Journal of Sleep Disorders & Therapy
ISSN: 2167-0277
OPEN ACCESS Freely available online
Research Article

Treatment with Very Low Intensity Transcranial Magnetic Stimulation in Patients with Fibromyalgia: Effects on Sleep Quality

Jose María Gomez-Arguelles[1,2], Blanca Travesí Bugallo[1], Marco Moreno-Zazo[3], Ceferino Maestu Unturbe[1]

[1]Department of Bioelectromagnetism, Biomedical Technology Centre, Polytechnic University of Madrid/Ciber BNN (Madrid); [2]Neurology Department, Hospital Universitario Quirón-Salud (Madrid); [3]Rheumatology Department, Hospital Universitario Quirón-Salud (Madrid)

ABSTRACT

The relationship between poor sleep quality and fibromyalgia is bidirectional; both processes constantly feed into each other. A treatment that improves both processes could be very useful. This study investigates the effectiveness of applying a very low-field transcranial magnetic stimulation treatment on patients with fibromyalgia, and to know what changes are produced in the quality of sleep of the patients, compared to two control groups. Methods: a total of 27 patients with fibromyalgia were recruited, all of them adult women. The treatment of magnetic stimulation was applied to them, 4 or 6 weekly sessions, and the results were compared against a group of 52 patients with fibromyalgia to whom no treatment was applied, along with another group of 52 women with the same bio demographic characteristics, but without any pathology. The results were compared in terms of pain improvement using clinical global impression scales, and in terms of sleep quality using the Pittsburgh scale. Results: an improvement in the parameters studied was obtained in 82% of the subjects to whom the treatment was applied, with a mean reduction in the total score of the sleep scale from 16 to 8 points. This improvement is close to the rates observed in healthy subjects. Conclusion: very low intensity transcranial magnetic stimulation in this group of patients with fibromyalgia produced a clinical improvement and an improvement in sleep quality, reaching levels similar to those of healthy subjects.

Keywords: Central sensitization; Chronic pain; Fibromyalgia; Sleep quality; Transcranial magnetic stimulation

INTRODUCTION

Fibromyalgia (FM) is a disease whose main characteristic is the widespread pain that patients suffer chronically. It is a very common syndrome, which can affect up to 4.8% of the population [1], mostly women (90%) [2]. Most authors nowadays consider that this condition has a central origin, caused by an altered signal processing [3-4]. Other factors that have been implicated in its development include central sensitization, genetic, endocrine, sleep disorders, psychosocial, and physical stress [5].

Although pain is the predominant symptom, other very prevalent symptoms in this pathology are fatigue, mood problems, and neurocognitive difficulties and sleep disorders [6]. In fact, for many authors, sleep problems are, after generalized pain, the most common symptom, being reported in more than 90% of patients [7-10]. This difficulty in achieving unrefreshing sleep has negative effects on the quality of life of patients, being related to the other symptoms described above, such as fatigue, neurocognitive problems and mood problems of patients [11-16]. In fact, for some authors, sleep disorders are the main cause of FM [17], while for most researchers the relationship is bidirectional [7,18], entering a vicious circle, in which continuous pain leads to sleep problems, and sleep disorders increase pain [19-21].

FM currently has no curative treatment. Therefore, all currently available treatments aim to alleviate symptoms. They are mainly based on medications with neuromodulatory action, such as antidepressants or antiepileptic drugs. It is also recommended to promote physical activity, patient education and neuropsychological therapies [22-25]. Among the new therapies for the treatment of this disease is transcranial magnetic stimulation of very low intensity (LITMS) [26]. Although it is not yet known exactly on which central mechanisms it acts, it is being used to improve the symptomatology of patients, such as pain or sleep. Our working hypothesis was that LITMS improved the sleep pattern of patients, and this would correlate with the general perception of improvement.

METHODS

Participants

The study was conducted according to the ethical standards

***Correspondence to**: Jose María Gomez Arguelles, Department of Bioelectromagnetism, Biomedical Technology Centre, Polytechnic University of Madrid/Ciber BNN (Madrid), 2Neurology Department, Hospital Universitario Quirón-Salud (Madrid), E-mail: jmgarguelles@yahoo.es

Received: October 23, 2021; **Accepted:** November 11, 2021; **Published:** November 22, 2021

Citation: Gomez Arguelles JM, Blanca TB, Marco MZ, Ceferino MU (2021) Treatment with Very Low Intensity Transcranial Magnetic Stimulation in Patients with Fibromyalgia: Effects on Sleep Quality. J Sleep Disord Ther 10:348. doi: 10.35248/2167-0277.21.10.348

required by the declaration of Helsinki. Patients and controls were recruited from January to December 2019. All of them gave their signed consent to participate in the study. A total of 79 fibromyalgia patients participated in it, and a total of 52 healthy women, as a control group.

All patients had to have been diagnosed with fibromyalgia prior to their participation in the study, with at least 2 years of evolution, and this diagnosis had to have been ratified by at least two specialists in this pathology, following the standard classification and diagnosis guidelines. In order to homogenize the sample as much as possible, only women between the ages of 18 and 65 years were selected, since this sex and age range is the most prevalent in this pathology. The participants should not have other diseases that could interfere with the final results, such as severe psychiatric problems, major sleep disorders, such as narcolepsy, or diseases that are associated with poorer sleep quality, as occurs in many other neurological diseases (e.g. Alzheimer's disease) or respiratory diseases (e.g. COPD).

All patients and controls completed the clinical global impression scales and the Pittsburgh questionnaire at the beginning and end of the study. Only one group of patients received treatment with EMTBI, with the principal investigator deciding whether they received 4 to 6 weekly sessions, depending on the characteristics of the participants. Therefore, 3 groups were established; G1: patients treated with LITMS, G2: patients not treated with LITMS, and G3: healthy women.

The groups of treated patients (G1) were those who agreed to undergo this treatment. The untreated group (G2) was selected as similar as possible to the previous group, in terms of bio demographic, clinical and therapeutic characteristics. The control group (healthy subjects) was also selected taking into account their bio demographic characteristics similar to G1 and G2, and that they did not have any other disease or treatment that could interfere with the study, as indicated above.

TREATMENT

This was a prospective experimental, interventional study with two arms and a control group. Patients who opted for treatment (G1) underwent 4 to 6 weekly sessions of LITMS. The decision on the number of sessions was determined by the clinician, depending on the severity of the case. Therefore, the group that needed 6 sessions were those patients who scored higher on the pain and sleep scales in the initial phase.

LITMS is a form of TMS that consists of applying a brain device that seeks neuronal stimulation with very low frequencies, typical of physiological brain activity, in the order of femtoteslas, i.e. 10-15 Teslas. Each application lasts 20 minutes, and must be performed in an appropriate enclosure, called a Faraday cage, where the electromagnetic field is practically null. The mode of action of the LITMS is believed to act through the so-called 'window effect', activating neural networks by resonance. These networks are selective, only those whose resonance matches the applied frequency will respond, not affecting the rest. It is a very safe, painless treatment, which has already been shown to be effective in this type of patient, and has been approved for use in fibromyalgia patients in our country [26].

Data collection

Sociodemographic characteristics of patients and controls were collected using a self-administered questionnaire, including sex, age, years of evolution, mean analgesic or neuromodulatory treatments, and patients/controls not taking any medication (Table 1).

Table 1: Baseline Data of Patients (G1 and G2) and Controls (G3).

GROUP	G1	G2	G3
Number	27	52	52
Range age	30-63	24-65	30-64
Middle age	46±9	48±9	45±10
Years of evolution	8,5	8	NP
Years of diagnostic	3,5	5	NP
None medication	8	11	NP
Medication average	2,5±2	2,1±2	NP

NP: Not applicable

To assess sleep quality, we used the *Pittsburgh Sleep Quality Index* (PSQI) [27], which was developed by Buysse et al. in 1989, and since then has been routinely used in multiple studies assessing sleep quality in countless pathologies. The results of this questionnaire are grouped into seven areas related to sleep: latency, duration, subjective quality, efficiency, associated sleep disorders, use of medication for sleep and daytime dysfunction. The results are evaluated on a scale from 0 to 3, with 3 being the most negative value. The subdomain values are summed to a total ranging from 0 to 21, with higher values indicating worse sleep quality. The scale is categorized into good sleep quality (0-5 points) and poor sleep quality (>5 points). The PSQI has demonstrated adequate internal consistency, sensitivity and specificity for sleep assessment [28]. To assess the general state of the patients, a global clinical scale (CGIp) was used, with a variation between 0 and 3, with 3 again being the worst value.

Statistical procedure

First, a descriptive (mean, standard deviation, frequencies and percentages) and inferential analysis was performed. The normality of the data distribution was verified using a Kolmogorov-Smirnov test. A multivariate analysis of variance (MANOVA) was performed to examine the relationship between different aspects of sleep with the PSQI scale and global improvement with the CGIp scale, in FM. The F statistical analysis was done by means of Wilks' lambda. Statistical significance was $p<0.05$. All analyses were performed using SPSS software (version 20.0).

RESULTS

The entire sample of patients completed the treatment and no side effects were reported in any case. To compare the data between the different scales, two Manova tests were performed. The first compared the Pittsburgh total score with the CGIp variation, with results respectively of $p1 = 0.0099$ and $p2 = 0.038$, indicating statistical significance in both cases. The Wilks' lambda resulting from this comparison was 0.754, again indicating that the results are statistically significant for 75.4% of the sample. Another Manova was also developed comparing the total variance on the Pittsburgh scale with the variance on the CGIp. In this case, $p1 = 0.0083$ and $p2 = 0.042$ were obtained, both below the established 0.05 significance, again indicating significant results. For this comparison, Wilks' lambda rises to 0.984, which implies that it is valid for 98.43% of the sample.

We also wanted to study in how many patients the treatment did

not work, either by worsening in any of the indexes studied, or by not experiencing an improvement in any of them (Pittsburgh or CGIp). For this purpose, different variations are studied:

The first variation (V1) comprises a study prior to the start of treatment and data collection on the day of the fourth session, at which time continuity is determined according to the results obtained. In this variation, there were 14.81% of women who did not experience improvement and no subject worsened their score on the Pittsburgh scale. As for the CGIp there were 22.22% of people who did not experience any improvement, although again none of them worsened the parameters studied.

The second variation comprises from the test of the fourth session to the last one carried out on the day of the sixth and last session, so that the period studied is two weeks. The Pittsburgh index remained the same in 44.44% of the cases and there were two subjects whose score worsened, which corresponds to 7.4% of the sample. As for the CGIp study, 70.37% remained the same and only one subject worsened (3.7%).

The last variation studied corresponds to the total treatment (from before the first session to the last one). 100% of the subjects experienced some improvement with respect to the General Pittsburgh index and one subject maintained his CGIp, as the rest of the participants improved. These variations are observable in the mean and standard deviation of the Pittsburgh index and the CGIp throughout the sessions for the group of treated women (recall that the Pittsburgh index is scored as 21 for poor sleep and 0 for optimal sleep, and that the CGIp is scored out of 3, with 3 being poor quality of life and 0 optimal) (Table 2).

In the case of the control group (G3), being a group of healthy women, their Pittsburgh score was 5.37 on average with a standard deviation of 3.21, significantly smaller than in women with fibromyalgia.

Table 2: Pittsburgh Scale and Clinical Global Impression data

Score Pittsburgh	Session 1	Session 4	Session 6
Media	15,67	10,41	8,29
Standard deviation	3,88	4,00	3,67
CGIp	Session 1	Session 4	Session 6
Media	2,93	1,89	1,63
Standard deviation	0,27	0,75	0,56

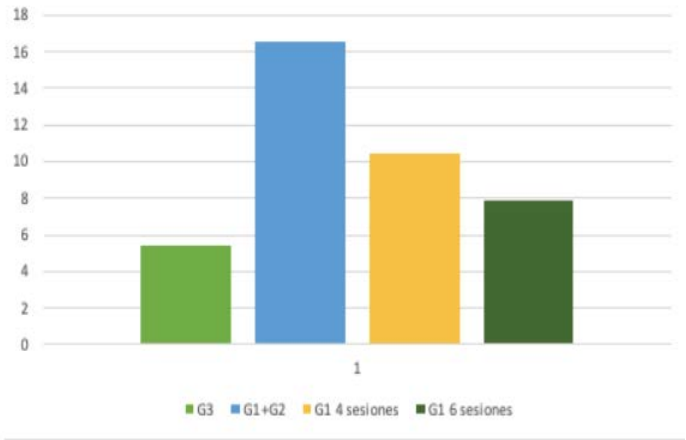

Figure 1: Bar chart with the total score on the Pittsburgh scale. G1: patients treated with CBTMS (4-6 sessions). G2: patients not treated with BCMS. G3: control group.

In the case of the Pittsburgh scale, in its total score, as can be seen in (Figure 1), a significant reduction was achieved both for G1 4 sessions, going from a score of 15.67 to 10.2 ($p < 0.05$) and above all for the patients who received 6 sessions, from 15.67 to 7.84 ($p < 0.005$), approaching values of control subjects.

When we analysed the group of patients treated (G1), we observed an improvement in all the subdomains of the Pittsburgh scale, in all of them with statistical significance ($p < 0.05$), except in item 6 (use of medication), being more striking the effect in patients who reached 6 sessions (Table 3).

Finally, when we compared the results of only the group of patients treated (G1), between the perceived global quality, through the CGIp and the global sleep quality, through the Pittsburgh scale, we found a direct correlation, being again more evident in those patients who completed the 6 sessions. As can be seen in (Figure 2),

Table 3: Scores by Areas (items) and the Pittsburgh Scale Total, according to the number of sessions, in the treated patients (G1). Items; I1: sleep latency. I2: sleep duration. I3: sleep quality. I4: sleep efficiency. I5: associated sleep disorders. I6: medication. I7: daytime dysfunction.

I1	2,59	1,41	129
I2	1,81	1,44	1,24
I3	1,89	0,93	0,76
I4	2	1,22	0,71
I5	2,48	1,70	1,41
I6	2,11	1,78	1,70
I7	2,78	1,93	1,65
TOTAL	15,67	10,41	7,84

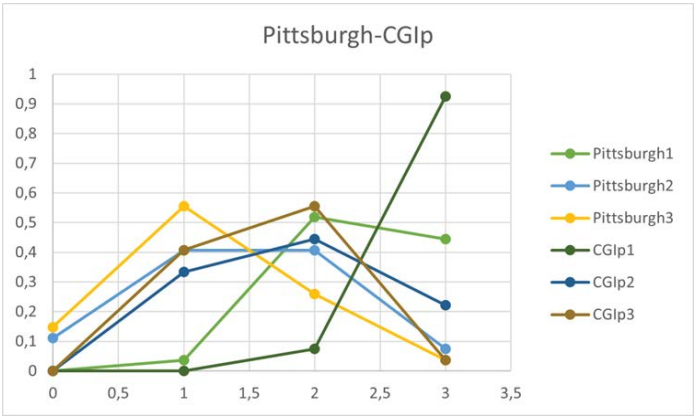

Figure 2: Dot plot comparing the variations with the Pittsburgh Scale with the CGIp in the treated patients. Abscissa axis: proportions. Ordinate axis: CGIp grading (between 0 and 3) and the Pittsburgh (a value of 0 is assigned if the score is between 0 and 5 included. Value 1, between 6 and 10 included. Value of 2, between 11 and 16 included and value of 3, between 17 and 21).

Legend of Pittsburgh and CGIp scales; 1: variation between visit 1 and 4.

2: variation between visit 4 and 6.

3: variation between visit 1 and 6.

at the end of the treatment, in both the CGIp and the Pittsburgh there were very few patients with high scores, contrary to what was observed at the beginning of the treatment

DISCUSSION

The aim of this study was to determine if there is a correlation between the general improvement of the patient and the quality of

sleep, in a group of women with FM, through a non-invasive brain stimulation treatment, such as LITMS, and comparing the effect to a control group of healthy women.

The results of the study show that after applying 4 or 6 weekly treatment sessions, patients perceive a clear general improvement, as well as in the different evaluation parameters of the Pittsburgh scale, except in the use of medication. Moreover, there is a positive correlation between these parameters, being more significant when 6 sessions were applied.

The various symptoms that occur in a patient with FM, in addition to pain, along with the rest of the symptoms, currently assume that there is an ongoing dysfunction of the central nervous system [28]. After widespread pain, the most common complaints in FM, next to fatigue, are sleep disturbances, described by more than 90% of patients in different studies [7-10].

Multiple experimental studies have demonstrated a bidirectional relationship between sleep and pain. Continued pain reduces the quality of sleep, and sleep deprivation maintained over time increases pain [18-19]. The causal relationship between the two is not completely clear, while some authors suggest that two thirds of cases of FM are due to sleep disorders [17], and these correlate with the severity of pain and even with the number of *tender points* [29], others, however, do not consider sleep as a pathogenic agent of FM [30-31].

The fact is that more than 45 years ago Moldofsky described experimentally that the disruption of deep sleep induced widespread pain and fatigue in healthy subjects [32], and concluded that changes in sleep/wakefulness can produce hyperalgesia or body hypersensitivity and fatigue. Since then, multiple studies have described the interaction between sleep and pain, some based on global sleep deprivation, others on specific deprivation of deep sleep or REM sleep, even in healthy subjects [28]. There is evidence that sleep fragmentation in healthy subjects interferes with the inhibitory response of the nervous system to painful stimuli, and increases sensitivity to different non-painful stimuli, such as noises, bright lights or intense smells [33-34], reflecting a sensitization of the CNS [35], and a concept common to the so-called central sensitization syndromes [28].

We know that sleep disruption in normal subjects can reduce inhibitory descending pathways [33,37], and even that sleep deprivation in a population of sedentary middle-aged women results in an alteration of these descending pathways similar to that observed in patients with FM [33]. As these modulatory circuits are also important in the pathophysiology of anxiety and depression, a study wanted to compare in patients with fibromyalgia and healthy subjects who had been subjected to experimental pain, as were their levels of anxiety, depression, sleep and other symptoms of FM. Sleep quality (measured with the Pittsburgh scale) was the only factor that significantly correlated with the reduction of descending inhibitory pathways in patients with fibromyalgia ($p = 0.006$) [38].

In addition, this vicious cycle leads to the onset or aggravation of other symptoms, such as mood and cognitive problems [11-12, 20-21]. Sleep deprivation affects mental alertness, memory, concentration, and the patient's general mood [39]. Patients with poor sleep quality are more likely to have pain and fatigue, defining symptoms of FM [10], as well as increased anxiety and depression [40-41]. Poor sleep quality has been reported to have a cumulative effect on the development of depression [42]. So much so, in fact, that along with cognitive symptoms, fatigue and an awakening with a sense of unrefreshing sleep are the cardinal symptoms of severity for the new American Academy of Rheumatology diagnostic criteria for FM [43]. This reflects a broader change in criteria than the old criteria for classification of FM by this Association, dating back to 1991, when nothing more than the symptom of pain was included [44].

A large number of studies have correlated different polysomnographic changes and FM. Altered sleep architecture has been described with delayed sleep onset [45-46], poor sleep efficiency [47], reduced deep and REM sleep [45-46,48] and various alterations in non-REM sleep, including prominent alpha, commonly called alpha rhythm intrusion or alpha-delta sleep [45,47-54]. This disturbance has been associated with increased number of pain points, increased pain duration and intensity, and decreased sleep duration and efficiency [51]. The significance of all these alterations in FM has not been fully elucidated, in fact other chronic diseases have been commonly associated with these sleep variations [49]. Even in patients with insomnia without other associated pathology, none are considered specific to FM [40, 55].

The Pittsburgh scale is the most commonly used self-administered questionnaire in research on the relationship between FM and sleep [31]. Researchers who have analysed sleep in FM with the PSQI have obtained assessments of poor subjective sleep quality in most cases and a significant prevalence of sleep problems in this population [8,10,56]. Osorio et al. assessed the sleep of 30 patients with FM and 30 healthy controls with this instrument, and highlighted that the group with FM, in addition to presenting poor sleep quality, had particularly affected dimensions of the PSQI related to sleep latency, the existence of sleep disorders and impaired daytime functioning [57], findings similar to those found in our patients.

It has been suggested that early recognition and subsequent treatment of sleep disorders helps to reduce the symptoms of this disease [58], as has been shown in various clinical trials that have succeeded in reducing insomnia [59-60]. In our case, after applying an experimental treatment, such as LITMS, an improvement was observed in the items related to sleep, and this correlated with the overall improvement of the patient. We cannot know which of the two processes originally leads to the improvement of the other, since both are intrinsically related. Due to the limited sample of patients we cannot draw definitive conclusions about efficacy, or how long the observed effect is maintained, but it opens an interesting avenue for future study.

CONCLUSIONS

Sleep disturbances are not only one of the most common symptoms in fibromyalgia. The relationship between sleep disturbances and fibromyalgia is possibly bidirectional. Patients with this pathology have systematically worse scores on the Pittsburgh scale than controls, and the improvement in the different sleep parameters assessed by this questionnaire could have a great significance in the overall improvement of the disease.

With our study, we have found that after the application of a non-invasive treatment, such as low-field transcranial magnetic stimulation, an improvement is obtained in different areas related to sleep, such as subjective quality, sleep duration, sleep efficiency and dysfunction during the day.

A second conclusion is that by applying a greater number of sessions, better results are obtained, although they are already

significant from the fourth session onwards.

Finally, the improvement in the different sleep parameters correlates with the overall improvement of the patient, both cardinal aspects of fibromyalgia.

It would be desirable to extend this study to a larger number of participants, and to describe in future studies how long these improvements are maintained. Even so, we believe that it opens an interesting field of study and progress in the coming years, in the knowledge of this pathology.

REFERENCES

1. Bergman S. A general practice approach to management of chronic widespread musculoskeletal pain and fibromyalgia (Revised). In: Adebajo OA, Dickson J, editors. Collected Reports on the Rheumatic Diseases. Series 4 (Revised) Halmstad (SW): Arthritis Research Campaingn. 2005. P.129-139.
2. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum. 1990;33(2):160-72.
3. Chinn S, Caldwell W, Gritsenko K. Fibromyalgia Pathogenesis and Treatment Options Update. Curr Pain Headache Rep. 2016;20(4):25.
4. Sluka KA, Clauw DJ. Neurobiology of fibromyalgia and chronic widespread pain. Neuroscience. 2016;338:114-129.
5. Fitzcharles MA, Yunus MB. The clinical concept of fibromyalgia as a changing paradigm in the past 20 years. Pain Res Treat. 2012;2012:184835.
6. Bennett RM, Jones J, Turk DC, Russell IJ, Matallana L. An internet survey of 2.596 people with fibromyalgia. BMC Musculoskelet Disord. 2007;8:27.
7. Andrade A, Vilarino GT, Sieczkowska SM, Coimbra DR, Bevilacqua GG, Steffens RAK. The relationship between sleep quality and fibromyalgia symptoms. J Health Psychol. 2020;25(9):1176-86.
8. Bigatti SM, Hernandez AM, Cronan TA, Rand KL. Sleep disturbances in fibromyalgia syndrome: relationship to pain and depression. Arthritis Rheum. 2008;59(7):961-7.
9. Rutledge DN, Jones K, Jones CJ. Predicting high physical function in people with fibromyalgia. J Nurs Scholarsh. 2007;39(4):319-24.
10. Theadom A, Cropley M, Humphrey KL. Exploring the role of sleep and coping in quality of life in fibromyalgia. J Psychosom Res. 2007;62(2):145-51.
11. Ambrose KR, Gracely RH, Glass JM. Fibromyalgia dyscognition: concepts and issues. Reumatismo. 2012;64(4):206-15.
12. Park DC, Glass JM, Minear M, Crofford LJ. Cognitive function in fibromyalgia patients. Arthritis Rheum. 2001;44(9):2125-33.
13. Bertolucci PH, de Oliveira FF. Cognitive impairment in fibromyalgia. Curr Pain Headache Rep. 2013;17(7):344.
14. Fortier BE, Beaulieu BS, Ivers H, Morin CM. Insomnia and daytime cognitive performance: a meta-analysis. Sleep Med Rev. 2012;16(1):83-94.
15. Yaffe K, Falvey CM, Hoang T. Connections between sleep and cognition in older adults. Lancet Neurol. 2014;13(10):1017-28.
16. Wolfe F, Ross K, Anderson J, Russell IJ. Aspects of fibromyalgia in the general population: sex, pain threshold, and fibromyalgia symptoms. J Rheumatol. 1995;22(1):151-6.
17. Mork PJ, Nilsen TI. Sleep problems and risk of fibromyalgia: longitudinal data on an adult female population in Norway. Arthritis Rheum. 2012;64(1):281-4.
18. Ohayon MM. Pain sensitivity, depression, and sleep deprivation: links with serotoninergic dysfunction. J Psychiatr Res. 2009;43(16):1243-5.
19. Smith MT, Haythornthwaite JA. How do sleep disturbance and chronic pain inter-relate? Insights from the longitudinal and cognitive-behavioral clinical trials literature. Sleep Med Rev. 2004;8(2):119-32.
20. Hamilton NA, Affleck G, Tennen H, Karlson C, Luxton D, Preacher KJ, et al. Fibromyalgia: the role of sleep in affect and in negative event reactivity and recovery. Health Psychol. 2008;27(4):490-7.
21. Nicassio PM, Ormseth SR, Kay M, Custodio M, Irwin MR, Olmstead R, et al. The contribution of pain and depression to self-reported sleep disturbance in patients with rheumatoid arthritis. Pain. 2012;153(1):107-112.
22. Borchers AT, Gershwin ME. Fibromyalgia: A Critical and Comprehensive Review. Clin Rev Allergy Immunol. 2015;49(2):100-51.
23. Fitzcharles MA, Yunus MB. The clinical concept of fibromyalgia as a changing paradigm in the past 20 years. Pain Res Treat. 2012;2012:184835.
24. Häuser W, Ablin J, Fitzcharles MA, Littlejohn G, Luciano JV, Usui C, et al. Fibromyalgia. Nat Rev Dis Primers. 2015;1:15022.
25. Van Oosterwijck J, Meeus M, Paul L, De Schryver M, Pascal A, Lambrecht L, et al. Pain physiology education improves health status and endogenous pain inhibition in fibromyalgia: a double-blind randomized controlled trial. Clin J Pain. 2013;29(10):873-82.
26. Maestú C, Blanco M, Nevado A, Romero J, Rodríguez-Rubio P, Galindo J, et al. Reduction of pain thresholds in fibromyalgia after very low-intensity magnetic stimulation: a double-blinded, randomized placebo-controlled clinical trial. Pain Res Manag. 2013;18(6):e101-6.
27. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28(2):193-213.
28. Spaeth M, Rizzi M, Sarzi-Puttini P. Fibromyalgia and sleep. Best Pract Res Clin Rheumatol. 2011;25(2):227-39.
29. Hauri P, Hawkins DR. Alpha-delta sleep. Electroencephalogr Clin Neurophysiol. 1973;34(3):233-7.
30. Diaz-Piedra C, Catena A, Sánchez AI, Miró E, Martínez MP, Buela-Casal G. Sleep disturbances in fibromyalgia syndrome: the role of clinical and polysomnographic variables explaining poor sleep quality in patients. Sleep Med. 2015;16(8):917-25.
31. Diaz-Piedra C, Di Stasi LL, Baldwin CM, Buela-Casal G, Catena A. Sleep disturbances of adult women suffering from fibromyalgia: a systematic review of observational studies. Sleep Med Rev. 2015;21:86-99.
32. Moldofsky H, Scarisbrick P, England R, Smythe H. Musculosketal symptoms and non-REM sleep disturbance in patients with "fibrositis syndrome" and healthy subjects. Psychosom Med. 1975;37(4):341-51.
33. Smith MT, Edwards RR, McCann UD, Haythornthwaite JA. The effects of sleep deprivation on pain inhibition and spontaneous pain in women. Sleep. 2007;30(4):494-505.
34. Geisser ME, Glass JM, Rajcevska LD, Clauw DJ, Williams DA, Kileny PR, et al. A psychophysical study of auditory and pressure sensitivity in patients with fibromyalgia and healthy controls. J Pain. 2008;9(5):417-22.
35. Yunus MB. Fibromyalgia and overlapping disorders: the unifying concept of central sensitivity syndromes. Semin Arthritis Rheum. 2007;36(6):339-56.
36. Smith MT, Edwards RR, McCann UD, Haythornthwaite JA. The effects of sleep deprivation on pain inhibition and spontaneous pain in women. Sleep. 2007;30:494–505.
37. Kundermann B, Spernal J, Huber MT, Krieg JC, Lautenbacher S. Sleep deprivation affects thermal pain thresholds but not somatosensory thresholds in healthy volunteers. Psychosom Med. 2004;66:932-937).

38. Paul-Savoie E, Marchand S, Morin M, Bourgault P, Brissette N, Rattanavong V, et al. Is the deficit in pain inhibition in fibromyalgia influenced by sleep impairments? Open Rheumatol J. 2012;6:296-302.

39. McEwen BS, Karatsoreos IN. Sleep Deprivation and Circadian Disruption: Stress, Allostasis, and Allostatic Load. Sleep Med Clin. 2015;10(1):1-10.

40. Choy EH. The role of sleep in pain and fibromyalgia. Nat Rev Rheumatol. 2015;11(9):513-20.

41. Sayar K, Arikan M, Yontem T. Sleep quality in chronic pain patients. Can J Psychiatry. 2002;47(9):844-8.

42. Yunus M B, Ahles TA, Aldag JC, Masi AT. Relationship of clinical features with psychological status in primary fibromyalgia. Arthritis Rheum. 1991;34:15-21).

43. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Katz RS, Mease P, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res (Hoboken). 2010;62(5):600-10.

44. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum. 1990;33(2):160-72.

45. Branco J, Atalaia A, Paiva T. Sleep cycles and alpha-delta sleep in fibromyalgia syndrome. J Rheumatol. 1994;21(6):1113-7.

46. Horne JA, Shackell BS. Alpha-like EEG activity in non-REM sleep and the fibromyalgia (fibrositis) syndrome. Electroencephalogr Clin Neurophysiol. 1991;79(4):271-6.

47. Onen SH, Alloui A, Gross A, EschallierA, Dubray C. The effects of total sleep deprivation, selective sleep interruption and sleep recovery on pain tolerance thresholds in healthy subjects. J Sleep Res. 2001;10:35–42.

48. Drewes AM, Nielsen KD, Taagholt SJ, Bjerregård K, Svendsen L, Gade J. Sleep intensity in fibromyalgia: focus on the microstructure of the sleep process. Br J Rheumatol. 1995;34(7):629-35.

49. Moldofsky H. The significance of the sleeping-waking brain for the understanding of widespread musculoskeletal pain and fatigue in fibromyalgia syndrome and allied syndromes. Joint Bone Spine. 2008;75(4):397-402.

50. Moldofsky H, Scarisbrick P, England R, Smythe H. Musculosketal symptoms and non-REM sleep disturbance in patients with "fibrositis syndrome" and healthy subjects. Psychosom Med. 1975;37(4):341-51.

51. Roizenblatt S, Moldofsky H, Benedito-Silva AA, Tufik S. Alpha sleep characteristics in fibromyalgia. Arthritis Rheum. 2001;44(1):222-30.

52. Roizenblatt S, Tufik S, Goldenberg J, Pinto LR, Hilario MO, Feldman D. Juvenile fibromyalgia: clinical and polysomnographic aspects. J Rheumatol. 1997;24(3):579-85.

53. Carette S, Oakson G, Guimont C, Steriade M. Sleep electroencephalography and the clinical response to amitriptyline in patients with fibromyalgia. Arthritis Rheum. 1995;38(9):1211-7.

54. Perlis ML, Giles DE, Bootzin RR, Dikman ZV, Fleming GM, Drummond SP, et al. Alpha sleep and information processing, perception of sleep, pain, and arousability in fibromyalgia. Int J Neurosci. 1997;89(3-4):265-80.

55. Cantero, JL, Atienza M, Salas R M. Human alpha oscillations in wakefulness, drowsiness period, and REM sleep: different electroencephalographic phenomena within the alpha band. Neurophysiol Clin. 2002;32:54-71.

56. Prados G, Miró E. Fibromialgia y sueño: una revisión. Rev Neurol. 2012;54(4):227-40.

57. Osorio CD, Gallinaro AL, Lorenzi-Filho G, Lage LV. Sleep quality in patients with fibromyalgia using the Pittsburgh Sleep Quality Index. J Rheumatol. 2006;33(9):1863-5.

58. Korszun A, Young EA, Engleberg NC, Brucksch CB, Greden JF, Crofford LA. Use of actigraphy for monitoring sleep and activity levels in patients with fibromyalgia and depression. J Psychosom Res. 2002;52(6):439-43.

59. Edinger JD, Wohlgemuth WK, Krystal AD, Rice JR. Behavioral insomnia therapy for fibromyalgia patients: a randomized clinical trial. Arch Intern Med. 2005;165(21):2527-35.

60. Martínez MP, Miró E, Sánchez AI, Díaz-Piedra C, Cáliz R, Vlaeyen JW, et al. Cognitive-behavioral therapy for insomnia and sleep hygiene in fibromyalgia: a randomized controlled trial. J Behav Med. 2014;37(4):683-97.