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The effect of electrotherapy on fatigue in people with multiple sclerosis

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Abstract
Multiple Sclerosis (MS) is one of the central nervous system disorders. Fatigue is one of the symptoms of MS. Intervention through electrotherapy can contribute to the best physiotherapy treatment of fatigue by improving the quality of life of the individual. The aim of this review is to describe recent research data on the efficacy of electrotherapy in reducing fatigue in people with MS. The Google Scholar, PubMed and PEDro databases were searched in English with the following keywords: Multiple sclerosis, fatigue, electrical stimulation, magnetic field. The review included clinical studies that referred to methods of intervention of electrotherapy.
Discussion-Conclusions: This review failed to identify a more general electrotherapy program (treatment dosage, frequency, protocols) that could be widely used in MS patients and reduce fatigue levels. The research done so far is short-term and compares electrotherapy with other intervention techniques. There is a need for longer-term research that will help to establish general guidelines for an electrotherapy protocol (treatment dosage, frequency) for people with MS that would help reduce fatigue.

Keywords: Multiple sclerosis, fatigue, electrical stimulation, magnetic field

Introduction
Multiple Sclerosis (MS) is an autoimmune, inflammatory, demyelinating disease of the central nervous system. It is a neurological abnormality caused by destruction of the myelin that surrounds the nerve fibers [1]. The disease shows great clinical inhomogeneity. Among the symptoms of the disease is fatigue, which can have a negative impact on daily activities and significantly affect quality of life [2].
The frequency of MS is related to the latitude of each region. Specifically, the incidence of the disease is higher in: northern Europe, Canada and the US Northern states (> 100/100000) and lower in East Asia and sub-Saharan Africa (2/100000). The global prevalence of the disease is increasing, from 30/100000 in 2008 to 33/100000 in 2013. In Europe, more than 500000 people are affected by the disease. In Greece, in data from 2011 to 2014, there were 3500 registered patients. MS usually affects people between the ages of 20-40 and is more common in women than in men (2.3–3.5:1) [3, 5].
Regarding fatigue, in a study in MS patients, 87% said they considered "fatigue" one of the problems of the disease. In various other studies the percentage of patients who report "fatigue" ranges from 76-92%. However, 14-21% of patients consider it as the most serious symptom that causes them the greatest functional impairment, while 55-75% classify it as one of the three most serious symptoms [6].
Physiotherapy has been shown to help treat fatigue in people with MS [2]. Functional Electrical Stimulation (FES) and magnetic field applications have been used in the past to treat fatigue in MS patients [1].
The aim of this review is to describe recent research data on the efficacy of FES and magnetic fields in reducing fatigue in MS patients.

Literature review
The Google Scholar, PubMed and PEDro databases were searched in English with the following keywords: Multiple sclerosis, fatigue, electrical stimulation, magnetic field.

The review included clinical studies and systematic reviews that referred to methods of electrotherapy intervention. Below are the main conclusions of the articles included in this review.

Firstly, De Carvalho *et al*. [7] evaluated the efficacy of a pulsed low-frequency magnetic field in reducing fatigue in people with MS in a randomized, double-blind, crossover trial with 50 individuals. Participants were randomly divided into two groups, the study group to which the magnetic field therapy was applied and the sham group to which a general treatment was applied. The Modified Fatigue Impact Scale (MFIS) and the Fatigue Severity Scale (FSS) were used to assess fatigue. Each session included 24 minutes of treatment. The treatment was done three times a week, for eight weeks. After five months, the groups did the treatment of the other group. The results of the study showed that treatment with a low-frequency magnetic field (as defined according to the protocol of this study) compared to sham treatment does not help to reduce fatigue more.

In the study of Lappin *et al*. [8], the efficacy of pulsed electromagnetic field therapy in fatigue associated with MS, spasticity, bladder control and overall quality of life was investigated. The study involved 117 people with MS and the design included a cross-trial. The intervention used in this study was the daily exposure to a pulsed electromagnetic field emitted by a small, portable generator; pulsed magnetic field therapy (PMFT). The Multiple Sclerosis Quality of Life Inventory (MSQLI) was used to record fatigue and quality of life. It was observed that daily exposure to a pulsed electromagnetic field reduced fatigue and improved quality of life.

In another study, Piatkowski *et al*. [9] studied the effect of a Bio-Electro-Magnetic-Energy-Regulation (BEMER) magnetic field on MS-related fatigue. Their study was a randomized controlled clinical trial involving 37 people. A BEMER magnetic field was applied Fatigue was measured with the MFIS and the FSS. There was a statistically significant difference in results between the two groups on the MFIS (26.84 vs. 36.67, p = .024). FSS values in the intervention group were significantly lower after 12 weeks (3.5 vs. 4.7, p = .016). After six weeks there was a follow-up and there was no difference in fatigue between the two groups. The MFIS has three subcategories (physical, cognitive and psychological). In the group that underwent the intervention there were significant differences for the first two subcategories ((p = .018) and (p = .041) respectively), but not for the third subcategory.

Furthermore, Mostert *et al*. [10] studied whether adding to the neurological rehabilitation program of people with MS additional treatment with PMFT provides an additional effect on fatigue. For the purposes of this study, a randomized controlled trial was performed with 25 individuals. The sample was randomly divided into two groups, the study group in which PMFT treatment was applied and the sham group in which some general treatment was applied. The FSS and the Visual Analog Scale (VAS) were used to assess fatigue. Each session included 16 minutes of treatment and the treatment was done twice a week, for 3-4 weeks. Fatigue levels were high for both groups at the beginning of the study. After treatment, fatigue was reduced by 18% in the treatment group and 11% in the control group. These changes are not statistically significant. According to the results of the research and because the cost for this treatment is high, as well as the placebo effect was important, the authors of the work do not recommend the use of pulses to reduce fatigue in a patient with MS.

In the study of Chang *et al*. [11] the effect of an 8-week program with FES on fatigue (general, central, peripheral) of MS patients was studied. For the intervention, FES was applied superficially to the quadriceps femoris muscle. The FSS, VAS, maximal voluntary contraction (MVC), voluntary activation level (VAL), twitch force (ITT), General Fatigue Index (FI), Central Fatigue Index (CFI), Peripheral Fatigue Index (PFI) and MFIS were the tools used to evaluate fatigue. The values of FI (p = .01), CFI (p = .02) and the MFIS score (p = .02) significantly improved after the implementation of the program. The study showed that when central fatigue improves, general fatigue can also improve significantly (p< .01). According to the results of the research, MS patients with significant central fatigue following an 8-week program of superficial FES can significantly reduce their fatigue, especially central fatigue.

Moreover, Backus *et al*. [12] studied the efficacy of the FES method in combination with cycling in reducing fatigue and improving the quality of life in people with MS who are non-ambulatory. The sample was divided into two groups (12 people in the intervention group and nine people in the control group). The intervention group followed a 30-minute program, 2-3 times a week, for 12 weeks. The MFIS and the Fatigue Scale for Motor and Cognitive Functions (FSMC) were used to measure fatigue. The MFIS and FSMC scores improved for the intervention group compared to the control group. The results of the research showed that a treatment program that includes FES combined with cycling is safe for non-ambulatory patients with MS. In addition, such a program can reduce fatigue and improve their overall quality of living.

Lastly, Bisht *et al*. [13] in a pilot study studied whether a multidimensional intervention has a positive effect on the fatigue of people with second-stage MS. The multidimensional intervention included a modified Paleolithic diet with supplements, stretching, resistance exercises with electrical stimulation of the muscles of the trunk and lower limbs, meditation and massage. The FSS was used to measure fatigue. In the first group the FSS score decreased from 5.7 to 3.32 (p = .0008) within 12 months, a statistically significant reduction in fatigue levels. In this small, pilot study, there was a significant improvement in fatigue in those who completed the study. Given the small sample size and the percentage of supplements, further evaluation of this treatment is required.

Discussion

FES is a tool that has been used in the past in research to reduce fatigue in MS patients. In the study of Chang *et al*. [11], after superficial application of FES to the quadriceps femoris muscle for 8 weeks there was a significant reduction in fatigue in patients with MS. Another very interesting FES application was the combination of FES with cycling [12]. During the session, the electrodes were placed on the muscles and at the same time there was an electrical stimulation of the muscles that were activated during movement. After 24 weeks of implementing this combined FES exercise program with cycling there was a positive effect on fatigue, cognitive function and pain. However, it should be noted that these studies were performed on a small sample size of patients, so there is a need for larger-scale research to confirm these findings. Finally, Bisht *et al*. [13] report that a multidimensional intervention has a positive effect on the fatigue of people affected by second-stage MS.

Other studies included in our review investigate the efficacy of the use of PMFT in reducing fatigue in MS patients. These studies have shown that PMFT can have a positive effect on reducing fatigue. In the study conducted by Lappin *et al*. [8], it was observed that daily exposure to a pulsed electromagnetic field, emitted by a small, portable generator, reduced fatigue and improved quality of life. A significant difference in the MFIS

results was also observed after 12 weeks of using BEMER magnetic field therapy for eight minutes, twice daily [9]. Although some studies show slight positive effects of PMFT on fatigue, their results were not statistically significant. Similar conclusions were drawn by De Carvalho *et al.* [7], as well as Mostert *et al.* [10], who evaluated the efficacy of a pulsed low-frequency magnetic field in reducing fatigue in people with MS.

Regarding the quality of the studies included in this review, the following were observed:

This review failed to identify a more general electrotherapy protocol (treatment dosage, frequency, regimens) that could be widely used in MS patients and that could reduce fatigue levels, because the above studies do not describe the exact protocols that were applied. Another problem is the short duration of the studies; most of them were implemented for eight weeks.

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