN), 200–300 ms] (Espuny et al., 2018; Imbir et al., 2017, 2021). Mid-latency ERPs are associated with early attention-related processes that index fast and automatic detection of salient (emotional) stimuli [P200, 200–250 ms] (Sarlo and Munafò, 2010; Zhu et al., 2015), decoding of complex facial features including those relevant to emotions and affect recognition [N250, 250–300 ms] (Balconi and Pozzoli, 2008, 2009; Blier et al., 2011; Güntekin et al., 2019; Schindler et al., 2019), the amount of cognitive effort and allocation of attentional resources, receptivity to emotional stimuli and conscious stimulus recognition, and categorization and organization of behavioral responses [P300, 340–600 ms] (Imbir et al., 2017; Wei et al., 2016). Further, long-latency ERPs are involved in the detection of semantic incongruity and conflict processing [N4, 350–500 ms] (Imbir et al., 2017, 2021; Zhao et al., 2015), complex cognitive processes such as evaluation of the intensity of expressed emotions and differentiation between emotions or sustained attention processes, persistent engagement in emotional and cognitive processing resources, conflict resolution and sensitivity to emotional valence [LPP/LPC, 500-800ms] (Espuny et al., 2018; Gootjes et al., 2011; Imbir et al., 2017, 2021; Moradi et al., 2017; Schindler et al., 2019).

1.3. Tasks and experimental paradigms for eliciting and studying emotional ERPs

The emotional Stroop task (EST), emotional Go/No-Go, emotional dot probe and emotional picture frame are the tasks most commonly used to elicit ERPs. The EST aims to evaluate the interference between emotional stimuli and related cognitive processes (Straub et al., 2022). Individuals must decide whether the colors of positive, negative, neutral words match with color words presented in black (Domes et al., 2006; Werner et al., 2014). The task includes two types of trials: congruent (concordance between the color of the emotional word and the color word) and incongruent trials (no concordance between the color of the emotional word and color word). Cognitive interference arises when the processing of the word prevents simultaneous processing of the color (Crombez et al., 2000). Longer delays in responding to negative than to neutral words indicate a negative attentional bias. On this basis, negative information requires a greater amount of cognitive resources, which subsequently leads to longer processing times (Imbir et al., 2021). Further, the magnitude of the interference effect is related to the extent to which the words are related to the participant's emotional state and/or pain (Crombez et al., 2000). As the words become more closely linked to the participant's emotional state and/or pain, a greater attention directed towards them is expected, potentially resulting in reduced processing of the color information (Crombez et al., 2000). The emotional dot probe task requires participants to decide as quickly and accurately as possible on which side of the screen an asterisk is displayed on. Participants must ignore the emotional picture/word-pairs, which are presented immediately before the asterisk on the left and right sides. Trials include a picture combination, composed of two pictures presented simultaneously on the left and right sides of the screen. Stimuli are divided into two conditions: emotional (emotional/pain and neutral pictures) and neutral (two neutral pictures) (Cisler and Koster, 2009; Jodd et al., 2018; Koster et al., 2004). Additionally, this task comprises two types of trials: congruent, where the asterisk aligns with the emotional picture's side, and incongruent, where the asterisk appears on the opposite side. Behaviorally, shorter reaction times to congruent trials indicate an inclination towards emotional stimulation, while longer reaction times to incongruent trials serve as an indicator of attentional disengagement (Fernandes-Magalhaes et al., 2022). In the emotional picture frame task, pictures of different emotions (pain, anger, happiness, etc.) and a neutral condition are displayed in a frontal view, while each picture is surrounded by a colored frame (red, yellow, green, blue). Individuals are asked to name (by pressing a target button) the frame color of the picture displaying a positive, negative or neutral picture/face, without paying attention to the actual picture/face (Feng et al., 2012; Fischer-Jbali et al., 2021). This paradigm can offer insights into task accuracy, participants' cognitive speed, and the specific processing of emotional content (Fischer-Jbali et al., 2021). The emotional Go/No-Go task, is composed of two types of cues (go cues, no-go cues) presented in a pseudorandomized order. Individuals must respond by pressing a target button for go cues and must inhibit their response during the presentation of no-go cues. Normally, the emotional component is task-irrelevant, while another task relevant aspect (e.g., male vs. female faces) is the element that participants have to respond to. Further, the relative numbers of false alarms (commission errors [CE]) and omission errors ([OE]; errors on go trials divided by the total number of go trials) are recorded, reflecting behavioral inhibition and execution, along with emotional modulation (Schulz et al., 2007; Sitges et al., 2018).

1.4. Findings in emotional processing research of Fibromyalgia Syndrome

Concerning FMS, studies exploring ERPs and using emotional picture paradigms* (e.g., masking or cognitive paradigms) have confirmed an influence of emotional stimuli on pain processing (greater P50, smaller N80 amplitudes) (Montoya et al., 2005b), maladaptive affective attention modulation (ssVEP, steady-state visually evoked potentials) (Goldway et al., 2022), and early cerebral modulation of pain associated with an increase in automatic attention [greater P100, P200a, P200b amplitudes] (Peláez et al., 2019). Other studies have investigated the processing of emotional words in FMS using language (decision) (Montoya et al., 2005a; Sitges et al., 2007), emotional Stroop (Fischer-Jbali et al., 2022b; Mercado et al., 2013) or dot probe tasks (Cardoso et al., 2021) tasks. In FMS, these studies have shown: 1) avoidance of threatening information [smaller P200 amplitude] (Montoya et al., 2005a), 2) specific difficulty in cognitive inhibition [greater P450 amplitude] (Mercado et al., 2013), 3) reduced allocation of attentional resources and subsequently greater emotional processing of stimuli [smaller P300, larger LPC amplitudes] (Cardoso et al., 2021), 4) increased allocation of CN resources to pain-related information [larger positive ERPs] (Sitges et al., 2007), and 5) greater cognitive effort and attentional mobilization to overcome reduced attentional resources caused by central nervous pain sensitization (CNPS), in addition to preferential cerebral processing of negative information (larger P300 and LPC amplitudes), which may be related to greater pain or affective symptoms in FMS (Fischer-Jbali et al., 2022b).

Emotional and pain facial expressions has also been a highly relevant research topic in FMS, as facial expressions are important for the communication of emotions between individuals, including pain (Williams et al., 2006). Deficits related to facial emotion processing are a potential source of interpersonal communication failure, which could increase vulnerability to interpersonal distress (Muñoz Ladrón et al., 2021; Weiß et al., 2013). Especially, expressions of pain seem to facilitate communication of suffering and enable the sufferer to obtain support from others (Williams et al., 2006). Nonetheless, outcomes regarding emotional facial expressions and FMS are diverse. Fischer-Jbali et al. (2021), using an emotional picture frame task, showed deficient mobilization of attentional resources and sustained attention, as well as greater engagement in the decoding of complex facial features to overcome attentional impairments, in FMS (smaller P200, larger N250, and smaller LPP amplitudes). In an emotional dot probe, a bias towards encoding negative rather than positive emotions, an increase of attentional resource allocation to pain-related information, and a nonspecific deficit in sustained attention (smaller N170, larger P200, and smaller LPC amplitudes) were further observed in FMS by Fischer-Jbali et al. (2022a). In the same task, Fischer-Jbali et al. (2022a, 2022b) observed that attentional bias to pain was caused by deficits in the allocation of attentional resources and automatic attention, accompanied by altered control of attentional processes (larger P200 amplitude). Gonzalez-Roldan et al. (2013) showed a bias towards CN processing of faces exhibiting negative affect in FMS. No differences between FMS patients and controls in emotional Go/No-Go ERPs were found by either Pidal-Miranda et al. (2019) or Sitges et al. (2018).

(Note: Please be advised that additional elucidation on paradigms, including a comprehensive examination of tasks, materials, and information pertaining to underlying cognitive and emotional processes, can be found in the Supplementary Material; see Supplementary Table 1 for details).*

1.5. Relationships among ERP components, symptoms and behavior/performance patterns in Fibromyalgia Syndrome

Some studies have also observed associations among emotional ERP components, symptoms of FMS and/or behavior/performance parameters. Namely, Fischer-Jbali et al. (2021) revealed that depression severity was a predictor of the P100 amplitude elicited by emotional faces. Further, N170, P200 and N250 amplitudes correlated positively with correct responses naming the frame color for happy and neutral faces pictures. Fallon et al. (2015) demonstrated that valence ratings mediated the relationship between the emotional picture type and central-parietal LPP. Goldway et al. (2022) suggested that maladaptive affective attention modulation may be a predictor of disease symptoms such as pain severity. Impaired fronto-occipital connectivity was further

associated with sleep difficulties in FMS during a paradigm assessing attention allocation in response to affective distractors (Goldway et al., 2022). Negative attentional bias, or preferential processing of negative information or pain, has been proposed to contribute to the aversive mood states (i.e., anxiety and depression) that characterize the disorder (Duschek et al., 2014; Galvez-Sánchez et al., 2019), as well as greater fear of pain, less physical activity, maladaptive coping strategies, mood impairments and functional disability (Crombez et al., 2012; Khatibi et al., 2009; Todd et al., 2018; Vlaeyen et al., 2016).

1.6. Objective of the study and its plausible scientific and clinical contribution

Alterations in emotional processing in FMS seem to play an important role in symptom development/maintenance and the magnitude of the experienced pain (Galvez-Sánchez et al., 2019). However, studies analyzing the mechanisms underlying CN emotional processing in FMS show promising but inconsistent results, with some of them even failing to detect any emotional processing alteration (Pidal-Miranda et al., 2019; Sitges et al., 2018). The emotional tasks used have also been diverse and the resulting ERPs evaluated have therefore varied. Systematic reviews related to this topic are scarce and no meta-analysis has been performed to date. Thus, the present systematic review and meta-analysis mainly intends to: 1) determine the extent of abnormalities in the emotional processing linked to emotional ERPs- encompassing the corresponding scalp topographic distributions- in FMS, and 2) integrate ERP data from analogous emotional tasks into a meta-analysis to clearly demonstrate the scientific and clinic value of measuring emotional ERPs by EEG in FMS. Secondary outcomes include qualitative exploration of the emotional tasks used, differences in the ERPs involved in the processing of different emotions, possible related attentional bias in FMS, differences in psychological, clinical, and functional factors, differences in performance data between FMS and controls, and associations of psychological, clinical and functional variables with emotional ERPs and performance.

In support of the Central Sensitization theory, this review and meta-analysis have the potential to uncover valuable insights into the comprehension of CN emotional peculiarities within the context of FMS. From a clinical standpoint, synthesizing diverse perspectives on abnormalities in emotional processing related to emotional ERPs in FMS can enhance the understanding of the cognitive and emotional dimensions in FMS, ultimately informing effective therapeutic strategies. Nevertheless, it is imperative to articulate a tangible implication of specific ERP components in the emotional alterations associated with FMS pathology. Therapeutic interventions and preventions endeavors can be directed towards enhancing cognitive abilities linked to ERPs with the greatest potential to influence emotional alterations in FMS. Given the presumed connection between emotional alterations, CN pain processing and FMS symptoms and well-being (Galvez-Sánchez et al., 2019; Montoro et al., 2018), such neuropsychological training initiatives could further potentially contribute to alleviating symptoms associated with FMS. It also should not be overlooked that the identification of objective markers in the FMS diagnosis remains to be a significant challenge in this disorder (Choy et al., 2010; Galvez-Sánchez et al., 2019; Moyano et al., 2014). Hence, evaluating the scientific and clinical utility of specific emotional ERPs could serve as a starting point in researching them as potential objective markers for FMS. This will ultimately contribute to an effective and timely diagnosis, thereby positively influencing the treatment and prognosis of FMS.

2. Materials and methods

2.1. Search strategy and selection of studies

The present systematic review and meta-analysis was conducted according to the guidelines of the Cochrane Collaboration and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis [PRISMA] (Page et al., 2021). The protocol was formerly registered in the Prospective Register of Systematic Reviews (PROSPERO) international database (Registration ID: CRD42023402466). The search terms–extracted by MeSH (Medical Subject Headings)–were: fibromyalgia OR FMS OR fibromyalgia syndrome, AND emotion OR emotional processing OR emotional word OR emotional picture OR emotional facial expression OR attentional bias, AND EEG OR ERP OR evoked potential. The articles were collected between 1 March 2023 and 1 September 2023* by four independent reviewers (L.R.F-J., A.A., C.M.G-S. and C.I.M.) from the Scopus, PubMed, and Web of Science (WOS) databases, using the following eligibility criteria: (1) studies written in English; (2) original, peer-reviewed studies; (3) samples comprising adult patients ($\geq$ 18 years old) with an official diagnosis of FMS, and without other severe physical and/or mental disorder; (4) studies focused on emotional processing and ERPs in FMS; and (5) publication date from 2003 to 2023. The exclusion criteria were as follows: (1) duplicated articles; and (2) letters, conference articles, commentaries, posters or unpublished studies. The exclusion criteria for the meta-analysis were as follows: (1) absence of a comparison group (healthy control group); and (2) studies measuring ERPs that were not examined beyond their own research.

All identified articles were reviewed, and those that did not meet the criteria for subsequent analysis of the full text were discarded. To eliminate irrelevant studies, all titles and abstracts of each study were analyzed in a first step. Afterwards, the remaining articles were screened in detail for eligibility; therefore, all the full texts were checked and analyzed based on the preset inclusion and exclusion criteria. Discrepancies during this review process were reviewed by the first author [L.R. F-J.]. The PRISMA flowchart (Fig. 1) displays the screening and selection process for study inclusion. An additional final examination of the selected articles based on eligibility criteria was conducted by the senior author [C.I.M.] prior to proceeding with data extraction and quality assessment. The research question (PICO) was as follows: What aspects of emotion processing are commonly altered in fibromyalgia patients compared to healthy individuals (e.g., differences in emotional ERPs or associated scalp topographic distributions)?

*(*Note. A final search for updates was conducted before the article's publication on February 7, 2024, and three additional articles were identified. However, they were subsequently excluded based on their abstracts. None of them directly addressed our research question framed using the PICO format. The study by* Balducci et al. *(2024) utilized fMRI,* Mercado et al. *(2022) focused on deficits in working memory rather than identifying commonly altered aspects of emotion processing in FMS and* Fernandes-Magalhaes et al. *(2023) employed a combination of EEG and a dot-probe task, with the primary goal of modifying attentional bias through an intervention in FMS. This last additionally lacked of a healthy control group).*

2.2. Data extraction and quality assessment

After initially selecting studies based on the inclusion and exclusion criteria, full texts were analyzed. Study characteristics, methodologies and results were extracted, and limitations of the studies were assessed by two independent researchers [L.R.F-J. and C.I.M.]. The following data extraction sequence was used: first author, study tittle, country, publication year, study objectives, diagnostic methodology, study design (e.g., randomized controlled trail, experimental-cross-sectional, or case-control), sample size, participant distribution across study groups, age (mean/standard deviation), gender distribution (% women), ERPs explored, electrode pools, scalp topographic distributions, psychological data (e.g. depression, state and trait anxiety, sensory and affective pain), symptoms data (e.g. clinical pain, disease impact, cognitive deficits), along with the pertaining scales utilized (e.g. Beck Depression Inventory (Beck et al., 1996); Emotion Regulation Questionnaire (Gross and John, 2003); Fibromyalgia Impact Questionnaire (Burckhardt et al., 1991); McGill Pain Questionnaire (Melzack, 1975)),

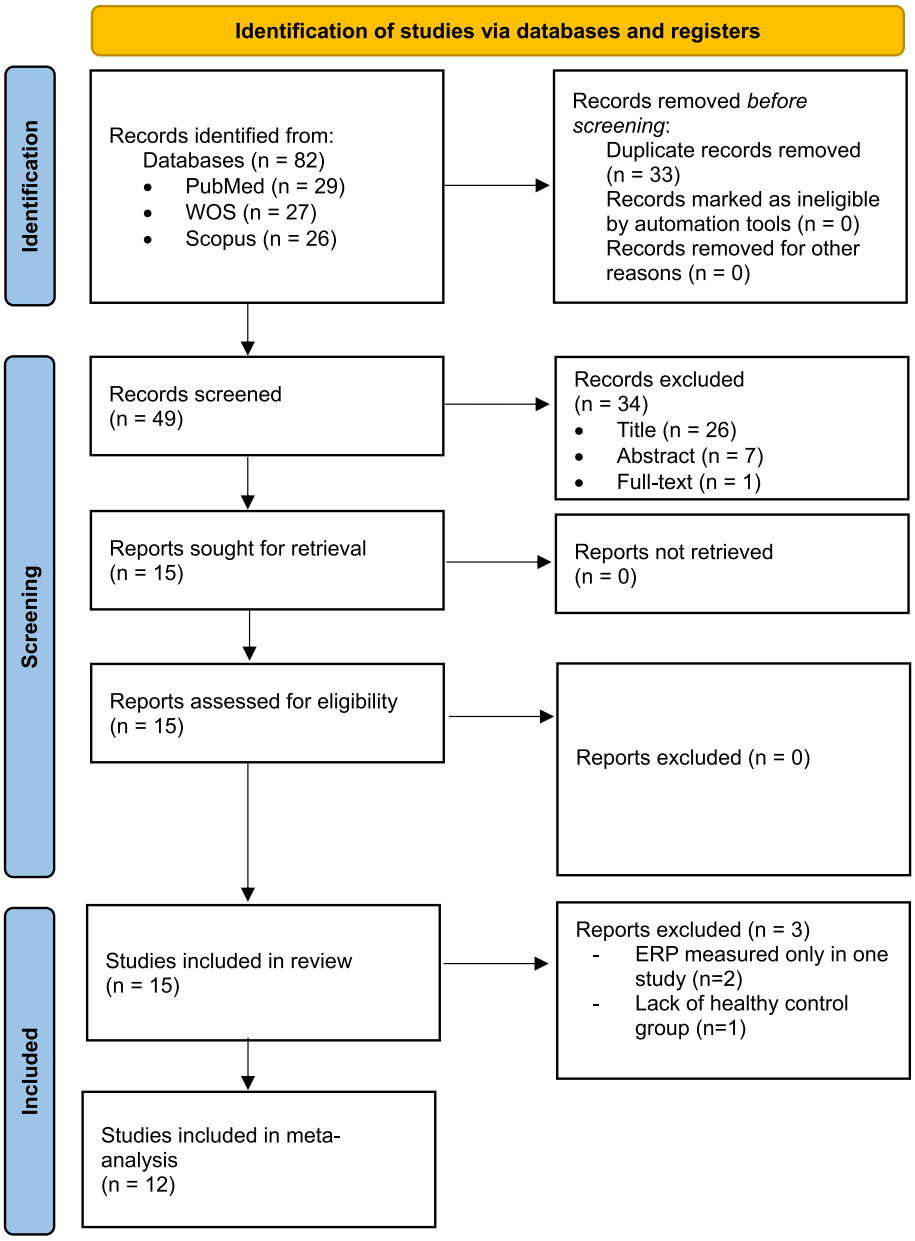

Fig. 1. Flow diagram of relevant eligible studies related to ERPs and emotional processing in fibromyalgia syndrome.

social and medical records (e.g., years of education, medication intake, pain duration), details of emotional tasks, stimulus types (words, faces, pictures), results on ERPs for each emotional stimulus (pain, angry, happy, positive, negative and neutral), task performance and quantitative ERP data for group comparisons. The data extracted from the articles that underwent review for the purpose of the meta-analysis is accessible at https://osf.io/bdux8. C.I.M. reviewed the data extraction to ensure accuracy. The characteristics of the included studies (displayed in Table 1) were manually extracted and tabulated. In order to obtain as much quantitative ERP data as possible, when these data were not available or incomplete in the articles reviewed, the corresponding authors were contacted via e-mail. Plot digitizer software was also used to extract missing data from figures/plots (Kadic et al., 2016).

For assessment of the quality of the selected articles, two authors (A. A. and C.M.G-S.) independently evaluated the risk of bias (ROB) in each study based on the Cochrane ROB assessment tool. L.R.F-J. and C.I.M. did not participate in the ROB assessment given that they authored papers included in the current systematic review. This tool includes the following seven items: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other bias. For each item, the ROB was graded as high (H), medium (M), or low (L). Discrepancies were resolved by further discussion with C.I.M. Any discrepancies in the ROB were reviewed by C.I.M, who made the final decision.

2.3. *Efficacy outcomes and data synthesis*

According to the primary and *secondary objectives** (reported in the Introduction section) of this review and meta-analysis, the characteristics (year of publication, country, study design, study groups, whether the sample of each study has a control group, sample size, age, type of ERPs measured, type of emotional task, etc.), findings (differences in ERP amplitudes between FMS patients and controls, emotional alterations reported, scalp topographic distributions, etc.), conclusions, and

Table 1
Characteristics of selected studies on event-related potentials from electroencephalography to evaluate emotional processing in fibromyalgia syndrome.

Event-related potentials by electroencephalography to evaluate emotional processing in fibromyalgia syndrome							
First author (publication year), study name, country	Objective	Study design/ diagnostic technique	Sample size, age (years)_ (Mean ± SD)	Task	EEG and ERP components	Results	Conclusion
Fernandes-Magalhaes et al., 2022, Neural correlates of the attentional bias towards pain-related faces in fibromyalgia patients: An ERP study using a dot-probe task. *Spain*	Investigation of neural temporal dynamics related to attentional bias in FMS	Cross-sectional BDI FIQ PCS STAI VAS (pain, fatigue) Questionnaire (current health; functional status)	*Total N* = 50 100 % female *FMS N* = 25; 53.0 ± 8.9 *HC* N = 25; 50.2 ± 9.1	Dot probe task (500-ms fixation cross, 500-ms stimuli, 300-ms interval, 200-ms probe, 1500-ms reaction, 300-ms interval) pain vs. non-pain stimuli (faces)	QuickCap-Neuroscan with 60 scalp electrodes P100/N100 (100 ms) N170 (150 ms) P200 (196 ms) N200a (274 ms) P300 (350 ms)	Generally greater P200 (frontal) for pain compared to neutral faces; In FMS group, greater P200 (fronto-central) for pain compared to neutral faces; greater P200 to pain for FMS patients compared to controls; generally shorter P200 latency (centro-parietal) for pain compared to neutral faces; smaller N200a for FMS patients to controls; in FMS, longer RT for incongruent than for congruent/ neutral trials	Presence of attentional bias in FMS caused by a deficit in the allocation of attentional resources to process pain-related information; attentional bias could be explained by automatic attentional mechanisms, which are accompanied by alterations of more strategic or controlled attentional components
Fischer-Jbali et al., 2022a, Central nervous activity during a dot probe task with facial expressions in fibromyalgia. *Austria*	Investigation of central nervous correlates of attentional and emotional processing in FMS	Cross-sectional ACR 2010 BDI MPQ SAM SCID STAI	*Total N* = 52 100 % female *FMS N* = 26; 50.4 ± 9.7 *HC* N = 26; 45.7 ± 7.5	Dot probe task (900–1000-ms fixation cross, 500-ms stimulus, 300-ms blank, 400-ms probe, reaction) Anger, pain, happiness, neutral stimuli (faces)	actiCHamp with 32 electrodes P100 (70–130 ms) N170 (120–200 ms) P200 (200–360 ms) N250 (300–460 ms) LPC (500–1000 ms)	In FMS, smaller N170 for anger/pain than for happy faces, and greater P200 for pain than for happy faces; N170 and P200 were unaffected by emotional expressions in controls; generally smaller LPC and longer RT in FMS; FMS with comorbid depression had less attentional interference due to emotional expressions and less difficulty disengaging from these stimuli than FMS without depression	Facilitated encoding of facial features representing negative rather than positive emotions in FMS; more automatized processing of pain expressions; greater attentional resource allocation to pain-related information nonspecific deficits in sustained attention in FMS confirmed by RT; shallower processing depth of emotional information in patients with comorbid depression
Fischer-Jbali et al., 2022b, Central nervous activity during an emotional Stroop task in fibromyalgia syndrome. *Austria*	Investigation of the influence of emotions on cognitive processing in FMS	Cross-sectional ACR 2010 MPQ SAM SCID	*Total N* = 71 100 % female *FMS N* = 36; 52.1 ± 12.1 *HC N* = 35; 54.1 ± 8.6	Emotional Stroop task (3000–5000-ms fixation cross, 1500-ms stimulus, 1500-ms response) Positive, negative, neutral stimuli (words)	Standard Brain Amp with 32 electrodes P100 (70–130 ms) EPN (130–250 ms) P300 (200–400 ms) N4 (430–730 ms) LPC (700–1300 ms)	In FMS, generally greater P300 and theta power; in FMS, negative words elicited greater LPC than positive words; no differences for P100, EPN, or N4; in FMS, generally longer RT	Greater cognitive effort and attentional mobilization in FMS needed to overcome the reduction of attentional resources caused by central nervous pain sensitization; behavioral outcomes do not support attentional bias but LPC reflects preferential processing of negative information, which may contribute to pain

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Table 1 (*continued*)

Event-related potentials by electroencephalography to evaluate emotional processing in fibromyalgia syndrome							
First author (publication year), study name, country	Objective	Study design/ diagnostic technique	Sample size, age (years)_ (Mean ± SD)	Task	EEG and ERP components	Results	Conclusion
							and affective symptoms
Goldway et al., 2022, Abnormal Visual Evoked Responses to Emotional Cues Correspond to Diagnosis and Disease Severity in Fibromyalgia. *United States/Israel*	Investigation of abnormalities in cognitive-emotional processing and their relation to disease severity in FMS	Cross-sectional ACR 2010 BDI MPQ PSQI STAI Self-report questionnaire for clinical manifestations	*Total N* = 58 87.93 % female *FMS N* = 39; 36.7 ± 12.5 (35 female) *HC N* = 19; 31.5 ± 9.2 (16 female)	ssVEP task (paradigm assessing attention allocation in response to affective distractors) (1-s scramble, 2.9-s scramble and dots, 5.8-s distractor and dots, 1–3-s interval) Superimposed on emotional vs. neutral background (pictures)	V-Amp EEG amplifier with 16 electrodes ssVEP (steady-state visually evoked potentials)	FMS showed impaired affective discrimination, sustained attention to negative distractors, decreased task-related EEG and decreased task-related connectivity (fronto-occipital); lack of adaptive attentional discrimination was predictive of pain severity; impairments in EEG connectivity (fronto-occipital) were predictive of sleep disturbances	Maladaptive affective attention modulation, which predicts disease symptoms; importance of centrality of cognitive-emotional dysregulation in pathophysiology of chronic pain
Fischer-Jbali et al., 2021, Central nervous activity during implicit processing of emotional face expressions in fibromyalgia syndrome. *Austria*	Investigation of central nervous correlates of affective and attentional processing in FMS	Cross-sectional ACR 2010 BDI MPQ SAM SCID STAI	Total *N* = 62 100 % female *FMS N* = 25, 50.5 ± 10 *HC N* = 37; 47.1 ± 7.9	Picture frame task (1750-ms fixation cross, 300-ms stimulus, decision task, 700–2300-ms interval) Angry, painful, happy, neutral stimuli (faces)	ActiCHamp with 32 electrodes P100 (70–150 ms) N170 (130–210 ms) P200 (200–380 ms) N250 (330–440 ms) LPP (470–990 ms)	In FMS, smaller P200/LPP, and greater N250 compared to controls; in FMS, N250 varied according to emotional stimuli; no differences for P100 or N170; in FMS, longer RT and fewer correct responses; task performance related to pain severity	Deficient short-term mobilization of attentional resources and sustained attention in FMS; greater engagement in the decoding of complex facial features needed to compensate for attentional impairments; neural mechanisms underlying complex visual processes are particularly susceptible to emotional influences in FMS; behavioral data support attentional deficits in FMS and implicate clinical pain therein
Cardoso et al., 2021, Emotional and Attentional Bias in Fibromyalgia: A Pilot ERP Study of the Dot-Probe Task. *Portugal*	Investigation of neural correlates of attentional bias in FMS.	Cross-sectional (pilot study) Semi-structured interview BDI FIQ PCS	*Total N* = 30 100 % female *FMS N* = 15; 51.9 ± 7.1 *HC* N = 15; 46.1 ± 8.4	Dot probe task (500-ms fixation cross, 500-ms pairs of words, 100–300-ms fixation cross, 150-ms probe, 1750-ms black screen) Pain vs. non-pain stimuli (words)	128 electrode HydroCel Geodesic Sensor Net, Net Amps 300 amplifier P300 (300–400 ms) LPP (400–600 ms; 600-800 ms)	No behavioral differences between groups; in FMS, smaller P300 and greater LPP compared to HC	Results show that FMS patients allocate less attentional resources to the task followed by an increased emotional processing of stimuli; outcomes support generalized attentional deficits in FMS
Peláez et al., 2019, Subliminal emotional pictures are capable of modulating early cerebral responses to pain in fibromyalgia. *Spain*	Investigation of the neural correlates of the influence of visual masking emotional stimulation on the processing of painful stimuli	Cross-sectional BDI FIQ FPQ-II PCS STAI TSK Questionnaire (current health;	*Total N* = 42 100 % female *FMS N* = 20; 48.7 ± 10.3;	Masking paradigm (400-ms mask 1, 33-ms subliminal prima, 400-ms mask 2, 2500-ms response [30-ms laser stimulus])	ElectroCap with 60 electrodes P100 80–120 ms) P200a (190–270 ms) P200b (280–360 ms) N200 (130–170	In FMS, greater P100 to painful stimuli preceded by pain-related pictures compared with painful trials preceded by other emotional pictures; FMS showed greater	Early cerebral modulation of pain in FMS, suggesting that only pain-related information (even unconscious) is able to enhance automatic attention; increasing neural

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Table 1 (*continued*)

Event-related potentials by electroencephalography to evaluate emotional processing in fibromyalgia syndrome							
First author (publication year), study name, country	Objective	Study design/ diagnostic technique	Sample size, age (years)_ (Mean ± SD)	Task	EEG and ERP components	Results	Conclusion
		functional status) VAS (pain perception, fatigue)	*HC N* = 22; 49.9 ± 8.8	Neutral, negative or pain-related stimuli (picture)	ms) LPP (500–920 ms)	P200a and P200b compared to HC	activity involved in the processing of painful stimulation
Pidal-Miranda et al., 2019, Pain Expressions and Inhibitory Control in Patients with Fibromyalgia: Behavioral and Neural Correlates. *Spain*	Investigation of preferential allocation of attention to information related to symptoms of FMS, particularly to pain cues	Cross-sectional semi-structured interview BDI MFE-30 PSQI PCS PSS VAS Edinburgh Handedness Inventory	*Total N* = 59 100 % female *FMS N* = 31; 50.1 ± 9.9; *HC N* = 28; 47.8 ± 11.1 *Total N* = 53 100 % female	Go/No-Go task (500-ms stimulus, 1.9–2.3-s interval) Pain, happy, neutral stimuli (faces)	actiCHamp with 32 electrodes Time-frequency decomposition N200 (250–340 ms) P300 (350–600 ms)	Pain expressions showed longer RT, more errors, greater theta and delta power, and greater P300 to No-Go stimuli; in controls, N200 greater for pain faces; no main group effects for N200, P300, or time-frequency data	Presentation of pain faces might be less conflicting for the patients, who are more used to encountering pain stimuli; could not confirm a greater effect of attentional bias towards negative stimuli over inhibitory performance in FMS
Sitges et al., 2018, Emotional influences on cognitive processing in Fibromyalgia patients with different depression levels: an event-related potential study. *Spain*	Investigation of the modulating role of depression in response execution and inhibition	ACR1990 BDI ERQ PANAS PVAQ SAM Numerical scale (0−10): pain intensity, duration, current level of pain	*FMS low depression N* = 17; 54.5 ± 10.7 *FMS high depression N* = 18; 50.3 ± 8.7 *HC* N = 18; 50.9 ± 6.2	Emotional Go/ No-Go task (500-ms stimulus, reaction, 1300–1500-ms fixation cross) Pain, happy, neutral stimuli (faces)	QuickAmp amplifier with 46 scalp electrodes N200 (200–350 ms) P300 (350–500 ms)	FMS with high depression showed lower positive affect scores, higher negative affect and pain vigilance scores, and slower RT than FMS with low depression/ controls; FMS rated pain faces as more arousing than controls; lack of group difference in N200 or P300	Depression is associated with higher affective dysregulation and deficits in information-processing speed in FMS; pain induces a bias to pain-related information, but pain intensity is not a predictor of cognitive dysfunctions; no significant impairment in response execution in response inhibition due to pain
Fallon et al., 2015, Altered Cortical Processing of Observed Pain in Patients With Fibromyalgia Syndrome. *United Kingdom*	Investigation of spatiotemporal patterns of brain activation in response to observed pain	Cross-sectional BDI FIQ PCS SAM	*Total* N = 37 100 % female *FMS N* = 19; 40.0 ± 8.0 *HC N* = 18; 39.2 ± 8.0	Simple viewing task (3-s black fixation cross, 3-s picture, 2-s resting interval, 4-s response period) Pain vs. non-pain stimuli (picture)	64-channel Biosemi Ag-Acl active 2 electrode system Short-latency P100 (110–170 ms) N100 (110–170 ms) Mid-latency P200 (210–230 ms) N200 (280–310 ms) P300 (370–420 ms) Long latency LPP (500–650 ms)	FMS attributed greater pain/ unpleasantness to pain pictures than controls; In FMS greater LPP and amplitude difference covaried with perceived unpleasantness of stimuli; In FMS greater Mid-latency positive potentials and smaller short-latency positive potentials	Increased central nervous activation of processes involved in emotional control and motivational salience in FMS; increased activation regardless of valence of stimuli suggest that even innocuous, everyday visual stimuli with somatic connotations may challenge the emotional state in FMS; importance of cognitive-emotional therapeutic approaches for FMS treatment
Gonzalez-Roldan et al., 2013, Altered Psychophysiological Responses to the View of Others´ Pain and Anger Faces in Fibromyalgia Patients. *Spain*	Investigation of psychophysiological responses when viewing others´ facial expressions	Cross-sectional semi-standardized interview BDI EHI STAI PANAS WHYMPI	*Total N* = 40 100 % female *FMS N* = 20; 53.4 ± 8.1	Simple viewing task (1-s fixation cross, 2-s stimulus, reaction) Pain, anger, happy, neutral stimuli (faces)	QuickAmp with 64 electrodes N100 (50–150 ms) N170 (150–200 ms) EPN (200–300 ms)	FMS show generally greater cardiac deceleration than pain-free controls; greater N100 to pain/anger faces in comparison with neutral faces; pain-free controls	Enhanced defensive reactions and increased mobilization of attention resources (to pain/anger faces); reduced allocation of attention (to happy faces);

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Event-related potentials by electroencephalography to evaluate emotional processing in fibromyalgia syndrome							
First author (publication year), study name, country	Objective	Study design/ diagnostic technique	Sample size, age (years)_ (Mean ± SD)	Task	EEG and ERP components	Results	Conclusion
			HC N = 20; 52.7 ± 9.9			showed greater N100 amplitudes to happy faces compared to patients, and more positive amplitudes (200–300 ms) to happy than to other faces; FMS showed greater theta power in response to pain/ anger faces and reduced alpha power relative to controls to all faces	both characterize information processing in FMS
Mercado et al., 2013, Brain correlates of cognitive inhibition in fibromyalgia: Emotional intrusion of symptom-related words. *Spain*	Investigation of cognitive inhibition mechanisms as part of the attentional control functions in FMS	Cross-sectional ACR 1990 FIQ STAI	*Total N* = 50 100 % female *FMS N* = 25; 47.8 ± 8.3 *HC* N = 25; 48.0 ± 7.5	Emotional Stroop task (300-ms stimulus, 3000-ms intertrial interval) Fibromyalgia symptom-related words, arousing-negative, arousing-positive and neutral stimuli (words)	ElectroCap International with 60 scalp electrodes P450	In FMS, symptom-related words elicited larger frontal P450; enhanced activation within right inferior frontal gyrus compared to the rest of the stimuli; no differences between groups in behavior/ performance	Presence of specific difficulty in cognitive inhibition in FMS (under conditions intimately linked with the core concerns of their disease); involvement of right inferior frontal cortices in this inefficient mechanism, which might require greater effort to achieve comparable performance to healthy people because of dysfunctional processing
Sitges et al., 2007, Abnormal brain processing of affective and sensory pain descriptors in chronic pain patients. *Spain*	Investigation of the abnormal brain processing of affective and sensory pain-related information seen in chronic pain	Cross-sectional BDI FIQ MPQ STAI PASS PVAQ WHYMPI	*Total* N = 52 *FMS N* = 18; 49.4 ± 6.5; *MSK* N = 18; 46.4 ± 9.2 *HC N* = 16; 49.2 ± 8.6	Word decision task (300-ms stimulus, response, 1800–2000-ms interval) affective, sensory pain descriptors, pleasant/non-pain-related words (words)	32 electrodes P200 (200–350 ms) LPC (500–800 ms)	Chronic pain patients used more affective and sensory pain descriptors, and were slower in responding to self-endorsed pain descriptors than to pleasant words; in MSK, greater positive ERPs for affective pain descriptors than for pleasant words; in controls, greater positive ERPs for sensory pain descriptors than for affective pain words No group effect in PPT;	Lack of dissociation between affective and sensory components of pain information; exaggerated rumination during the encoding of self-referent information related to pain; both characterize abnormal information processing in chronic pain patients
Montoya et al., 2005a, Altered processing of pain-related information in patients with fibromyalgia. *Spain*	Investigation of pressure pain thresholds (PPTs) and event-related potentials (ERPs) elicited by emotional words	Cross-sectional ACR1990 BDI STAI WHYMPI Measure of pain intensity and duration	*Total N* = 24 100 % female *FMS N* = 12; 50.6 ± 6.2 *HC* N = 12;	Language decision task (800-ms cue, 200-ms stimulus, 2-s reaction, 2.5-s inter-trial interval) unpleasant pain-related vs. neutral stimuli (words)	ElectroCap with 9 electrodes N100 (100–250 ms) P200 (150–300 ms) N4 (250–400 ms) P300 (450–650 ms) LPC (500–800 ms)	FMS have enhanced pain sensitivity; for N4 and P300, unpleasant words elicited more positive amplitudes than neutral words; in FMS, generally smaller P200; in controls, greater LPC for unpleasant	Altered cognitive processing of pain-related information; abnormal adaptation to mechanical pain stimuli

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Table 1 (*continued*)

Event-related potentials by electroencephalography to evaluate emotional processing in fibromyalgia syndrome							
First author (publication year), study name, country	Objective	Study design/ diagnostic technique	Sample size, age (years)_ (Mean ± SD)	Task	EEG and ERP components	Results	Conclusion
			51.8 ± 5.7			pain-related compared to neutral words	
Montoya et al., 2005b, Abnormal affective modulation of somatosensory brain processing among patients with fibromyalgia. *Spain*	Investigation of the influence of emotional states (pleasant and unpleasant) on brain activity	Cross-sectional BDI MPQ STAI WHYMPI	Total *N* = 43 100 % female *FMS N* = 27; 51.3 ± 6.8; *MSK N* = 16; 49.2 ± 8.3	Oddball paradigm (6-s stimulus, 6-s blank) Pleasant vs. unpleasant stimuli (picture, IAPS)	32 electrodes somatosensory-evoked potentials (SEPs) P50 (20–80 ms) N80 (60–110 ms) P200 (135–260 ms)	In FMS, generally greater P50 to tactile stimuli compared to MSK; in FMS, greater P50 and smaller N80 for unpleasant than pleasant pictures	Abnormal processing of nonpainful somatosensory information in FMS, especially when somatic signals are arising from the body within an aversive stimulus context; Support for the use of biopsychosocial models for understanding chronic pain and FMS

Note: FMS = fibromyalgia; HC = healthy controls; MSK = musculoskeletal pain; BDI = Beck Depression Inventory; EHI = Edinburgh Handedness Inventory; ERQ = Emotion Regulation Questionnaire; FIQ = Fibromyalgia Impact Questionnaire; FPQ-II = Fear of Pain Questionnaire; MFE-30 = Memory Failures of Everyday Questionnaire; MPQ = McGill Pain Questionnaire; PANAS = Positive and Negative Affect Schedule; PASS = Pain Anxiety Symptoms Scale; PVAQ = Pain Vigilance and Awareness Questionnaire; PCS = Pain Catastrophizing Scale; PSS = Perceived Stress Scale; PSQI = Pittsburgh Sleep Quality Index; SAM = Self-Assessment Manikin Scale; SCID = Structured Clinical Interview; STAI (State & Trait) = State-Trait Anxiety Inventory; TSK = Tampa Scale for Kinesiophobia; VAS = visual analog scale; WHYMPI = West Haven-Yale Multidimensional Pain; RT = reaction time.

limitations of the selected studies were synthetized and qualitatively analyzed. In addition, the target population, and the proportions of male and female participants, were ascertained. A general overview of the main characteristics, results and limitations of the studies is shown in Table 1. The differences in the ERPs measured between FMS and controls were further integrated and statistically analyzed (see Section 2.4. for more detailed information).

(Note: Secondary outcomes are not expounded upon in the main document of this manuscript but are detailed and discussed in the Supplementary Material; see supplementary results and discussion for detail).*

2.4. Statistical analysis

According to the main objective of the present review and the corresponding PICO question (What aspects of emotion processing are commonly altered in fibromyalgia patients compared to healthy individuals [e.g., differences in emotional ERPs or associated scalp topographic distributions]?), ERP data from the reviewed studies were integrated and differences between FMS and controls were analyzed. Given that the ERP data extracted from the selected studies mostly related to the different kinds of emotional stimuli, a mixed effect meta-analysis was performed using rma.mv function from the metaphor package (Viechtbauer, 2010) within R 3.6.2 software; specifically, a three-level meta-analysis was conducted using study as the cluster variable (level 3) and the effect sizes for FMS vs. control comparisons for each emotion in the study (level 2). Given the anticipation of potential heterogeneity among the included studies, a random-effects model was employed to compute the pooled effect sizes. Restricted maximum likelihood (RMEL) was used to calculate the heterogeneity of variance $\tau 2$, as it has demonstrated a reduction in bias across various scenarios with continuous data (Veroniki et al., 2016). Between and within study heterogeneity was evaluated using Cochran's Q and Higgins' I^2 (IntHout et al., 2016). A Cronbach's Q p value $< .050$ implies between-study heterogeneity, an I^2 between 25 % and 50 % implies low heterogeneity, an I^2 between 50 % and 75 % implies moderate heterogeneity and $I^2 > 75$ % implies high heterogeneity. Age, emotion, stimuli, task, year of study and country were tested as moderators and the results of significant comparisons are reported. Results from the meta-analysis are reported in Section 3.3.1.3 (Differences in ERPs amplitudes between FMS patients and controls).

Note that not all authors responded to the data request. Moreover, in the study of Montoya et al. (2005b), the groups were not FMS patients and controls, but rather FMS and musculoskeletal pain (MSK) patients. The study by Gonzalez-Roldan et al. (2013) only assessed N100, while the study conducted by Mercado et al. (2013) exclusively measured P450. Given the absence of additional studies measuring N100 or P450, both studies were consequently excluded from the quantitative meta-analysis. Hence, the number of the studies used in the statistical analysis of each ERP differed slightly from the total included in the qualitative reporting.

3. Results

3.1. Literature search and characteristics of studies included in qualitative and quantitative analyses

In total, 82 articles were identified in the databases after an extensive search. After deleting all duplicates, 49 articles were selected for review. The PRISMA flow diagram (Fig. 1) offers insight into the study exclusion process at each screening stage. Finally, a total of 15 full-text articles were included in the systematic review and meta-analysis. These articles were checked for suitability based on the predefined inclusion criteria and then subjected to data extraction (Table 1) as well as quality assessment.

Regarding the characteristics of the selected studies, the publication year ranged between 2005 and 2022. Most studies included a control group of healthy participants (Cardoso et al., 2021; Fallon et al., 2015; Fernandes-Magalhaes et al., 2022; Fischer-Jbali et al., 2021, 2022a, 2022b; Goldway et al., 2022; Gonzalez-Roldan et al., 2013; Mercado et al., 2013; Montoya et al., 2005a; Peláez et al., 2019; Pidal-Miranda et al., 2019; Sitges et al., 2007, 2018); only one study did not include a control group (Montoya et al., 2005b). Further, one study included another chronic pain condition (Sitges et al., 2007) and another one differentiated between different degrees of depression severity (Sitges

et al., 2018). Regarding the locations of the studies, nine were conducted in Spain (Fernandes-Magalhaes et al., 2022; Gonzalez-Roldan et al., 2013; Mercado et al., 2013; Montoya et al., 2005a, 2005b; Peláez et al., 2019; Pidal-Miranda et al., 2019; Sitges et al., 2007, 2018), three in Austria (Fischer-Jbali et al., 2021, 2022a, 2022b), one in Portugal (Cardoso et al., 2021), one in the United Kingdom (Fallon et al., 2015), and one in the United States/Israel (Goldway et al., 2022). Regarding the study design, all included studies used a cross-sectional design. Additional information related to the characteristics of the selected studies is reported in Table 1.

3.2. Participants

Among the 15 selected articles, 12 analyzed ERPs to evaluate emotional processing by comparing FMS patients and controls (Cardoso et al., 2021; Fallon et al., 2015; Fernandes-Magalhaes et al., 2022; Fischer-Jbali et al., 2021, 2022a, 2022b; Goldway et al., 2022; Gonzalez-Roldan et al., 2013; Mercado et al., 2013; Montoya et al., 2005a; Peláez et al., 2019; Pidal-Miranda et al., 2019). Of the remaining three studies, one compared FMS patients with MSK (Montoya et al., 2005b) and another study compared FMS patients, controls and patients with MSK (Sitges et al., 2007). Finally, Sitges et al. (2018) compared FMS patients with high and low depression groups and controls.

The largest FMS sample size among the studies reviewed was 39 (Goldway et al., 2022) and the smallest was 12 (Montoya et al., 2005a). Similarly, the largest control group comprised 37 participants (Fischer-Jbali et al., 2021) and the smallest comprised 12 participants (Montoya et al., 2005a). The control sample was notably smaller compared to that of FMS patients in the study of Goldway et al. (2022). The sample size (mean + SD) of each study is displayed in Table 1.

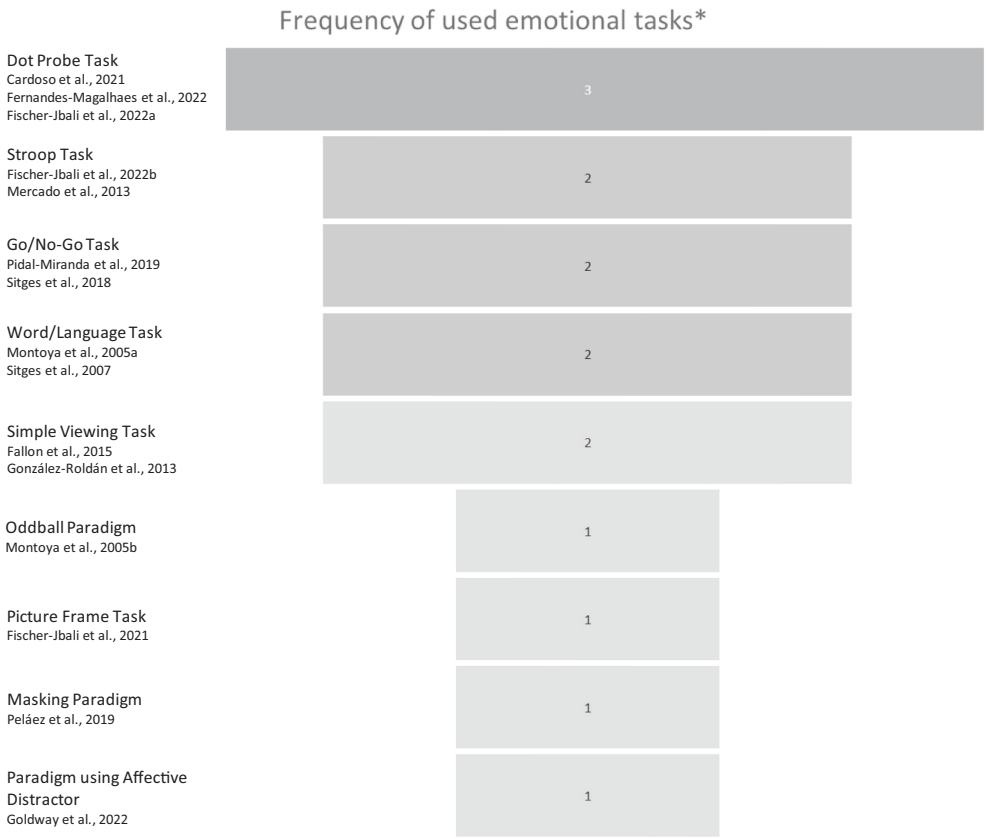
Considering all the reviewed studies together, the total sample (N = 668) was divided into two main groups, FMS patients (N = 360) and controls (N = 308, along with a small group of patients with MSK (N = 34) that is not further considered. The mean age of the entire sample was 48.3 years, and the FMS patients were slightly older (M = 49.21) than the controls (M = 47.17). Participants ranged between 18 and 70 years old. Regarding sex, there were more female than male participants (total sample = 98.92 % women). Notably, only two studies included men (Goldway et al., 2022; Sitges et al., 2007), neither of which had a sample composed entirely of men.

3.3. Qualitative and quantitative analysis of the selected studies

3.3.1. ERPs to evaluate emotional processing in FMS

3.3.1.1. Emotional tasks used. The most frequently used emotional task was the dot probe task (Cardoso et al., 2021; Fischer-Jbali et al., 2022a; Fernandes-Magalhaes et al., 2022), followed by the emotional Stroop task (Fischer-Jbali et al., 2022a, 2022b; Mercado et al., 2013), the Go/No-Go task (Sitges et al., 2018; Pidal-Miranda et al., 2019) and the Word/language decision task (Sitges et al., 2007; Montoya et al., 2005a). Other tasks used included the oddball paradigm (Montoya et al., 2005b), the simple viewing task (Fallon et al., 2015), the emotional face task (Gonzalez-Roldan et al., 2013), the picture frame task (Fischer-Jbali et al., 2021), the masking paradigm (Peláez et al., 2019) and a paradigm assessing attention allocation in response to affective distractors (Goldway et al., 2022). Each of these tasks was only in only one study.

3.3.1.2. ERPs analyzed. In total, 14 different ERPs, which varied in time range from 20 ms up to 3700 ms after stimulus onset, were identified to evaluate emotional processing in FMS. Among the most frequently analyzed amplitudes were P200 (Fallon et al., 2015; Fernandes-



Graphic 1. Frequency of used emotional tasks. *(*Note. Emotional tasks refer to classical tasks of cognitive psychology manipulated by incorporated additional emotional elements).*

Magalhaes et al., 2022; Fischer-Jbali et al., 2021, 2022a; Montoya et al., 2005a, 2005b; Peláez et al., 2019; Sitges et al., 2007) and LPP/LPC (Cardoso et al., 2021; Fallon et al., 2015; Fischer-Jbali et al., 2021, 2022a, 2022b; Montoya et al., 2005a; Peláez et al., 2019; Sitges et al., 2007), which were analyzed by eight studies (53.3 % of all studies included); P300 (Cardoso et al., 2021; Fallon et al., 2015; Fischer-Jbali et al., 2022b; Montoya et al., 2005a; Pidal-Miranda et al., 2019; Sitges et al., 2018), which was analyzed by six studies (40 %); P100 (Fallon et al., 2015; Fischer-Jbali et al., 2021; Fischer-Jbali et al., 2022b; Fischer-Jbali et al., 2022a; Peláez et al., 2019) and N200 (Fallon et al., 2015; Fernandes-Magalhaes et al., 2022; Peláez et al., 2019; Pidal-Miranda et al., 2019; Sitges et al., 2018), which were analyzed by five (33.3 %) studies; and N170, which was analyzed by four studies (26.6 %) (Fernandes-Magalhaes et al., 2022; Fischer-Jbali et al., 2021; Fischer-Jbali et al., 2022a; Gonzalez-Roldan et al., 2013). The other ERPs (P50, N80, P100/N100, N100, EPN, N250, N4, P450, ssVEP) were analyzed by one or two studies *(see* Table 1*: EEG and ERP Components, for further details)*. Additionally, P50 and N80 were analyzed in a study comparing FMS and MSK patients, instead of controls (Montoya et al., 2005b). Therefore, these ERPs are not further reported, except the results related to the ERPs involved in the processing of different emotional stimuli within the FMS group.

ERPs were identified by seven studies using peak maximum detection (Fischer-Jbali et al., 2021, 2022a, 2022b; Gonzalez-Roldan et al., 2013; Montoya et al., 2005a; Sitges et al., 2007, 2018). Among these, four studies employed global maxima detection (Fischer-Jbali et al., 2021, 2022a, 2022b; Sitges et al., 2018), peak maximum baseline-to-peak (Sitges et al., 2007), peak maximum within a specific time-window (Gonzalez-Roldan et al., 2013), and peak maximum without a closer definition (Montoya et al., 2005a) were exclusively each employed in one study. Additionally, eight studies employed a mean amplitude measure for detecting ERPs (Cardoso et al., 2021; Goldway et al., 2022; Gonzalez-Roldan et al., 2013; Montoya et al., 2005a, 2005b; Peláez et al., 2019; Pidal-Miranda et al., 2019; Sitges et al., 2007). Among these studies, two used a mean amplitude baseline-to-peak measure (Goldway et al., 2022; Montoya et al., 2005b), one study employed a mean amplitude within a specific time-window (Montoya et al., 2005a), and five studies did not provide a more detailed definition of the mean amplitude computation (Cardoso et al., 2021; Gonzalez-Roldan et al., 2013; Peláez et al., 2019; Pidal-Miranda et al., 2019; Sitges et al., 2007). Finally, three studies used PCS methods (tPCS and sPCS) for ERP detection (Fernandes-Magalhaes et al., 2022; Mercado et al., 2013; Peláez et al., 2019).

Concerning additional EEG measures, eleven studies also reported scalp topographies (Cardoso et al., 2021; Fallon et al., 2015; Fernandes-Magalhaes et al., 2022; Fischer-Jbali et al., 2021, 2022a, 2022b; Gonzalez-Roldan et al., 2013; Mercado et al., 2013; Montoya et al., 2005b; Pidal-Miranda et al., 2019; Sitges et al., 2018). Three studies conducted additional analyses related to peak latencies (Fernandes-Magalhaes et al., 2022; Mercado et al., 2013; Sitges et al., 2018), other three studies (Fischer-Jbali et al., 2022b; Gonzalez-Roldan et al., 2013; Sitges et al., 2018) performed additional power analyses, two studies conducted source analysis (sLoreta) (Mercado et al., 2013; Peláez et al., 2019), and one study reported results related to EEG connectivity (Goldway et al., 2022).

3.3.1.3. Differences in ERP amplitudes between FMS patients and controls. In the course of the qualitative analysis (systematic review), eight ERP components (P100, P200, N200, N250, P300, LPP/LPC, ssVEP) were recognized for their featured potential to identify significant differences between FMS patients and controls by authors. However, the subsequent quantitative analysis (meta-analysis) demonstrated that only two ERP components (N250 and LPP/LPC) exhibited significant differentiation between FMS patients and controls. Notwithstanding the aforementioned and considering the nature of the present study, which involves a systematic review and meta-analysis, and its overarching aim, both sets of findings: the qualitative and quantitative are detailed. The data for the calculated effect sizes is accessible at https://osf.io/g2pxf/.

In qualitative analysis, the P100 component showed greater amplitudes for FMS patients compared to controls in one study (Peláez et al., 2019), while another study revealed the opposite (Fallon et al., 2015). The remaining four studies did not show differences between FMS patients and controls (Fischer-Jbali et al., 2021, 2022a, 2022b; Peláez et al., 2019). In quantitative analysis, a total of 14 results were recovered for P100 in four studies (level 3). The results showed non-significant effects in the FMS vs. control comparison for P100 (r = -.170, 95 % CI: -.45, 0.11, p = .226; *see Supplementary Fig. 1*). There was no significant heterogeneity (total I^2 = 0 %, Q = 1.40, p = .999), and Egger's test showed that there was no publication bias (b = -1.63, p = .369; *see Supplementary Fig. 2*).

Within qualitative analysis, one study showed greater P200 amplitudes (Peláez et al., 2019), while two studies reported smaller P200 amplitudes (Fischer-Jbali et al., 2021; Montoya et al., 2005a), for FMS patients compared to controls. No effects of group were found in five studies (Fallon et al., 2015; Fernandes-Magalhaes et al., 2022; Fischer-Jbali et al., 2022a; Sitges et al., 2007). The quantitative analysis of this ERP returned a total of 15 results obtained from five studies (level 3). The results were not significant (r= -.100, 95 % CI: -.42, 0.23], p = .547; *see Supplementary Fig. 1*) and showed no heterogeneity (total I2 = 0 %, Q = 2.76, p = .999). Moreover, Egger's test showed that there was no publication bias (b = -1.29, p = .498; *see Supplementary Fig. 2*).

Regarding qualitative outcomes, for the N200 component, two studies reported smaller amplitudes (Fernandes-Magalhaes et al., 2022; Fallon et al., 2015), whereas three studies showed no significant differences between FMS patients and controls (Peláez et al., 2019; Pidal-Miranda et al., 2019; Sitges et al., 2018). Sitges et al. (2018) divided FMS participants into high and low depression groups, and no group differences were found between controls and these FMS subgroups. In the quantitative analysis of this ERP, a total of 13 results were extracted from five studies (level 3). Non-significant differences were found in the FMS vs. controls comparison (r = 0.161, 95 % CI: -.29, 0.61], p = .452; *see Supplementary Fig. 1*). The results showed no heterogeneity (total I^2 = 19.71 %, Q = 7.121, p = .849), and Egger's test showed that there was no publication bias (b = -1.34, p = .434; *see Supplementary Fig. 2*).

Regarding qualitative analysis of N250, one study showed greater amplitudes for FMS patients compared to controls (Fischer-Jbali et al., 2021), while another study was unable to detect differences between FMS patients and controls related to this ERP component (Fischer-Jbali et al., 2022a). In the quantitative analysis, a total of eight results for N250 appeared in the two studies (level 3) showing significant effects (r = -.391, 95 % CI: -.76, -.02, p = .037; *see* Fig. 2). FMS had greater N250 amplitudes than controls. The results showed no heterogeneity (total I^2 = 0 %, Q = 2.668, p = .976), and Egger's test revealed no publication bias (b = -8.11, p = .297; *see Supplementary Fig. 2*). Country and stimuli were the same in both studies. Meta-regression showed no effect of age, emotion, task or year of publication (all ps > .050).

In the qualitative analysis for P300, Fischer-Jbali et al. (2022b) and Fallon et al. (2015) found greater amplitudes for FMS patients compared to controls, while one study showed smaller amplitudes in FMS patients for this ERP component (Cardoso et al., 2021). Three other studies did not find significant differences between FMS patients and controls (Montoya et al., 2005a; Pidal-Miranda et al., 2019; Sitges et al., 2018). As with N200, Sitges et al. (2018) did not find group differences between controls and any of the FMS subgroups (high and low depression). The quantitative analysis of this ERP returned a total of 13 results distributed among five studies (level 3). The results were not significant in the FMS vs. controls comparison for P300 (r = 0.092, 95 % CI: -.38, 0.57, p = .680; *see Supplementary Fig. 1*). The results showed no heterogeneity (total I^2 = 24.46 %, Q = 8.16, p = .773), and Egger's test revealed no publication bias (b = 1.48, p = .123; *see Supplementary Fig. 2*).

Regarding qualitative outcomes for LPP/LPC, three studies found

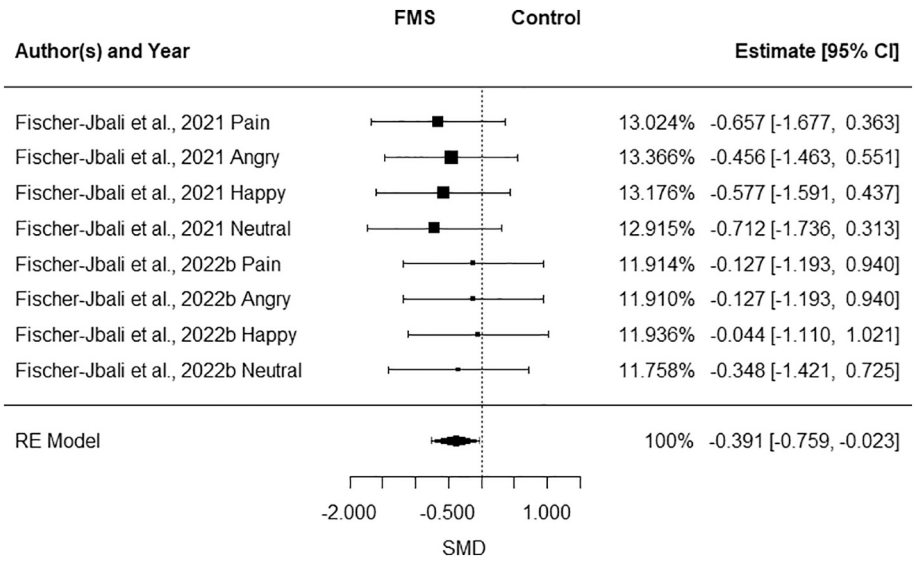


Fig. 2. Forest plot for the comparison of N250 amplitude between fibromyalgia syndrome (FMS) patients and controls.

smaller amplitudes (Fischer-Jbali et al., 2021; Fischer-Jbali et al., 2022a; Sitges et al., 2007), whereas two studies reported greater LPP/LPC amplitudes (Cardoso et al., 2021; Fallon et al., 2015), for FMS patients compared to controls. Another three studies did not find significant differences between FMS and controls (Fischer-Jbali et al., 2022b; Montoya et al., 2005a; Peláez et al., 2019). In the quantitative analysis of LPP, a total of 19 level 2 effect sizes were obtained from seven studies (level 3). FMS patients had significantly smaller amplitudes than controls for this ERP (r = -.261, 95 % CI: -.52, -.01, p = .049; *see* Fig. 3). The results were homogeneous (total I^2 = 0 %, Q = 7.46, p = .999), and Egger's test revealed no publication bias (b = -1.23, p = .178; *see Supplementary Fig. 2*). Meta-regression showed no effect of age, country, emotion, task or year of publication (all ps > 0.050). Additionally, stimuli showed a trend towards a moderating effect (p = .054), where *emotional faces* had a negative association with the pooled effect size (b = -049, p = 008), and *emotional pictures* had a positive association with the pooled effect size (b = 1.178, p = 019); i.e., in FMS, *emotional pictures* were related to greater LPP/LPC amplitudes, whereas *emotional faces* were related to smaller LPP/LPC amplitudes. However, it is relevant to highlight that this trend did not reach statistical significance.

Based on qualitative analysis, Goldway et al. (2022) observed reduced responsivity (ssVEP) to task stimuli for FMS patients compared to controls. However, that was the only study to analyze this ERP. Given the relative lack of studies exploring this component, no further exploration (i.e., quantitative analysis) was conducted.

Qualitative analysis revealed no group effect for the remaining five ERP components (P100/N100, N100, N170, EPN, N4, P450) in any of the studies. Among these ERPs, the only one analyzed by several studies was N170 (Fernandes-Magalhaes et al., 2022; Fischer-Jbali et al., 2021, 2022a; Gonzalez-Roldan et al., 2013). Results from the meta-analysis (eight results recovered from two studies [level 3]) were congruent with the reported studies; i.e., were not significant (r= -.226, 95 % CI: -.59, 0.14, p = .226; *see Supplementary Fig. 1*) and showed no heterogeneity (total I^2 = 0 %, Q = 2.27, p = .943). Egger's test revealed no

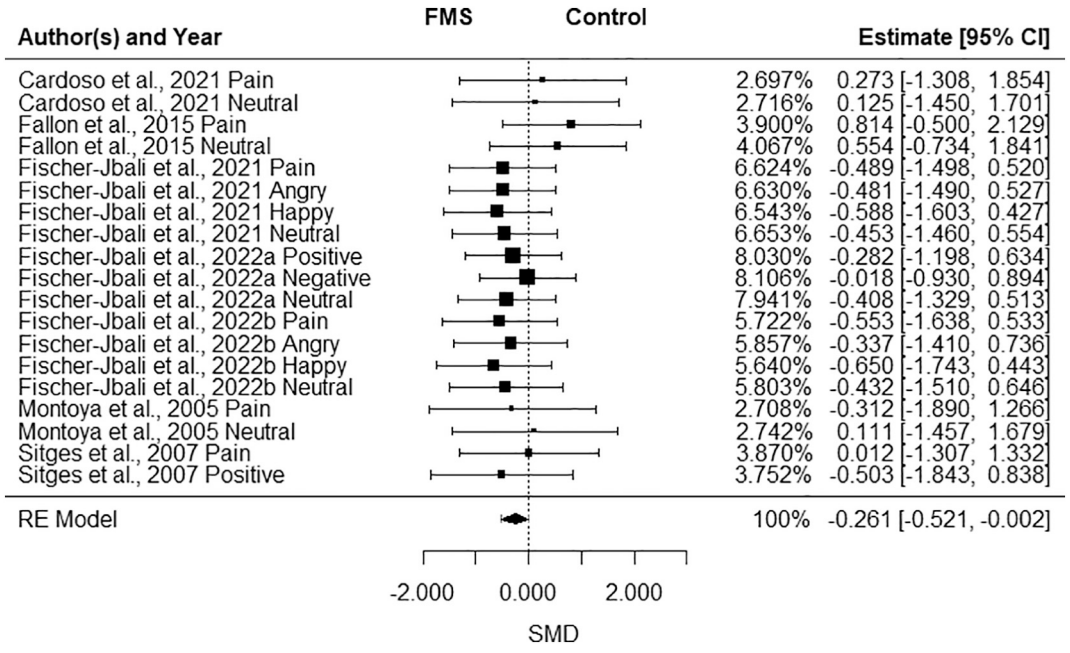


Fig. 3. Forest plot for the comparison of LPP/LPC amplitude between fibromyalgia syndrome (FMS) patients and controls.

publication bias (b = 1.42, $p = .775$; *see Supplementary Fig. 2*).

3.3.1.4. Scalp topographic distributions of the emotional processing abnormalities observed in FMS. Different scalp topographic distributions of ERP's were seen related to the differences in emotional ERP processing between FMS patients and controls, and therefore to the emotional processing abnormalities observed in FMS (Table 2). Abnormalities in the processing of emotional words were mostly reported in central (P200), centro-parietal (P300, LPP) and parieto-occipital (P300) regions of scalp topographic (Cardoso et al., 2021; Fischer-Jbali et al., 2022b; Montoya et al., 2005a). Abnormalities in the processing of emotional faces were mainly distributed over fronto-central (N200), parieto-temporal (P200, N250, LPC) and parieto-occipital (P200, LPC) scalp topographies (Fernandes-Magalhaes et al., 2022; Fischer-Jbali et al., 2021, 2022a). In addition, abnormalities related to the processing of emotional pictures were reported in fronto-central (P200), centro-parietal (P100/N100, P200, LPC), parietal (P300), parieto-occipital (P100) and occipital (N200) scalp topographic regions (Fallon et al., 2015; Peláez et al., 2019). Abnormalities in distractor valence were seen in occipital regions of scalp topographic (Goldway et al., 2022).

3.4. Quality of selected studies

The ROB evaluation revealed that 12 studies were of low quality (Cardoso et al., 2021; Fernandes-Magalhaes et al., 2022; Fischer-Jbali et al., 2021; Fischer-Jbali et al., 2022a; Fischer-Jbali et al., 2022b; Goldway et al., 2022; Gonzalez-Roldan et al., 2013; Mercado et al., 2013; Montoya et al., 2005b; Peláez et al., 2019; Sitges et al., 2007; Sitges et al., 2018), and 3 were of moderate quality (Fallon et al., 2015; Montoya et al., 2005a; Pidal-Miranda et al., 2019). More detailed information about the ROB assessments can be found in Table 3.

The analyzed papers had several limitations, including: 1) a lack of information about the possible influence of medication (Fernandes-Magalhaes et al., 2022; Fischer-Jbali et al., 2021; Fischer-Jbali et al., 2022a; Fischer-Jbali et al., 2022b; Mercado et al., 2013; Peláez et al., 2019; Pidal-Miranda et al., 2019) and psychiatric comorbidities (Fischer-Jbali et al., 2021) on the assessed variables, 2) the small sample size (Cardoso et al., 2021; Fischer-Jbali et al., 2022a; Montoya et al., 2005a; Sitges et al., 2007), 3) the inability to analyze patient subgroups because of the small sample size (Fischer-Jbali et al., 2021; Fischer-Jbali et al., 2022a; Fischer-Jbali et al., 2022b), 4) the small sample sizes of the psychiatric comorbidity subgroups (Fischer-Jbali et al., 2022b), 5) the presence of samples entirely composed of female patients (Fernandes-Magalhaes et al., 2022; Peláez et al., 2019), 6) the non-control of the possible small effects of depression (Fischer-Jbali et al., 2022a), anxiety (Fischer-Jbali et al., 2022b), or both disorders on ERP amplitudes (Fischer-Jbali et al., 2022b) and the menstrual cycle phase or menopausal status, which can influence pain in FMS (Fallon et al., 2015), 7) difficulties in discerning the possible influence of negative mood in FMS on the results, given the prevalence and variability of affective symptoms (i.e., anxiety and depression) in this population (Gonzalez-Roldan et al., 2013), 8) the absence of a healthy control group to compare the effects of mood induction on brain activity during the oddball paradigm (Montoya et al., 2005b), a measure related to illness or pain beliefs in chronic pain patients (Sitges et al., 2007), who suffer from a chronic pain disease different from FMS (Cardoso et al., 2021), and the lack of analysis of the influence of social factors, such as level of education (Fallon et al., 2015), 9) the non-assessment of symptom severity in the healthy control group (Goldway et al., 2022) and participants' eyesight (Fischer-Jbali et al., 2021), 10) the limited suitability of the tasks used (Fernandes-Magalhaes et al., 2022; Sitges et al., 2018) and 11) the potential lack of suitability of the Beck Depression Inventory (overlapping symptoms of chronic pain and depression), especially in relation to the defined cut-off scores (Sitges et al., 2018).

Regarding the different tasks, the studies also reported some limitations. For instance, in the Stroop task, the three stimulus categories were not matched in terms of affective arousal (Fischer-Jbali et al., 2022b), while in the dot probe task there were limitations in the timing of the task, specifically the long delay (300 ms) between the face offset and probe onset (Fischer-Jbali et al., 2022a), and the exposure time to the dot-probe was too short to induce the effects of interest (Cardoso et al., 2021). Moreover, the interruption in pain medication prior to the testing session might have influenced emotional and attentional processing (i.e., via a transient increase in pain severity) (Fischer-Jbali et al., 2022a), and the use of verbal stimuli may have induced motor artifacts (Cardoso et al., 2021). In the picture frame task, a control condition of frames without pictures was not included (Fischer-Jbali et al., 2021; faces extracted from the Montreal Pain and Affective Face Clips), and familiarity or priming effects may have influenced the ratings attributed to images because affective valence and arousal ratings for pictures were made after the initial EEG presentations (Fallon et al., 2015; pain images). In the Go/No-Go tasks, equiprobable Go and No-Go trials might have not been sufficiently sensitive to capture differences between groups (Pidal-Miranda et al., 2019), and in the language decision task the design did not allow inference regarding how the two experimental tasks (pain pressure threshold (PPT) assessment and language decision task) influenced each other (Montoya et al., 2005a). Finally, in the masked emotional picture task, the negative picture condition was based on stimuli belonging to various negative categories of emotion, such as sadness, fear, and disgust; without taking into account that the brain's responses may be differentially influenced by these categories (Peláez et al., 2019).

Other limitations not mentioned by the authors were identified, such as a small sample size (Cardoso et al., 2021; Pidal-Miranda et al., 2019), imprecise specification of diagnostic criteria (Cardoso et al., 2021; Fernandes-Magalhaes et al., 2022), no indication of the sample sex ratio (Sitges et al., 2018), failure to report analyses by sex (Goldway et al., 2022), failure to specify the method used to determine the sample size (Fischer-Jbali et al., 2021; Montoya et al., 2005a, 2005b), failure to report any measure of the effect size (Gonzalez-Roldan et al., 2013; Mercado et al., 2013), non-reportage of the non-significant statistical data (Goldway et al., 2022; Sitges et al., 2007), partial reporting of the data related to non-significant results (Fernandes-Magalhaes et al., 2022; Fischer-Jbali et al., 2022a; Fischer-Jbali et al., 2022b; Fischer-Jbali et al., 2021; Cardoso et al., 2021; Peláez et al., 2019; Pidal-Miranda et al., 2019; Sitges et al., 2018; Fallon et al., 2015, Gonzalez-Roldan et al., 2013; Mercado et al., 2013; Montoya et al., 2005a; Montoya et al., 2005b), and no explicit limitations paragraph (Fernandes-Magalhaes et al., 2022; Sitges et al., 2018).

4. Discussion

The present review and meta-analysis **mainly aimed to** analyze studies on emotional processing alterations (linked to emotional ERPs) in FMS patients over 18 years of age, and integrated them into a meta-analysis. Based on the **systematically reviewed literature**, the most frequently analyzed ERP amplitudes were P200, LPP/LPC, P300, N200, P100, and N170. The tasks used were diverse. The frequency of use of the tasks was in the following (descending) order: dot probe task, emotional Stroop, Go/No-Go and the Word/language decision task. Out of the 15 analyzed articles, 9 were able to find differences in emotional processing between FMS and controls, and hence disturbances in emotional processing in FMS (Cardoso et al., 2021; Fallon et al., 2015; Fernandes-Magalhaes et al., 2022; Fischer-Jbali et al., 2021, 2022a, 2022b; Goldway et al., 2022; Montoya et al., 2005a; Peláez et al., 2019). These emotional disturbances were distributed over the whole range of ERP latencies (20—3700 ms). Abnormalities in emotional processing observed in FMS patients compared to controls were mainly reported in central, parietal, temporal and occipital areas. From the most frequently analyzed ERP amplitudes in the reviewed literature, the **quantitative analysis** identified only two ERP components (N250, LPP/LPC) capable

Table 2
Scalp topographic distributions of ERP's related to differences in emotional ERP processing in Fibromyalgia patients compared to controls.

ERPs	Scalp topographic distributions	Latency	Electrodes	Variance effect	Stimuli	Study
P100	Parieto-occipital	70-150 ms	P7, P3, O1, O2, P4, P8	–	Faces	Fischer-Jbali et al., 2021
	Parieto-occipital	70-130ms	P7, O1, Oz, O2, P8	–	Faces	Fischer-Jbali et al., 2022a
	Parieto-occipital	70-130ms	PO3, PO4, O1, O2, P3, P4, P7, P8	–	Words	Fischer-Jbali et al., 2022b
	Parieto-occipital	80-120ms	O1, Oz, O2, POz, PO3, PO4	Main effect group and interaction (FMS)	Pictures	Peláez et al., 2019
	Centro-parietal	135-155ms	CP6, P4, P6	Main effect group	Pictures	Fallon et al., 2015
N100	Frontal, central	50-150 ms	Fz, Cz	Interaction (both)	Faces	Gonzalez-Roldan et al., 2013
	–	100-150 ms	–	–	Words	Montoya et al., 2005a
P100/ N100		100 ms	–	–	Faces	Fernandes-Magalhaes et al., 2022
N170	–	150 ms		–	Faces	Fernandes-Magalhaes et al., 2022
	Parieto-occipital	130-210ms	P7, P3, O1, Oz, O2, P4, P8	–	Faces	Fischer-Jbali et al., 2021
	Parieto-occipital /left/right)	120-200ms	L: T7, P7, O1; R: T8, P8, O2	Interaction (FMS)	Faces	Fischer-Jbali et al., 2022a
	Temporo-parietal	150-200ms	T7, T8, P7, P8	–	Faces	Gonzalez-Roldan et al., 2013
EPN	Parieto-occipital	130-250ms	PO3, PO4, O1, O2, P7, P8	–	Words	Fischer-Jbali et al., 2022b
	Frontal	200-300 ms	F3, Fz, F4; (FC3, FCz, FC4, C3, Cz, C4; P3, Pz, P4; O1, Oz, O2)	Interaction (controls)	Faces	Gonzalez-Roldan et al., 2013
P200	——	210-230ms	——	——	Pictures	Fallon et al., 2015
	Frontal, fronto-central	196ms	——	——	Faces	Fernandes-Magalhaes et al., 2022
	Centro-parietal	200-360ms	Pz, CP1, CP2	Interaction (FMS)	Faces	
	Parieto-occipital, parieto-temporal (left/right)	200-380 ms 150-300 ms	P3, Pz, P4, O1, Oz, O2; P7, CP5, T7; P8, CP6, T8	Main effect group Main effect group	Faces Words	Fischer-Jbali et al., 2022a
	Central	200-350 ms	Cz, C3, (C4)	Interaction (controls)	Words	
	Frontal, central, centro-parietal	P200a: 190-270ms, P200b: 280-360ms	F4, C4, CP4, F3, C3, CP3	P200a: Main effect group	Pictures	Fischer-Jbali et al., 2021
	Centro-parietal, fronto-central		P200a: C1, Cz, C2, CP1, CPz, CP2, CP4 P200b: FC1, FCz, FC2, C1, Cz, C2	P200b: Main effect group		Montoya et al., 2005a Sitges et al., 2007 Peláez et al., 2019
N200	**Fronto-central**	274 ms	——	Main effect group	Faces	Fernandes-Magalhaes et al., 2022
	Frontal	250-340 ms	Fz	Interaction (controls)	Faces	
	Occipital	280-310 ms	POz, Oz, O1, O2	Main effect group	Pictures	
	Parieto-occipital	130-170 ms	——	——	Pictures	Pidal-Miranda et al., 2019
	Fronto-central	200-350 ms	Fz, FCz, FC1, FC2, Cz	——	Faces	Fallon et al., 2015 Peláez et al., 2019 Sitges et al., 2018
N250	**Parieto-temporal (left/ right**), occipital	330-440ms	O1, Oz, O2; T7, CP5, P7, P3; T8, CP5, P8, P4	Main effect group and interaction (FMS)	Faces	Fischer-Jbali et al., 2021
	Parietal (left/right)	300-460ms	L: P3, P7, CP5; R: P4, P8, CP6	–	Faces	Fischer-Jbali et al., 2022a
P300	Frontal, **Posterior**	200-400 ms	(FP1, FP2, F3, F4, Fz, AFz, FC5, FC6, F7, F8); Pz, P3, P4, PO3, PO4	Posterior Main effect group	Words	Fischer-Jbali et al., 2022b
	Centro-parietal	300-400 ms			Words	
	Central	350-600 ms	54, 55 (CPz), 61, 62 (Pz), 78, 79	Main effect group	Pictures	Cardoso et al., 2021
	Posterior parietal (right)	370-420 ms	Cz	——	Pictures	Pidal-Miranda et al., 2019
	Central, parietal	450-650 ms	CPz, CP2, CP4 Cz, C3, C4; Pz, P3, P4	Main effect group ——	Words	Fallon et al., 2015 Montoya et al., 2005a
	Fronto-central	350-500ms	Fz, FCz, FC1, FC2, Cz	–	Faces	Sitges et al., 2018
N4	Central	430-730ms	Cz, C3, C4, CP1, CP2, FC1, FC2	–	Words	Fischer-Jbali et al., 2022b
	Central, parietal	250-400 ms	(Cz), C3, C4; (Pz), P3, P4	–	Words	Montoya et al., 2005a
P450	frontal	488 ms	–	Interaction (only FMS)	Words	Mercado et al., 2013
LPC	Frontal, posterior	700-1300ms	FP1, FP2, AFz, F7, F3, F4, F8, Fz (Pz, P3, P4, PO3, PO4)	Frontal interaction (FMS)	Words	Fischer-Jbali et al., 2022b
	Parieto-temporal	500-1000ms	P7, T7, P8, T8	Main effect group	Faces	Fischer-Jbali et al., 2022a
	Parieto-occipital	470-990ms	P7, P3, O1, Oz, O2, P4, P8, Pz, CP1, CP2	Main effect group	Faces	Fischer-Jbali et al., 2021

(*continued on next page*)

Table 2 (*continued*)

ERPs	Scalp topographic distributions	Latency	Electrodes	Variance effect	Stimuli	Study
	Centro-parietal	LPPe: 400-600 ms; LPPl: 600-800ms	54, 55 (CPz), 61, 62 (Pz), 78, 79	LPPe:—— LPPl: Main effect group	Words	Cardoso et al., 2021
	Posterior parietal, **centro-parietal**	500-650 ms	Cz, CPz, C2, CP2	Main effect group	Pictures	Fallon et al., 2015
	Central, centro-parietal, parietal	500-800ms	C4, CP4, P4, C3, CP3, P3	Interaction (controls)	Words	Sitges et al., 2007
	Frontal, central	500-800ms	Fz, F3, (F4); Cz, C3, (C4)	Interaction (controls)	Words	Montoya et al., 2005a
	Central	500-920ms	–	–	Pictures	Peláez et al., 2019
ssVEP	**Occipital**	3600-3700ms	O1, O2, Oz	Main effect group and interaction	Distractor valence	Goldway et al., 2022

Table 3
Risk of bias assessment of relevant eligible studies.

First author (year)	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	General Assessment (Low, Medium, High)
Fernandes-Magalhaes et al., 2022	H	H	H	H	L	M	Yes	Low
Fischer-Jbali et al., 2022a	H	H	H	H	L	M	Yes	Low
Fischer-Jbali et al., 2022b	H	H	H	H	L	M	Yes	Low
Goldway et al., 2022	H	H	H	H	L	H	Yes	Low
Fischer-Jbali et al., 2021	H	H	H	H	L	M	Yes	Low
Cardoso et al., 2021	H	H	H	H	L	M	Yes	Low
Peláez et al., 2019	H	H	H	H	L	M	Yes	Low
Pidal-Miranda et al., 2019	H	H	L	M	L	M	Yes	Moderate
Sitges et al., 2018	H	H	H	H	L	M	Yes	Low
Fallon et al., 2015	H	H	M	L	L	M	Yes	Moderate
Gonzalez-Roldan et al., 2013	H	H	H	H	L	M	Yes	Low
Mercado et al., 2013	H	H	H	H	L	M	Yes	Low
Sitges et al., 2007	H	H	H	H	L	H	Yes	Low
Montoya et al., 2005a	H	H	M	L	L	M	Yes	Moderate
Montoya et al., 2005b	H	H	H	H	L	M	Yes	Low

Note: L: Low, M: Medium, H: High.

of significantly distinguishing between FMS and controls.

In the ensuing sections of the discussion, both the qualitative (non-significant in our analyses but featured prominently in the reviewed manuscripts) and quantitative (derived to our statistical analyses) outcomes of this systematic review and meta-analysis are addressed collectively to provide an integrated overview of all pertinent aspects related to the PICO question and objectives of the present manuscript.

4.1. Findings on short-latency event-related potentials

Pertaining to the qualitative results, the literature reviewed showed alterations in **short-latency ERPs** (P100, P100/N100) arose in FMS according to tasks using **emotional pictures**. Regarding the different tasks using emotional pictures and according to authors, only the emotional Go/No-Go task was unable to detect short-latency ERP differences between FMS patients and controls (Pidal-Miranda et al., 2019). Indeed, among all the emotional tasks used by the authors, the Go/No-Go task was the only one that did not exhibit differences between FMS and controls, in terms of general performance or the emotional stimuli and latency (Pidal-Miranda et al., 2019; Sitges et al., 2018). The simple viewing task (Fallon et al., 2015) and the masking paradigm (Peláez et al., 2019) detected differences in short-latency ERPs over centro-parietal and parieto-occipital sites between FMS patients and controls. In general, alterations in this latency signify dysfunction in early sensory/basic visual processing, visuospatial orienting or stimulus detection (Carretié et al., 2004; Schindler et al., 2019). Particularly, in the study of Peláez et al. (2019), a painful stimulus was preceded by masking emotional pictures. FMS patients showed greater P100 amplitudes than controls in response to a painful stimulus when it was preceded by pain-related pictures compared with the rest of the emotional conditions. This latter finding led the authors to infer that salient subliminal emotional information affects attention, leading to enhanced

processing of pain in FMS. Fallon et al. (2015) found an association between impairments in short-latency ERPs and the subsequent augmentation of later ERPs. They concluded that the early processing stages were affected in FMS patients, even though the spatiotemporal pattern of brain activation highlights augmentation mainly of mid- and long-latency ERPs for non-pain and pain stimuli.

In spite of these observations, upon combining and quantitative analyzing the outcomes on P100 and P100/N100 derived from the independently reported studies, no notable distinctions arose between individuals with FMS and their healthy counterparts. This finding raises doubts regarding the reliability and generalizability of alterations in short-latency ERPs and, consequently, in the basic early stages of emotional stimulus processing for FMS.

4.2. Findings on midlatency event-related potentials

Alterations of mid-latency ERPs (P200, N200, P300, N250) in FMS were also detected by authors of the reviewed studies, for each stimulus type (emotional pictures, faces, words) as well as for each task (excluding the Go/No-Go task) used. In greater detail, mid-latency ERPs alterations during the processing of **emotional pictures** were seen in centro-parietal and fronto-central P200 (Peláez et al., 2019), in occipital N200 (Fallon et al., 2015) and in parietal P300 (Fallon et al., 2015). Consequently, Peláez et al. (2019), using a masking paradigm, identified an increase in cognitive processes related to pain stimulation and emotional picture processing in FMS patients; similarly, Fallon et al. (2015) suggested augmented allocation of top-down resources for emotional picture processing in FMS patients during a simple viewing task. These suggestions and identifications were attained given the involve of N200 in cognitive control mechanisms such as regulation of attentional engagement and disengagement (Eldar and Bar-Haim, 2010; Fu et al., 2017) and P300 in the amount of cognitive effort, allocation of attentional resources, receptivity and conscious recognition of emotional stimuli, and organization of behavioral responses (Imbir et al., 2017; Wei et al., 2016).

During the processing **of emotional faces,** mid-latency ERP alterations were seen in parieto-occipital and parieto-temporal P200 (Fischer-Jbali et al., 2021), in fronto-central N200 (Fernandes-Magalhaes et al., 2022) and in parieto-temporal N250 (Fischer-Jbali et al., 2021). Fernandes-Magalhaes et al. (2022) found smaller N200 amplitudes in FMS patients during an emotional dot probe task. The authors suggested low-efficiency regulation of the allocation of attentional resources towards emotional stimuli in FMS. Fischer-Jbali et al. (2021) used an emotional picture frame task and observed a reduction of P200 amplitude and an increase of N250 amplitudes in FMS patients. The reduction in P200 indicated deficient short-term mobilization of attentional resources, while the increased N250 amplitudes seemed to reflect greater engagement in the decoding of complex facial features to overcome the attentional impairments (Fischer-Jbali et al., 2021). These suggestions were considered given the general involve of N250 in the decoding of complex facial features as well as the recognition of emotions and affect (Balconi and Pozzoli, 2008, 2009; Blier et al., 2011; Güntekin et al., 2019; Schindler et al., 2019), while P200 has been associated with early attentional processes involved in the fast and automatic detection of relevant stimuli (Sarlo and Munafò, 2010; Zhu et al., 2015).

Finally, mid-latency ERP alterations during the processing **of emotional words** were also evident in central P200 (Montoya et al., 2005a) and in parieto-occipital (Fischer-Jbali et al., 2022b) and centro-parietal (Cardoso et al., 2021) P300, according to reviewed studies. In the study of Montoya et al. (2005a), reduced P200 during an emotional language decision task cooccurred with reduced engagement and attentional resource allocation to emotional stimuli in FMS. The authors suggested that FMS patients might be adopting a cognitive strategy to avoid more intense processing of the presented affective stimuli (Montoya et al., 2005a). Interestingly, while Fischer-Jbali et al. (2022b), using an emotional Stroop task, observed a greater P300 in FMS, Cardoso et al. (2021) using an emotional dot probe task, observed the opposite, i.e., reduced P300. Fischer-Jbali et al. (2022b) explained the result as greater cognitive effort and attentional mobilization in FMS patients to overcome the reduced attentional resources available owing to CNPS. Cardoso et al. (2021) reported reduced allocation of attentional resources to the task in FMS.

When data from the multiple studies was pooled in the meta-analysis and quantitative analyzed, only significant differences were obtained for N250 between individuals with FMS and healthy controls. Higher N250 amplitudes were determined in FMS compared with controls. Neither P200, nor N200 and P300 were significant. P200, N200 and P300 ERPs have been associated with attentional mobilization while N250 has been related to the decoding of complex facial features as well as the recognition of emotions and affect (Eldar and Bar-Haim, 2010; Fu et al., 2017; Imbir et al., 2017; Wei et al., 2016). Both attention to emotional stimuli, and decoding and recognition are complex cognitive processes (Phillips et al., 2008; Styles, 2006). However, this result suggests that attentional resources towards emotional stimuli are not altered in FMS but the ability to interpret, understand and assigning meaning to the signals expressed by others. This ability is integral to social and emotional intelligence, enabling individuals to comprehend the feelings and intentions of others; a crucial aspect of social interaction (Phillips et al., 2008). This finding would be congruent with the extensive reports of FMS patients of loneliness and negative daily social relations (Wolf and Davis, 2014).

4.3. Findings on long-latency event-related potentials

Alterations of long-latency ERPs (LPP/LPC, ssVEP) were observed for each stimulus type (emotional pictures, faces, words, distractor valence), but only in three tasks (dot probe task, simple viewing task, distractor valence) by authors of the reviewed studies. LPP/LPC is a component involved in complex cognitive processes, as well as in higher affective processes such as intensity evaluation, differentiation, engagement, and sensitivity to emotional valence (Espuny et al., 2018; Gootjes et al., 2011; Imbir et al., 2017, 2021). ssVEP is used for evaluation of the level of distraction induced by the emotional background pictures (Goldway et al., 2022), where reduced amplitudes indicate greater distraction. The simple **emotional picture** viewing task was able to detect alterations in centro-parietal long-latency ERPs (LPC) in FMS patients (Fallon et al., 2015). According to the conclusion provided by Fallon et al. (2015), this late cognitive evaluation of pain cues seems to be especially affected in FMS patients and the related brain area seems to play a role in integrating perception, action and cognition, which points to its particular relevance to FMS mechanisms. Alterations in long-latency ERPs during the processing of **emotional faces** were seen in parieto-temporal (Fischer-Jbali et al., 2022a) and parieto-occipital (Fischer-Jbali et al., 2021) LPP/LPC in FMS. Both studies showed reduced LPP/LPC amplitudes and nonspecific deficits in sustained attention in FMS patients using a picture frame task (Fischer-Jbali et al., 2021) and an emotional dot probe task (Fischer-Jbali et al., 2022a).

Alterations in long-latency ERPs related to the processing of **emotional words** were seen in the centro-parietal LPP during an emotional dot probe task (Cardoso et al., 2021), and in the occipital ssVEP during a paradigm assessing attention in response to affective distractors (Goldway et al., 2022). Cardoso et al. (2021) observed greater LPP in FMS patients during the task and considered that the patients showed increased processing of the presented stimuli (pain-related and neutral words). This result, along with the reduced P300 (related to attentional resources; previously reported in the context of mid-latency ERP alterations) led the authors to propose two possible explanations: 1) greater emotional involvement of FMS in the task than controls, despite the reduced allocation of attentional resources; or 2) an increase of the affective influence on cognitive processing of the words used in FMS, negatively impacting the attentional resources allocated

for task performance. Alterations (smaller amplitudes for FMS) related to the distractor valence task (ssVEP) were also related to impaired affective discrimination and sustained attention (Goldway et al., 2022).

The lower LPP/LPC amplitude in FMS under emotional processing was supported by the quantitative analysis. This confirmation underscores alterations in the ability to differentiate between emotions, sustain engagement, resolve conflicts, or evaluate emotional intensity in individuals with FMS. Interestingly, quantitative analysis also showed that emotional pictures were related to greater amplitudes, whereas emotional faces were related to smaller amplitudes, in LPP among FMS patients. Congruent with the previously observed lower N250 and in line with prior research (Muñoz Ladrón et al., 2021; Weiß et al., 2013), this result would corroborate the lower sensitivity of FMS patients to emotion recognition, leading to misinterpretation of the emotional state of other people.

4.4. Conclusions, clinical implications and future directions

In conclusion, though the literature reviewed herein demonstrated the presence of aberrations in emotional ERP processing in FMS, based on the meta-analysis, notably, N250 (mid-latency) and LPP/LPC (long-latency) were the only ERPs showing significant differences between FMS and controls. No heterogeneity or publication bias were found. N250 amplitude was greater, while LPP/LPC amplitude was smaller, in FMS patients compared to controls. These quantitative findings indicate that despite the range of qualitative findings presented, from among all the emotional ERPs related to FMS, N250 and LPP/LPC are those which the most potential to determine emotional alterations in FMS. They are associated with complex cognitive processes such as decoding features crucial for affect recognition (N250) and differentiation between emotions, sustained engagement, conflict resolution, or evaluation of emotional intensity (LPC/LPP). These findings do not support the notion of a CN system more responsive to emotional stimuli in FMS (Pinto et al., 2023) but the presence of cognitive impairments in FMS that encompass CN emotional processing. It is important to emphasize that our quantitative analysis did not confirm an effect of emotions on ERPs, which would also call the notion of a CN system more responsive to emotional stimuli into question.

The training and enhancement of these cognitive abilities might offer a potential avenue for mitigating symptoms and emotional difficulties associated with FMS. In this context, a recent study employing attentional bias modification (ABM) training in individuals with FMS has indicated its efficacy in altering bias-associated event-related potentials (ERPs) (Fernandes-Magalhaes et al., 2023). Additionally, neuromodulation through transcranial direct current stimulation and/or EEG-neurofeedback techniques can be proved beneficial in this context. With respect the transcranial direct current stimulation, as far we know, no studies have been developed integrating it in the course of emotional ERPs in FMS. Within the second, research focused in EEG-neurofeedback of N250 and LPP/LPC could aid in formulating a distinctive EEG-neurofeedback protocol in FMS. The significance of a uniquely designed EEG-neurofeedback approach in FMS has been recently emphasized by Torres et al. (2023). By tailoring neurofeedback techniques to the specific neural patterns associated with N250 and LPP/LPC, a more EEG-neurofeedback personalized and targeted approach can be developed for FMS.

In a similar line with the last, it is important to note that in the reviewed studies task setup had an important impact on the various ERP outcomes (amplitude, latency and emotional effect). As pointed out in the Results section, the number of studies reporting group differences in one direction versus those reporting opposite outcomes, or even not reporting differences at all, were highly similar. The diversity of the tasks and emotional stimuli used, the evaluated potentials, as well as their locations and time-windows, might be potential confounding factors. This implies a necessity to create and optimize emotional tasks protocols for use by all researchers to confirm the extent of the emotional deficiencies in FMS. Systematization of the protocols and tasks is indispensable for future studies.

Furthermore, although numerous studies analyzed LPP/LPC, only two analyzed N250. Also, the quality assessment ultimately determined that 12 out of the 15 studies included in the meta-analysis were of low-quality according to the "general assessment." Consequently, findings derived from this systematic review and meta-analysis should be interpreted with caution. The present meta-analysis should be replicated in the future when more studies emerge with high quality and analyzing N250.

4.5. Limitations and strengths

Several limitations of this study should be acknowledged. First, the majority of the participants were females, such that there was an unequal gender ratio in the studies. However, this gender bias is explained by the well-known high prevalence of FMS in females ($\leq$60 % in the unbiases studies) and the tendency of health professionals to underestimate FMS in men and overestimate it in women (Srinivasan et al., 2019; Wolfe et al., 2018). Accordingly, studies frequently include more female than male patients. It is also noteworthy that 9 out of the 15 studies were conducted in Spain. Nevertheless, no additional manuscripts from countries different than those reported were published in the reviewed period Second, the present review and meta-analysis included studies using similar, but not identical, tasks, which prevented a more extensive meta-analysis. The only data in the majority of the studies suitable for meta-analysis were the emotional ERPs. A future meta-analysis could use stricter criteria, extracting data only from studies using the same designs and tasks. However, no such studies are currently available. As shown by this review, task setup plays an important role in ERP outcomes and behavior/performance. Also, despite our requests, the quantitative data necessary to conduct the meta-analysis were unfortunately not obtained from all authors. Third, the author responsible for resolving discrepancies in the conducted quality assessment was the author of three of the manuscripts. This circumstance could potentially have introduced a conflict of interest. However, it is important to note that actual discrepancies only emerged in relation to the "Incomplete Outcome Data" issue, which became evident during the meta-analysis and facilitated their resolution, thereby mitigating any potential conflict of interest.

The main strength of this review and meta-analysis was strict adherence to the systematic methodological approach proposed in the study protocol. Furthermore, the study protocol was registered in PROSPERO and prepared in accordance with the updated PRISMA guidelines (Page et al., 2021). Additionally, this is the first review and meta-analysis to attempt to determine the extent of abnormalities in emotional processing linked to ERPs in FMS patients.

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CRediT authorship contribution statement

L.R. Fischer-Jbali: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – original draft, Writing – review & editing. **A. Alacreu:** Conceptualization, Data curation, Formal analysis, Software, Validation, Visualization, Writing – original draft, Methodology. **C.M. Galvez-Sánchez:** Conceptualization, Data curation, Methodology, Validation, Visualization, Writing – original draft. **C.I. Montoro:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare no conflict of interest.

Data availability

The protocol was formerly registered in the Prospective Register of Systematic Reviews (PROSPERO) international database (Registration ID: CRD42023402466). The data extracted from the articles that underwent review for the purpose of the meta-analysis (https://osf.io/bdux8) and the computed effect sizes (https://osf.io/g2pxf/) are available at Open-Source Framework.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijpsycho.2024.112327.

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