

Literature review

Physical training and multiple sclerosis

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Abstract

For many years, patients with multiple sclerosis (MS) were advised to avoid exercise because of the risk of increased neurological impairment. This article reviews the literature related to MS and physical exercise. Physical exercise depends on patients' physiological tolerance and response to exercise. MS patients can exhibit dysfunction of cardiovascular adjustment accompanied by respiratory involvement, which can alter aerobic capacity. These abnormalities tend to increase with the neurological impairment. Muscle weakness is the consequence of not only altered central motor drive but also disuse. Several studies have shown the benefits of physical training, with improvements in aerobic capacity, gait parameters and fatigue, and an influence on quality of life. Regular aerobic physical activity is necessary to maintain the benefit of physical training.

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1. Introduction

Multiple sclerosis (MS) is an inflammatory disease of the central nervous system that affects young people, especially women. The consecutive handicap varies depending on the locality and course of disease: relapsing, remitting or progressive. Motor disorders are frequent, with muscle weakness, balance problems and spasticity [9]. Fatigue is one of the symptoms most frequently reported by MS patients, sometimes isolated at the onset of MS or associated with other neurological disorders. The most likely causal mechanism, whether psychological and psychiatric disorders, sleep disorders, pain, comorbidities, medications, or deconditioning, has never been validated [3].

People with MS often limit their physical activity because of the risk of exacerbation of this chronic illness. In fact, decreased physical activity tends to increase deconditioning and alters fitness [17,27,35,39]. Thus the benefit of physical activity for people with MS must be questioned.

We aimed to describe physiological responses to exercise in MS and then review published research to explore the efficacy of physical activity for people with MS. The response to disability depends on the level of handicap generally evaluated by the Expanded Disability Status Scale (EDSS), although it is probably not the best scale for patients with limited disability [19].

2. Physiological response to exercise in MS

The appropriateness of physical activity for people with MS largely depends on patients' physiological tolerance and response to exercise. Ponichtera-Mulcare [27], in a review of literature published between 1951 and 1993, found four main areas related to exercise: cardiorespiratory fitness, autonomic function, skeletal muscle function and the effect of exercise-induced temperature increase. This review stressed the importance of the level of neurological impairment, which influences physical capacities.

Approximately 80% of patients with MS show evidence of dysfunction of the autonomic nervous system with documented abnormalities in sexual and bladder function [7–9].

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During physical stress, cardiovascular adjustments are almost entirely mediated by the autonomic nervous system. Only moderate abnormalities have been observed in heart rate and blood pressure in MS patients at rest [2,25,34,36]. Pepin et al. [25] examined blood pressure and heart rate variation during isometric muscular exercise in patients with mean EDSS of 4. Over half the patients exhibited abnormalities in blood pressure adaptation, which was also described during dynamic exercise [27,36]. Ponichtera-Mulcare et al. [28] found no difference in heart rate in nine people with MS and nine non-disabled individuals with EDSS ranging from 1 to 4. Among studies of abnormalities, variations may be explained by differences in neurological impairment, probably due to the presence of highly impaired individuals. Muscle weakness can also limit strength output during exercise [20]. Moreover, the severity of the illness increases the risk of lesions located on or near neurons involved in autonomic cardiovascular function [27,28].

Deficit in cardiorespiratory fitness is observed. Several studies have found a diminished aerobic capacity in MS, with a significantly lower $VO_{2\text{ peak}}$. Respiratory involvement can affect cardiorespiratory fitness. Little attention is generally paid to the pulmonary system, probably because patients with MS rarely exhibit pulmonary symptoms or disease [12]. Respiratory dysfunction is mainly due to respiratory muscle weakness, especially in cases of high cervical cord lesions [13]. Bulbar dysfunction, obstructive sleep apnea, and abnormalities of respiratory control could also be involved [12]. Respiratory involvement generally occurs with advanced MS but may occur earlier in the course of the disease, particularly during relapses. Koseoglu et al. [18], in a study of patients with mean EDSS of 4, found results slightly below the predicted value for spirometric parameters; however, results reflected muscle weakness, with a low peak expiratory flow rate. Foglio et al. [6] demonstrated exercise capacity appearing to be reduced in conjunction with reduced respiratory muscle function.

Ponichtera-Mulcare et al. [28] found that aerobic capacity may be altered by peripheral factors such as muscle weakness and fatigue, with an inverse relationship between oxygen uptake ($VO_{2\text{ peak}}$) and EDSS. Maximum voluntary contraction force is reduced in MS [20,30]. Muscle weakness is the consequence of altered central motor drive. Isokinetic assessment shows this muscle weakness even in patients with low EDSS [1,14,30,31] and may play a role in the attenuated response to maximal exercise testing. Atrophy exceeding that observed with short-term disuse and approaching that reported in spinal cord injury was observed in MS patients. Muscle showed fewer type I fibers; fibers of all types were smaller, with reduced enzyme activity, which is consistent with results observed in models of disuse [15,16]. This deficit may affect the ability of people with muscle to benefit from physical training. Thus, specific muscle strengthening must probably be included in a protocol of physical training to improve the benefit. Some studies have indicated that muscle strengthening can positively influence skeletal muscle performance [4,31].

3. Physical training effects

Gehlsen et al. [11] found a real benefit in 10 patients with EDSS < 6 after a 10-week program of aerobic training in balneotherapy for 3 hours/week, with a heart rate under 65–70% of the theoretical maximal rate. Schapiro et al. [33] confirmed these results with an open study of the $VO_{2\text{ max}}$ without controls. Gappmaier et al. [10] studied 13 patients participating in three supervised sessions per week of combined leg and arm cycling for 15 weeks. Training consisted of 40 min of cycling per session at approximately 60% $VO_{2\text{ max}}$, with a significant increase of $VO_{2\text{ max}}$ of 21% from baseline. Petajan et al. [24] prolonged this study and evaluated cardiorespiratory responses in 46 patients randomly assigned to exercise or non-exercise groups. The training consisted of three training sessions per week of cycling with a 5-min warm-up at 30% of $VO_{2\text{ max}}$, then 30 min at 60% of $VO_{2\text{ max}}$, followed by a 5-min cool-down. The exercise group demonstrated a significant increase in $VO_{2\text{ max}}$ of 22%, with increased isometric muscle strength and also an impact on fatigue and quality of life. Furthermore the overall EDSS scores did not change during the course of study. Ponichtera-Mulcare et al. [29], using a similar exercise program of 24 weeks, found a similar increase, of 15%, in $VO_{2\text{ max}}$. The sample was divided into ambulatory patients (EDSS 1–4.5) and semi-ambulatory patients (EDSS 5–6.5). The ambulatory group experienced an improvement of 22%, and the semi-ambulatory group an increase of only 5%. Thus, neurological disability affects exercise training, and more severely impaired individuals may experience a gain in aerobic fitness with such a program. Mostert and Kesselring [21] and Romberg et al. [32] reported results close to those of Petajan. Some variations in results were probably linked to methodology such as duration of the study or modalities of physical training.

Mean exercise time was only 327 min distributed over 14 training units and 3–4 weeks in the study by Mostert and Kesselring [21]. Subjects participated in five supervised training sessions per week, consisting of 30-min bicycle exercise training. Maximal aerobic capacity was not significantly changed, fatigue tended to decrease, and health-related quality of life improved.

Romberg et al. [32] investigated 91 patients with EDSS 1–5.5 [32]. The intervention consisted of strength and aerobic training initiated during 3-week inpatient rehabilitation and continued for 23 weeks at home with three weekly sessions of strength training and one aerobic exercise session without supervision. Health-related quality of life, gait and muscle strength were improved. Mean $VO_{2\text{ peak}}$ was not changed, but some of the exercise patients demonstrated a significant increase. The study was based on self-reports and some of the exercisers may have not recorded their training conscientiously.

Van den Berg et al. [40] recently investigated a 4-week supervised treadmill aerobic training, three sessions of 30 min/week. Individuals were encouraged to train at 55–85% of age-predicted maximal heart rate. The authors showed a significant increase in speed and walking endurance, without

significant variation in the Fatigue Severity Scale score, and with a return toward baseline scores 4 months later.

All these studies confirmed the value of physical training for MS patients and stress the importance of these patients maintaining regular physical exercise to conserve benefits for the long-term. Furthermore, fatigue, muscle strength and quality of life are improved by physical training. The self-reported health-related quality of life is decreased in MS patients, by 30–40% as compared with subjects without impairment, particularly in domains of physical activity, general health, energy and mental health on the MOS SF-36 and SEP-59 scales [23, 41,42]. Depression and neurological disability negatively affect self-reported health-related quality of life.

In a descriptive study examining exercise and well being, Stuijbergen [37] found that regular exercise positively influenced general perceptions of health, vitality and physical and social functioning. Physical activities were evaluated by the Human Activity Profile and quality of life by the SF-36. MS patients had less physical activity than subjects without disability, but MS patients with regular physical activity had a better physical score on the SF-36. The increase for other domains such general health, vitality, social function was not significant. The results of a consecutive study on a larger population support the potential positive impact of exercise on the long-term progression of functional limitation and quality of life for people with MS [38]. In a recent study [17], we found, using the SF-36, the best quality of life scores in patients taking part in physical activity at least 1 hour/week.

4. Exercise and temperature

Heat may induce an increase of symptoms in MS, and cold may improve symptoms. Little variations can result in a great change on neurological deficits. Namerow [22] and Davis et al. [5] reported spontaneous daily variations in clinical symptoms as a consequence of the circadian fluctuation of endogenous temperature, independent of physical exercise. In fact, the influence of temperature varies among patients with MS, as we noticed in a previous epidemiologic study [26].

Ponichtera-Mulcare et al. [28] measured patients' body temperature during exercise and found participants reporting no symptoms during or after the exercise testing, although a variation in the body temperature was noticed. Actually, there is no argument to say that the temperature change can affect physical exercise. Much of the published exercise and MS research reports noted that people with MS can exercise without exacerbating MS-related symptoms [39].

5. Conclusion

For many years people with MS have limited their physical activity because of the fear of increased disability. In fact, lack of physical activity tends to increase muscle weakness and fatigue. Several studies have demonstrated that physical training can benefit people with MS with EDSS < 6, with improved muscular performance, exercise capacity, health-related quality

of life and less impact on fatigue. Regular aerobic physical activity is necessary for maintaining the benefit of the physical training.

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