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Association between pain, anxiety, and alpha2 frontal activity in women with fibromyalgia

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ABSTRACT. Fibromyalgia is a disorder of the central nervous system, with the presence of chronic generalized pain, fatigue, morning stiffness, anxiety and depression symptoms. Higher amplitudes of the frequency band alpha2 have been associated with higher relaxation in this population. In the present study, we analysed the association between pain, anxiety, and the spectral power of alpha2 frontal in women with fibromyalgia. Thirty-one women diagnosed with fibromyalgia, for at least three months, took part in the study. Results revealed a statistically significant positive relationship between pain and anxiety levels. However, we found no association between the spectral power of alpha2 in the frontal cortex and the measures between anxiety and pain in the patients. Present findings emphasize the importance of understanding the cortical activity and the central control mechanisms in fibromyalgia.

Keywords: Fibromyalgia; pain; anxiety; electroencephalogram.

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Introduction

Fibromyalgia (FM) is a disorder of the central nervous system, characterized by chronic pain in the musculoskeletal system at specific painful areas (tender points), without inflammation, and related to a sensitization of the central nervous system to pain. The prevalence in the population is estimated between 0.7 and 4.4%, being more frequent in women (Marques, Santo, Berssaneti, Matsutani, & Yuan, 2017). In general, musculoskeletal and neurological tests do not show abnormalities (Bellato et al., 2012). Thus, the FM can be confused with several other disorders that have chronic pain and chronic fatigue as symptoms (Helfenstein, Goldenfum, & Siena, 2012). In this case, it is necessary to do a detailed investigation to exclude similar clinical conditions.

Patients with FM present anxiety and depression, which can disturb them in functional and work activities, increasing the severity of the disorder (Helfenstein et al., 2012). The prevalence of depression in patients with FM is estimated between 50 to 70% (Goldenberg, Bradley, Arnold, Glass, & Clauw, 2008). According to Helfenstein et al. (2012), patients may also experience various other symptoms, such as fatigue, morning stiffness, edema sensation, concentration problems, headaches, sleep disturbances, and tingling.

The Visual Analog Scale (VAS) is the most used instrument to measure pain in the past 10 years (Pinheiro et al., 2016). The VAS is configured as a subjective measure, but there is a need for complementing the self-report with more objective measures, such as the identification of physiological biomarkers in the clinical evaluation of pain.

The identification of biomarkers by the electroencephalogram (EEG) may configure a promising tool for helping in the diagnosis and clinical monitoring of pain (Jones, Huneke, Lloyd, Brown, & Watson, 2012). Moreover, EEG biomarkers may be used to predict responses to the treatment in FM (Hunter et al., 2009). EEG waves result from the sum of the excitatory and inhibitory postsynaptic potentials, which depolarize and hyperpolarize the neuronal membrane, respectively. In general, EEG studies report altered alpha wave amplitudes at rest in FM in the frontal, occipital, and parietal regions of the cerebral cortex (Pinheiro et al., 2016). The alpha frequency band is subdivided into alpha1 (8-10 Hz) and alpha2 (10-12Hz) (Vanneste, Ost, Van Havenbergh, & Ridder, 2017), and has been associated with a state of relaxation in the individual (Caro & Winter, 2011). Abnormalities in alpha and beta frequencies seem to contribute to central nervous system sensitization (Vanneste et al., 2017).

In the present study, we analysed the relationship between the levels of pain and anxiety with the spectral power of the alpha2 frequency band in the frontal region in women with FM. We hypothesized that a greater synchronization of frontal alpha activity would be associated to lower levels of pain and anxiety in FM. Although previous studies have correlated electrophysiological activity with pain symptoms (Villafaina, Collado-Mateo, Fuentes-García, Cano-Plasencia, & Gusi, 2019; Uygur-Kucukseymen et al., 2020), there is still a lack of evidence regarding other symptoms, such as anxiety, present in the disorder.

Material and methods

We carried out an experimental, cross-sectional, descriptive research, with a quantitative approach, in the city of João Pessoa - PB. The project was approved by the Research Ethics Committee of the Health Sciences Center of the Federal University of Paraíba under the CAAE: 39796914.5.0000.5188. The participants signed the Informed Consent Form (ICF) to take part in the research.

The study comprised a non-probabilistic convenience sample of 31 volunteers, following the inclusion criteria: having been diagnosed with FM according to the criteria of the American College of Rheumatology (Wolfe et al., 2010); having been diagnosed for at least three months by a medical team; and being female. The exclusion criteria were: cognitive deficit; illiterate women; history of seizure and major depression, which might affect the EEG patterns.

The instruments used for data collection were: the Sociodemographic and Clinical Questionnaire, to characterize the sample in social and FM-related issues, such as time of diagnosis, medication use, pain characteristic, among other factors; the Cumulative Illness Rating Scale, to verify the presence of other diseases in addition to FM; the Visual Analog Scale, to verify the level of pain at the time of the evaluation; the Beck Anxiety Inventory (BAI) to measure the level of anxiety symptoms; the Mini Mental State Examination (MMSE) to exclude participants with cognitive impairment (score lower than 24) and the Beck Depression Inventory (BDI) to exclude participants with severe depression symptoms (score higher than 36).

We used a 32-channels EEG device (ActiChamp32), at a sampling rate of 500 Hz. The high-pass filter of 0.5 and low-pass filter of 60 Hz were applied at the time of data acquisition, with participants' eyes closed. Impedance was kept below 20 k Ω (Tiemann et al., 2012).

Data collection was performed individually. Initially, the participants were instructed about the research procedures and invited to sign the ICF to take part in the study. Afterwards, the questionnaires were applied and data collection with the EEG was started. The 32 electrodes were placed on the scalp following the International 10-20 EEG System and the reference electrodes were placed on TP9 and TP10, left and right mastoids (Montoya et al., 2006; Fallon, Chiu, Li, Nurmikko, & Stancak, 2015), respectively.

EEG data was collected at rest, 6 minutes with the participant's eyes open, and 6 minutes with eyes closed (Hargrove et al., 2010). In order to avoid sleepiness during the acquisition of electroencephalographic data, the time was divided into blocks of 2 minutes, repeating this procedure three times, the data acquisition ending in 12 minutes (Hassan, Fraser, Conway, Allan, & Vuckovic, 2015). The data presented in the present study corresponded only to the collection with eyes closed, as the results with eyes opened and closed present essentially the same in FM, as reported in previous literature (Hargrove et al., 2010). The data output from the amplifiers was directed to a 15-inch laptop computer with BrainVision Pycoder software for recording the obtained recordings.

Analysis of the EEG data was performed using EEGLAB, a MATLAB toolbox. Noise and muscle artifacts, such as blinking and lateral eye movements, were removed, and data was filtered between 10 and 12 Hz, in order to gecd sfvgt the frequency range alpha2. Subsequently, re-referencing of the electrodes to mean reference was performed in order to remove possible spatial biases (Stevens, Batra, Kötter, Bartels, & Schwarz, 2000; Tiemann et al., 2012; González-Roldán, Munoz, Cifre, Sitges, & Montoya, 2013). In the data processing phase, the mean analyses of the alpha2 frequency band power spectra were performed for the frontal cortex.

Statistical analyses were performed using IBM Statistical Package for the Social Sciences (SPSS) software version 24. Descriptive analyses were performed, through measures of central tendency and dispersion, as well as Pearson's correlation analysis between the variables ‘Pain’, ‘Anxiety’ and ‘Alpha2’.

Results

Regarding sociodemographic characteristics, it was found that most women were married (58.1%, n = 18), 35.5% (n = 11), had a complete high school education, 45.2% (n = 14), a monthly income of one minimum wage, and a mean age of 44.81 (SD = 8.8) years. The average time of diagnosis of FM was 79.77 months (SD = 64.64). In addition, 29.1% (n = 9), received their FM diagnosis 96 to 120 months ago and 25.8% (n = 8), received their diagnosis 3 to 23 months ago.

The results of the CIRS showed that the participants had no serious pathologies associated with FM. From the BDI assessment, six participants were excluded due to the presence of severe symptoms of depression, and there was no exclusion due to cognitive impairment.

Regarding anxiety and depression levels, the mean values for the BAI and BDI questionnaires were 25.42 (SD = 11.00) and 19.35 (SD = 9.46), respectively. The participants had a mean pain level of 6.66 (SD = 1.70) on the VAS. Regarding the electroencephalographic data, the mean for alpha 2 spectral power in the frontal region was 1.5553 (SD = 2.82).

By performing the Shapiro-Wilk test, it was found that the data followed a normal distribution. Hence, Pearson's correlation test was performed between the variables 'Pain', 'Anxiety', and 'Alpha2'. A statistically significant positive relationship was observed between the levels of pain and anxiety [r = 0.462; p = 0.010], in which the higher the level of pain, the more symptoms of anxiety the sample had. There was no significant correlation between pain and frontal alpha2 [r = -0.055; p = 0.774] and between anxiety and frontal alpha2 [r = -0.089; p = 0.641].

Discussion

The present study assessed the relationship between the mean spectral power of alpha2 in the frontal brain regions of women with FM with pain and anxiety symptoms. No correlations were observed between the electroencephalographic activity of alpha2 and the measures of pain and anxiety. However, a positive correlation between pain and anxiety was found in women with FM.

Anxious symptoms are often present in FM patients, and they are many times associated with depression (Santos, Junior, Fraga, Macieira, & Bonjardim, 2012). Previous studies have reported that chronic pain can be initiated or aggravated by situations of anxiety or tension experienced by the patient (Andrade et al., 2013). In this sense, anxiety is directly related to pain states, sometimes associated with psychological factors. Anxiety modulate pain, changing its threshold, causing patients with FM to feel more intense and disturbing somatic sensations (Santos et al., 2012).

The increase in alpha activity has been reported as a representation of the reduction in cortical activation, as it reflects a synchronization of this frequency range (Bonini-Rocha et al., 2008). According to Navarro López, Bergós, and Marijuán (2015), a lower level of alpha activity becomes an indicator of decreased sensory-motor integration in brain processing with a need for extra effort for attenuation of the chronic pain sensation. Thus, alpha synchronization is related to brain activation in a more organized way, indicating that decreased levels of alpha2, namely greater desynchronization of alpha2, leads to higher levels of pain and anxiety.

Villafaina et al. (2019) suggested that pain symptoms are related to the alpha2 spectral power in various cortical regions, finding negative correlations in the central and parietal regions. However, they found no association between the frontal alpha2 activity and the pain levels, corroborating the findings of the present study. Vanneste et al. (2017), when analysing brain connectivity and activity in the other frequency bands related to pain scores, observed an increase of the spectral density only for the beta band, but no relationships with the alpha activity.

The correlation between frontal alpha2 activity and anxiety symptoms has been investigated in the literature, although not specifically to the FM population. Differences between the right and left hemispheres in alpha amplitude in the frontal region may be suggested as a possible biomarker of the anxiety disorders (Cheremushkin et al., 2018). Demerdzieva and Pop-Jordanova (2015) found a greater activation in the right frontal area of children with generalized anxiety disorder. In this respect, Adolph and Margraf (2016) found an expressive frontal alpha asymmetry in individuals with anxiety. These previous studies focused on interhemispheric differences, unlike the present experiment, which focused on the relationship between anxious symptoms and the alpha2 spectral power.

A potential limitation of the present study was the type of electroencephalographic analysis performed. In this regard, we consider that future studies may perform the analysis of the brain asymmetry for the alpha activity. We also suggest an analysis of possible interference factors, such as the time of diagnosis and use of medication in the sample.

Conclusion

In conclusion, we observed that anxiety and pain presented a positive correlation, as previously reported in literature. With regard to the electroencephalographic measures, we found no association between the spectral power of alpha2, in the frontal cortex, with the measures of pain and anxiety in women with FM. Our findings highlight the importance of further studies on the relationship between the symptoms of the FM and the brain activity as a way to understand the central control mechanisms in the disorder.

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