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Is the Transcranial Magnetic Stimulation an Adjunctive Treatment in Fibromyalgia Patients?

Transkraniyal Magnetik Stimulasyon Fibromiyalji Hastalarında Ek Bir Tedavi Yöntemi mi?

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Abstract

Objective: To investigate the effectiveness of low-frequency (LF) repetitive transcranial magnetic stimulation (rTMS) to the motor cortex area in fibromyalgia patients who are resistant to medical treatment.
Material and Methods: A total of 25 patients were randomly assigned to the study, who were in the active rTMS (n=13) or sham stimulation (n=12) group. For the rTMS group, the main stimulation parameters were 90% of motor threshold for 60 seconds at 1 Hz and a 45-second interval between each train. Ten sessions of low-frequency rTMS, which had a total of 1200 pulses at each session, were applied to the left primary motor cortex area daily over a period of 2 weeks. For the sham group, the same parabolic coil was placed at 90° angles to the motor cortex area, and the patients received 10 sessions of sham stimulation. The outcome parameters were pain intensity, which was measured by visual analog scale (VAS), Fibromyalgia Impact Questionnaire (FIQ), and the Beck Depression Inventory (BDI).
Results: A significant improvement in pain intensity, FIQ, and BDI scores was seen at the 10th day and first and third months in both groups. Although the mean of parameters of the rTMS groups was better than the sham group, the difference did not reach statistical significance, except FIQ scores at the 10th day in the real rTMS group.
Conclusion: Patients with fibromyalgia who enroll in real TMS did not present significant differences in long-term follow-ups with respect to those who enrolled in the sham TMS group.
Key Words: Fibromyalgia, transcranial magnetic stimulation, pain

Özet

Amaç: Medikal tedaviye dirençli fibromiyalji hastalarında motor korteks alana uygulanan düşük frekanslı tekrarlayıcı transkraniyal manyetik stimülasyonun (tTMS) etkinliğini araştırmak.
Gereç ve Yöntemler: Toplam 25 hasta randomize olarak aktif ve plasebo gruplarına ayrılarak çalışmaya alındı. Aktif tTMS grubu için stimülasyon sol primer motor korteks üzerinden motor eşik değerin %90'ı hesaplanarak 1 Hz ve 20 dakika uygulandı. Her seansta 1200 uyarı olmak üzere, iki hafta boyunca toplam 10 seans tedavi uygulandı. Plasebo grup için, parabolik koil 90° açı ile motor kortekse yerleştirildi ve aynı şekilde toplam 10 seans stimülasyon uygulandı. Sonuçlar, ağrı için vizüel analog skalası (VAS), Fibromiyalji Etkinlik Anketi (FIQ) ve Beck Depresyon Skalası (BDS) ile değerlendirildi.
Bulgular: Her iki grupta da tedavi sonunda, 1 ve 3. ay sonunda ağrı derecesinde, FIQ ve BDS'de anlamlı iyileşme gözlendi. Ancak, aktif tTMS grubunda iyileşme plasebo gruba göre daha iyiydi. Tedavi sonu FIQ skorlarında aktif grupta, plasebo gruba göre istatistiksel olarak anlamlı iyileşme gözlendi. Diğer değerlendirmelerde gruplar arasında istatistiksel farklılık saptanmadı.
Sonuç: Primer motor korteks üzerine düşük doz tTMS uygulamasının uzun süreli takiplerde fibromiyalji hastalarında plaseboya göre anlamlı iyileşme göstermediği görülmüştür.
Anahtar Kelimeler: Fibromiyalji, transkraniyal manyetik stimülasyon, ağrı

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Introduction

Fibromyalgia (FM) is a disease characterized by generalized musculoskeletal pain, feeling of stiffness, sleep disorders associated with awaking unrefreshed, fatigue, and the presence of tender points (1,2).

A number of hypotheses have been proposed regarding the pathophysiology of FM, which includes dysfunction of pain modulatory systems within the central nervous system, neuroendocrine dysfunction, and dysautonomia (3-5). However, there is no concept that provides a full explanation of the pathogenesis of the disease. Management of FM is frequently multidisciplinary, such as employing education, medications, physical therapies, and cognitive behavioral therapy (6). Usually, the most appropriate treatment is using both pharmacological and non-pharmacological methods together (7).

In the diagnosis of fibromyalgia, chronic widespread pain (in the axial skeleton, right and left side of the body, below and above the waist, and tender points) is the main criterion. In addition to pain disorders, affective disorders, anxiety, and somatic syndromes can often be observed (8). In recent years, repetitive transcranial magnetic stimulation (rTMS), which is a non-invasive, simple applicable method, has taken attention in the treatment of depression. After recent studies, the FDA approved the application of rTMS in the treatment of major depression disorders (9). As we know, the prevalence of depression is increased 30% to 80% in fibromyalgia patients compared with medically healthy individuals (10). Therefore, we thought that it can also be used as an adjunctive treatment in FM. This hypothesis was supported by a few studies that reported that non-invasive direct transcranial current stimulation and high-frequency (HF) rTMS of the motor cortex have analgesic effects in fibromyalgia patients (11,12).

In this randomized, double-blind, sham-controlled parallel group study, we aimed to investigate the effectiveness of low-frequency (LF) repetitive TMS to the motor cortex area in FM patients who are resistant to medical treatment.

Material and Methods

Patients and Study Design

Inclusion criteria were: diagnosing FM according to American College of Rheumatology (ACR) 1990 classification criteria, being 18-60 years of age, and no improvement in cases of using medical treatment for FM for at least 3 months. The patients who had inflammatory rheumatic disease, current primary psychiatric disease, previous surgical treatment to the cranial area, pregnancy, or history of substance abuse were excluded.

The sample size was calculated by Power and Sample Size Program version 3.0.43 before the study, based on data of previous studies. It was found that 12 patients and 12 controls were necessary to have 80% power (2-tailed test with an alpha of 0.05; with delta: 2; sigma: 1.7). All patients signed written informed consent forms to participate in the study, which was approved by the local ethics committee of Marmara University, Faculty of Medicine (date:07.04.2011 / No:B.30.2.MAR.0.01.02/AEK/65). The patients continued to their stable medications during the study. A masked clinician evaluated the patients clinically and provided the diagnosis of FM. The patients were randomly assigned to be in either a real stimulation group or a sham stimulation group by another clinician. The patients were evaluated by the first clinician on the tenth day of treatment and 1 and 3 months after treatment.

In the standardized assessment; pain intensity was measured with the visual analog scale (VAS) (0=no pain, 10=maximum pain imaginable). The effects of the treatment on the health domains were assessed with the Turkish version of the Fibromyalgia Impact Questionnaire (FIQ) (13). Depression and mood were assessed with the Beck Depression Inventory (BDI) (14).

Transcranial Magnetic Stimulation

Patients were seated in a comfortable reclining chair and told to keep their hands as relaxed as possible. Magnetic stimulation was applied with a MagVenture MagPROX100 machine (MagPROX100, MagVenture, Farum, Denmark) using a parabolic coil that was oriented at a tangent to the scalp. The resting motor threshold (rMT) was determined before each session using single-pulse stimulation over the left primary motor cortex. Motor-evoked potentials were recorded from the thenar muscles of the right hand, using a standard EMG machine and surface electrodes.

The rMT was defined as the minimal intensity required to evoke MEPs of 50 mV peak-to-peak amplitude in 5 out of 10 consecutive trials (15). The main stimulation parameters were 90% of motor threshold for 60 seconds at 1 Hz and a 45-second interval between each trains. In this way, we administered a total of 1200 pulses in each session. Ten sessions of low-frequency rTMS were applied daily from Monday to Friday over a period of 2 weeks. The stimulation area was the left primary motor cortex area that triggered a more selective right thumb abduction response in the left motor cortex. Sham stimulation was carried out with the same parabolic coil, which was placed at 90° angles to the motor cortex area. The patients were questioned for the safety of the treatment.

Statistical Analysis

The statistical analysis was performed with Statistical Package for the Social Science Program (SPSS Version 11.5 SPSS, Chicago, IL, USA). The main characteristics of patients were evaluated with descriptive studies, and categorical values were analyzed with chi-square tests. The treatment effects on pain, BDI, and FIQ were assessed with a general linear model. P values lower than 0.05 were accepted as statistically significant.

Results

A total of 28 female patients (mean age: 44 years) were enrolled into the study. One of them dropped out because of low back pain surgery, and two of them were excluded because of not coming to the follow-up visits. The study was completed with 25 patients who were in the active rTMS (n=13) or sham stimulation (n=12) group. The demographic data of each group are listed on Table 1. There was no significance between groups regarding age, body mass index, pain intensity, symptom duration, Beck depression inventory, and FIQ scores (p=0.662, 0.29, 0.127, 0.64, 0.254, 0.456, consecutively). Previous medical treatments were very similar in both groups (Table 2).

Table 1. Demographic data of groups

	Active rTMS group (n=12)	Sham stimulation group (n=13)	p value
Age (years)	45.25±9.33	43±7.63	0.66
Gender (female/male)	12 female	13 female	
Body mass index (kg/m^2)	28.91±4.87	31.15±10.43	0.29
Symptom duration (months)	53±29.15	54.92±30.44	0.64
Medical treatment duration (months)	14.91±19.36	14.07±22.02	0.78

rTMS: repetitive transcranial magnetic stimulation

Table 2. Previous medical treatments

	Sham stimulation group (n=13)	Active rTMS group (n=12)
1	Fluoxetine	Fluoxetine
2	Citalopram	Venlafaxine
3	Escitalopram	Amitriptyline
4	Venlafaxine	Venlafaxine
5	Escitalopram	Sertraline
6	Amitriptyline	Escitalopram
7	Sertraline	Duloxetine
8	Venlafaxine	Escitalopram
9	Amitriptyline	Venlafaxine
10	Sertraline	Escitalopram
11	Escitalopram	Escitalopram
12	Venlafaxine	Sertraline
13		Fluoxetine

rTMS: repetitive transcranial magnetic stimulation

The VAS scores at all follow-ups were statistically lower than before treatment in both groups (VAS before treatment- end of treatment: F=40.946 p=0.001, VAS before treatment- first month: F=22.904 p=0.001, VAS before treatment- third month: F=40.936 p=0.001). There was no statistical significance between groups at any time (VAS before treatment- end of treatment: F=10,566 p=0.079, VAS before treatment- first month: F=0.123 p=0.729, VAS before treatment- third month: F=0.696 p=0.413) (Figure 1).

Both of the groups had statistically improvements in FIQ scores (FIQ before treatment- end of treatment: F=30.244 p=0.001, FIQ before treatment- first month: F=29.986 p=0.001, FIQ before treatment- third month: F=32.357 p=0.001). At the end of the treatment, there was a statistically significant improvement in the FIQ scores in the real rTMS group than control group (FIQ before treatment- end of treatment F=8.891 p=0.006). However, this effect did not continue at the first and third months (FIQ before treatment- first month: F=2.506 p=0.127, FIQ before treatment- third month: F=2.255 p=0.147) (Figure 2).

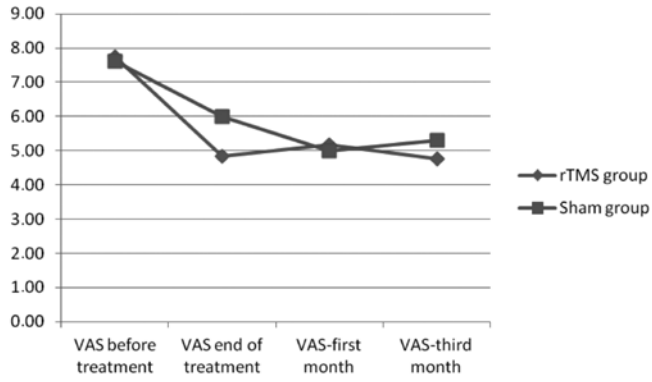

Figure 1. VAS scores of the groups. According to general linear model, there were statistical differences between baseline and the follow-ups for both groups. But, there was no statistical difference between groups at any time

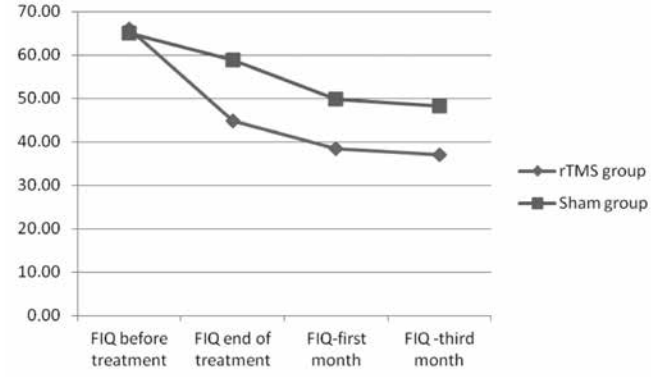

Figure 2. The FIQ scores in both groups were decreased statistically from baseline. At the end of the treatment, there was a statistically significant improvement in the FIQ scores in the real rTMS group than control group. However, this effect did not continue at the first and third months

The Beck Depression Inventory scores at all follow-ups were statistically lower than before treatment in both groups (BDI before treatment- end of treatment: F=21.921 p=0.001, BDI before treatment- first month: F=16.143 p=0.001, BDI before treatment- third month: F=43.455 p=0.001). The rTMS group had better BDI scores at the end of the treatment (F=5.927 p=0.023). There was no statistical difference between groups at the first and third months (BDI before treatment- first month: F=0.285 p=0.599, BDI before treatment- third month: F=1.391 p=0.25) (Table 3).

Three patients in the real rTMS group and one patient in the sham group reported adverse events. Two of the real group patients complained of transient headache, which was over in 24 hours, and the other patients complained about daily tinnitus. However, these complaints did not lead to changes in the treatment program.

Discussion

To treat chronic widespread pain in patients with FM is difficult, which usually requires a multidisciplinary approach using

Table 3. Mean±standard deviation of parameters

	rTMS group	Sham group	General linear model for repeated measures
VAS before treatment	7.75±1.54	7.61±2.14	Within groups: before treatment- end of treatment: F=40.946 p=0.001
			before treatment- first month: F=22.904 p=0.001
			before treatment- third month: F=40.936 p=0.001
VAS end of treatment	4.83±1.74	6±3.05	Between groups: VAS before treatment- end of treatment: F=10,566 p=0.079
VAS- first month	5.16±2.91	5.38±2.63	VAS before treatment- first month: F=0.123 p=0.729
VAS- third month	4.75±2.76	5.3±2.49	VAS before treatment- third month: F=0.696 p=0.413
FIQ before treatment	66.09±15.13	65.1±12.92	Within groups: before treatment- end of treatment: F=30.244 p=0.001
FIQ end of treatment	44.8±15.77	58.83±16.1	before treatment- first month: F=29.986 p=0.001
FIQ- first month	38.35±23.25	49.8±17.17	before treatment- third month: F=32.357 p=0.001
FIQ- third month	36.95±24.27	48.13±16.79	Between groups: end of treatment F=8.891 p=0.006
BDI before treatment	25.91±12.61	20.53±8.92	first month: F=2.506 p=0.127
			third month: F=2.255 p=0.147).
BDI end of treatment	19.58±9.33	18.53±9.7	Within groups: before treatment-end of treatment: F=21.921 p=0.001
BDI- first month	19.08±13.35	15.30±8.9	before treatment- first month: F=16.143 p=0.001
BDI- third month	16.75±10.6	14.15±8	before treatment- third month: F=43.455 p=0.001)
			Between groups: end of the treatment F=5.927; p=0.023
			first month: F=0.285 p=0.599
			third month: F=1.391 p=0.25

VAS: visual analog scale; FIQ: fibromyalgia impact questionnaire; BDI: beck depression inventory

both pharmacological and non-pharmacological interventions (16). Repetitive transcranial magnetic stimulation is a rapidly developing technique for the investigation of brain function, and several studies have been performed focusing on the use of rTMS to obtain clinical gains in neuropsychiatric diseases, such as major depression, Parkinson's disease, and epilepsy. As it is known, rTMS is a non-invasive, easily applicable, and relatively safe method (17). High-frequency rTMS (greater than 1 Hz) usually activates neurons and increases cerebral perfusion, whereas LF-rTMS (1 Hz or less) does the opposite (18,19). In recent years, the use of repetitive transcranial magnetic stimulation in depression and chronic pain treatment has excited scientists for the use of rTMS in FM patients. There is evidence of anti-depressive efficacy of HF-rTMS to the left dorsolateral prefrontal area and LF-rTMs to the right dorsolateral prefrontal area (20-22). In pain treatment, the motor cortex that is proven to be efficacious in chronic pain treatment should be the first cortical target. Extensive literature shows that stimulation of this area with either invasive or noninvasive brain stimulation is associated with pain improvement (23,24).

We therefore hypothesized that LF-rTMS of the motor cortex can reduce chronic widespread pain in patients with fibromyalgia, according to knowledge from previous studies. This hypothesis is supported by recent reports that non-invasive direct transcranial current stimulation of the motor cortex has analgesic effects in fibromyalgia patients (12,25). In the previous studies of Passard (25), Lefaucher (26,27), Mhalla (28), André-Obadia (29), and Nahmias (30), HF-rTMS was used, and analgesic effects of high-frequency stimulation of primary motor cortex were demonstrated. There were also studies that used low frequency for pain relief in FM. A study that had four patients found pain improvement, but in a second study, no difference was reported between the sham and real treatment groups (31,32). However, in both studies, LF-rTMS stimulation was applied to the prefrontal cortex area. We also used LF-rTMS to the motor cortex area, and to our knowledge, this is the first study in the literature.

We found significant improvements in pain intensity, FIQ, and BDI scores at the 10th day and first and third months in both groups. Although the mean parameters of the rTMS groups were better than the sham group, the difference did not reach statistical significance, except FIQ and BDI scores on the 10th day in the real rTMS group (p=0.006, p=0.023, consecutively). The sham group also had improvements, which suggested the placebo effect of the treatment.

Tamura et al. (33) demonstrated that 1 Hz rTMS to the left motor cortical area has beneficial effects on acute pain induced by capsaicin. On the other hand, there was no evidence about long-term follow-up in that study. We also found a significant analgesic effect in early control, but it did not take long.

The most common adverse effects of rTMS are headache and neck pain. There was no significant adverse effect in our study. Low-frequency rTMS to the prefrontal area may be associated with a higher incidence of headache and neck pain (17).

There are some limitations in our study. This study was done with patients with FM who are resistant to other treatment modalities. Therefore, it may be inadequate for assessing recently

diagnosed FM patients. Additionally, all patients were treated with a pharmacological agent. Because of these limitations, our results can not be generalized to all patients with FM. Moreover, the sham group had also demonstrated some amount of improvement. These improvements suggested that there was a placebo effect. Another possibility is that sham therapy, applied 90 degrees perpendicular to the primary motor cortex, may also have had some kind of unexpected effect on pain perception.

Conclusion

It seems that stimulating the primary motor cortex improves the patients' complaints, and it may be an adjunctive treatment for FM. It is clearly evident that more studies are necessary to clarify the questions about rTMS, such as technical considerations, stimulation site, and dosing schedule, in the treatment of FM.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Marmara University Faculty of Medicine.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - İ.Y.; Design - İ.Y., M.A.; Supervision - İ.Y., M.A.; Funding - M.A.; Materials - İ.Y., M.A.; Data Collection and/or Processing - M.A., D.Ö., B.E.; Analysis and/or Interpretation - İ.Y., M.A., D.Ö., B.E.; Literature Review - M.A.; Writer - İ.Y., M.A.; Critical Review - İ.Y., M.A., D.Ö., B.E.

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References

1. Podolecki T, Podolecki A, Hrycek A. Fibromyalgia: pathogenetic, diagnostic and therapeutic concerns. Pol Arch Med Wewn 2009;119:157-61.
2. Guymer E, Littlejohn G. Fibromyalgia: current diagnosis and management. Expert Rev Clin Immunol 2009;5:181-92. [CrossRef]
3. Lawson K. Treatment options and patient perspectives in the management of fibromyalgia: future trends. Neuropsych Dis Treat 2008;4:1059-71. [CrossRef]
4. Sarzi-Puttini P, Atzeni F, Diana A, Doria A, Furlan R. Increased neural sympathetic activation in fibromyalgia syndrome. Ann N Y Acad Sci 2006;1069:109-17. [CrossRef]
5. Tanriverdi F, Karaca Z, Unluhizarci K, Kelestimur F. The hypothalamo-pituitary-adrenal axis in chronic fatigue syndrome and fibromyalgia syndrome. Stress 2007;10:13-25. [CrossRef]
6. Sampson SM, Rome JD, Rummans TA. Slow-frequency rTMS reduces fibromyalgia pain. Pain Med 2006;7:115-8. [CrossRef]
7. Häuser W, Arnold B, Eich W, Felde E, Flügge C, Henningsen P, et al. Management of fibromyalgia syndrome--an interdisciplinary evidence-based guideline. Ger Med Sci 2008;9:6-14.
8. Häuser W, Eich W, Herrmann M, Nutzinger DO, Schiltenwolf M, Henningsen P. Fibromiyalgia syndrome: classification, diagnosis, and treatment. Dtsch Arztebl Int 2009;106:383-91.
9. Guidance for Industry and FDA Staff - Class II Special Controls Guidance Document: Repetitive Transcranial Magnetic Stimulation (rTMS) Systems. Available from: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm265269.htm
10. Santos Dde M, Lage LV, Jabur EK, Kaziyama HH, Iosifescu DV, Lucia MC, et al. The association of major depressive episode and personality traits in patients with fibromyalgia. Clinics 2011;66:973-8. [CrossRef]
11. Passard A, Attal N, Benadhira R, Brasseur L, Saba G, Sichere P, et al. Effects of unilateral repetitive transcranial magnetic stimulation of the motor cortex on chronic widespread pain in fibromyalgia. Brain 2007;130:2661-70. [CrossRef]
12. Fregni F, Gimenes R, Valle AC, Ferreira MJ, Rocha RR, Natalle L, et al. A randomized, sham-controlled, proof of principle study of transcranial direct current stimulation for the treatment of pain in fibromyalgia. Arthritis Rheum 2006;54:3988-98. [CrossRef]
13. Sarmer S, Ergin S, Yavuzer G. The validity and realibility of the Turkish version of the Fibromyalgia Impact Questionnaire. Rheumatol Int 2000;20:9-12. [CrossRef]
14. Hisli N. Beck Depresyon Envanteri'nin geçerliliği üzerine bir çalışma. Psikoloji Dergisi 1988;6:118-22.
15. Rossini PM, Barker AT, Berardelli A, Caramia MD, Caruso G, Cracco RQ, et al. Non-invasive electrical and magnetic stimulation of the brain, spinal cord and roots: basic principles and procedures for routine clinical application. Report of an IFCN committee. Electroencephalogr Clin Neurophysiol 1994;91:79-92. [CrossRef]
16. Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum 1995;38:19-28. [CrossRef]
17. Machii K, Cohen D, Ramos-Estebanez C, Pascual-Leone A. Safety of rTMS to non-motor cortical areas in healthy participants and patients. Clin Neurophysiol 2006;117:455-71. [CrossRef]
18. Kobayashi M, Pascual-Leone A. Transcranial magnetic stimulation in neurology. Lancet Neurol 2003;2:145-56. [CrossRef]
19. Jose RR, David A, Roland S, Massimo G, Pascual-Leone A. Subthreshold low frequency repetitive transcranial magnetic stimulation selectively decreases facilitation in the motor cortex. Clin Neurophysiol 2002;113:101-7. [CrossRef]
20. Chae JH, Nahas Z, Li X, George MS. Transcranial magnetic stimulation in psychiatry: research and therapeutic applications. International Rev Psychiatry 2001;13:18-23. [CrossRef]
21. Fitzgerald P. Is it time to introduce repetitive transcranial magnetic stimulation into standard clinical practice for the treatment of depressive disorders? Aust N Z J Psychiatry 2003;37:5-11. [CrossRef]

22. Hemond CC, Fregni F. Transcranial Magnetic Stimulation in neurology: what we have learned from randomized controlled studies. Neuromodulation 2007;10:333-44. [CrossRef]
23. Lefaucheur JP, Antal A, Ahdab R, Ciampi de Andrade D, Fregni F, Khedr EM, et al. The use of repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) to relieve pain. Brain Stimul 2008;1:337-44. [CrossRef]
24. Roizenblatt S, Fregni F, Gimenez R, Wetzel T, Rigonatti SP, Tufik S, et al. Site-specific effects of transcranial direct current stimulation on sleep and pain in fibromyalgia: a randomized, sham-controlled study. Pain Pract 2007;7:297-306. [CrossRef]
25. Passard A, Attal N, Benadhira R, Brasseur L, Saba G, Sichere P, et al. Effects of unilateral repetitive transcranial magnetic stimulation of the motor cortex on chronic widespread pain in fibromyalgia. Brain 2007;130:2661-70. [CrossRef]
26. Lefaucheur JP. The use of repetitive transcranial magnetic stimulation (rTMS) in chronic neuropathic pain. Neurophysiol Clin 2006;36:117-24. [CrossRef]
27. Lefaucheur JP, Drouot X, Menard-Lefaucheur I, Zerah F, Bendib B, Cesaro P, et al. Neurogenic pain relief by repetitive transcranial magnetic cortical stimulation depends on the origin and the site of pain. J Neurol Neurosurg Psychiatry 2004;75:612-6. [CrossRef]
28. Mhalla A, Baudic S, Ciampi de Andrade D, Gautron M, Perrot S, Teixeira MJ, et al. Long-term maintenance of the analgesic effects of transcranial magnetic stimulation in fibromyalgia. Pain 2011;152:1478-85. [CrossRef]
29. André-Obadia N, Peyron R, Mertens P, Mauguière F, Laurent B, Garcia-Larrea L. Transcranial magnetic stimulation for pain control. Double-blind study of different frequencies against placebo, and correlation with motor cortex stimulation efficacy. Clin Neurophysiol 2006;117:1536-44. [CrossRef]
30. Nahmias F, Debes C, de Andrade DC, Mhalla A, Bouhassira D. Diffuse analgesic effects of unilateral repetitive transcranial magnetic stimulation (rTMS) in healthy volunteers. Pain 2009;147:224-32. [CrossRef]
31. Sampson SM, Rome JD, Rummans TA. Slow-Frequency rTMS reduces fibromyalgia pain. Pain Med 2006;7:115-8. [CrossRef]
32. Carretero B, Martín MJ, Juan A, Pradana ML, Martín B, Carral M, et al. Low-frequency transcranial magnetic stimulation in patients with fibromyalgia and major depression. Pain Med 2009;10:748-53. [CrossRef]
33. Tamura Y, Okabe S, Ohnishi T, N Saito D, Arai N, Mochio S, et al. Effects of 1-Hz repetitive transcranial magnetic stimulation on acute pain induced by capsaicin. Pain 2004;107:107-15. [CrossRef]