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Article

Physical exercise for management of cognitive impairment in multiple sclerosis patients

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Abstract: Multiple sclerosis (MS) is an immunological disease affecting the nerves and leads to impaired cognition, walking, balance, fatigue, and depression. The most applicable symptom to all daily living, yet often overlooked, is cognitive impairment. Current research has looked in on the effectiveness physical exercise can have in managing MS. By conducting a literature review of the research, studies show exercise significantly improves several aspects of cognitive function, as well as aerobic fitness, fatigue resistance, ambulatory ability, and mood. All patients are affected differently by MS, so an individualized exercise plan should be prescribed to accommodate needs and disabilities. For mild to moderate impairment, 30 minutes of aerobic exercise 2-3 times per week is recommended. There are a variety of exercises that can be modified to have the same benefits. Theories suggest exercise has this effect by increasing neuroplasticity in the brain and releasing brain derived neurotropic factor, which contributes to the synthesis of neurons. Further studies need to be done on the direct neurological factors influencing cognition as data is limited. This paper reviews the current literature on the impact of physical exercise on multiple sclerosis and its therapeutic implications.

Keywords: Multiple Sclerosis, Cognitive, Exercise, Neurology, BDNF

1. Introduction

Multiple sclerosis is a progressively degenerative autoimmune disease that affects the myelin sheath of neurons. This causes several impairments that lead to difficulty in everyday functioning. Disabilities range from loss of coordination, optic neuritis, loss of memory, muscle degeneration, and more. Currently, there are no cures for the disease. Despite that, there are treatments to help manage the symptoms and slow down its path of progression. Recent studies have been recognizing beneficial results from simple exercise activity on the prevention of the progression of the disease. The purpose of this review is to determine the effectiveness of physical activity as an intervention treatment for multiple sclerosis for daily functioning, especially in the cognitive and muscular functioning aspects, as well as find areas that need more focus for future studies to hopefully one day find a cure.

2. Methods

For this review, a Google Scholar and PubMed search was done. My main search was for "multiple sclerosis" and "physical exercises interventions". I found more precise definitions of what multiple sclerosis is. There are several versions of MS, so I narrowed my research studies to relapsing-remitting multiple sclerosis since it is the most common. Secondly, I searched for the specific cognitive impairments that develop as the disease progresses. I wanted to find the actual effects this disease is to analyze the validity and potential effectiveness of the research treatment interventions. When it came to the physical exercise interventions, my goal was to discover a variety of physical activities used to determine which were most effective and appropriate considering the disabilities that patients experience. All of the relevant information was then compiled to develop an all-around approach to using physical activity for symptom management of multiple sclerosis and find new directives to take. The criteria for the research articles I looked at are limited mostly to peer-reviewed research. I did also include a few review articles to get a holistic stance of what other doctors have already analyzed to compare their analysis with mine. In the primary research done I looked for the use of randomized trials and valid tests for the purpose of those studies.

3. Multiple Sclerosis: The Autoimmune Disease

3.1. Definition, Signs, and Symptoms of Multiple Sclerosis

Multiple sclerosis (MS) is an autoimmune disease where the body's immune system attacks the myelin sheath of the nerve in the central nervous system (CNS). The CNS is made up of the brain, spinal cord, and optic nerves [6]. Myelin is important in the propagation of action potentials along nerve cells enabling them to communicate sufficiently. Therefore, when damaged, nerve signals are slowed or even stopped completely. MS affects each person differently. There are four courses it can possibly take, but the most common is relapsing-remitting (RRMS) [6], so most studies focus on this type.

MS causes several functional impairments. Loss of cognitive function is one of the major debilitating symptoms of the disease. To confirm that there MS causes significant impairment, scientists conducted a study of 40 patients with MS matched to 40 normal controls according to age, sex, and education and gave them a battery of neuropsychological tests [18]. They confirmed that patients with MS do experience memory loss, which can be attributed to their poor performance on the cognitive tests. They also acknowledged impairments in perceptual-motor functioning and increased fatigue among individuals with multiple sclerosis. In a blind clinical judgement, 17.5% of the MS patients tested as definitely impaired, whereas none of the normal controls did [18].

Furthermore, the seriousness of the cognitive impairment in MS patients is an aspect that needs awareness. A study in Holland created a battery of tests and imaging to "The3omains frequently impaired in people with MS are information-processing speed, working memory, verbal and visual memory, verbal fluency, and executive functions" [1]. This makes it difficult to be independent and perform daily life functioning. MRI studies show that these impairments are due to lesions in the brain. What region these lesions are is what determines how the patient is effected and to what extent their disabilities are which is why the disease effects everyone differently [16]. It is important to start treatment early in order to slow down the progression and prevent disabilty symptoms before they occur since there is no actual cure for the disease [15].

3.2. Theories about Causes of Multiple Sclerosis

Understanding what causes the loss of functionality and cognitive ability is important in combatting the symptoms. It is not well understood why patients' cognitive function improves after exercise. Andrew Borror of the Department of Exercise Science at the University of North Carolina developed a hypothesis. He proposed that brain—derived neurotropic factor (BDNF) gets released when exercising [2], which is the main factor contributing to this cognitive improvement. BNDF is a nerve growth agent with a role to support, grow, and differentiate existing neurons of the central and peripheral nervous system [10]. He argues that it gets released from the cerebral endothelium due to cerebral blood flow (CBF) in combination with oxidative stress. That means the cerebral endothelium play a key role in producing and secreting BDNF and therefore in improving cognitive function. If this hypothesis proves to be true, then future research can be done to "optimize" release in order to treat patients with MS, along with those who have had a stroke and in the elderly [10]. Other studies can verify the benefit of exercise in increasing BDNF. A study conducted by Ozkul et al measured the serum levels of suppressors of cytokine signaling (SOCS) 1 and 3 and BDNF before and after 8 weeks of exercise in 36 MS patients and 18 healthy individuals [22]. Their results show significant improvement in BDNF serum, with an average increase of 12.63% for the MS patients after exercise as compared to the control group that only had 0.28% increase. Patients also resulted in improved physcial functionality [22].

4. Physical Exercise as Management of Cognitive Impairment Symptoms

4.1. The Effect of Exercise as Treatment for Multple Sclerosis

There have been several recent studies analyzing the effectiveness of physical exercise as a form of treatment to help with some of the symptoms of multiple sclerosis. Scientists in the department of Neurology at Louisiana State University conducted a study showing that cognitive rehabilitation and L-amphetamine seems to be beneficial in symptomatic treatment for cognitive impairment in MS patients [16]. The use of these drugs is limited though. They noted patients receiving disease-modifying therapies for MS such as cholinesterase inhibitors and memantine have failed, and Ginkgo and exercise have limited data [16]. This research was done in 2012 and since then, there has been extensive work to determine the possibilities the effect of exercise can have on patients with MS.

In a pilot study conducted in 2018 by experts of the Italian Neurological Society, they found a routine cycle ergometer training program to have therapeutic use in individuals with MS [1]. It also showed to improve overall quality of life and depressive symptomatology while ameliorating cognitive disturbances [1]. Another pilot study by Briken et al used patients with moderate disablity (Expanded Disability Status Scale of 4-6) and grouped them in a control, arm ergometry, rowing, and bicycle egrometry group to train for 8-10 weeks [3, 24]. The primary finding was improvement in their aerobic ability. This leads to overall better health and quality of life. The secondary findings were improved walking ability, cognitive function as measured bya neuropsychological test battery, depression, and fatigue [3]. More specifically, it improved "aspects of verbal learning and delayed memory, as well as alertness and shift of attention, but not in working memory or executive function" [3].

Another study by Sandroff et al looked more into why exercise "drives adaptive central nervous system neuroplasticity" [25]. A framework was developed to analyze where cognitive improvements oroginated from when exercise was involved. They argue that "exercise can be viewed as an integrative, systems-wide stimulus for neurorehabilitation because impaired mobility and cognition are common and cocurring in MS" [25]. In other words, exercise stimulates connectivity in the brain, therefore increasing neuroplasticity "based on the integrative processing of multisensory input and associated complex motor output that is required for the regulation of physiological systems during exercise behavior" [25].

4.2. Exercise Prescription for Multiple Sclerosis

There is a variety of activities that showed improvement of cognitive functioning, along with physical fitness benefits as well. Previously, "MS patients were advised not to participate in physical exercise" [5]. A review article that studied research mainly on moderately impaired patients with MS found the recommended exercise to benefit patients is aerobic training at low to moderate intenstiy [5]. Resistence training did show benefit, but the amount of studies conducted on this was low. They did not that when resistence training was combined with aerobic training, conclusions regarded that modality as impossible [5].

For patients with more progressive physical impairments, aquatic therapy showed to be more accessible than resistance training or running [9, 20, 17, 23]. Aquatic therapy also demonstrated a much more significant increase in BDNF when compared to a land-exercise group [9]. They were able to perform more of the exercises which had the same endurance benefit as jogging or walking would have. For imporoving aerobic fitness, between arm ergometry, rowing, and bicycle ergometry, the bicycle was the only one to show significant difference when compared to the control group [3]. Since the disease effects each person differently, it is important to have an idividualized program to assess what each patient needs to focus on improving while accommodating for any disabilities [15].

4.3. Complications for Physical Exercise as Treatment

One problem faced with patients who have multiple sclerosis is rapid fatigue from physical exertion. Multiple sclerosis related fatigue is repoted in 70-80% of patients [19]. For example, in the pilot study by Briken mentioned ealier, only 42 of the 47 participants were able to finish the exercise trials [3]. Sometimes the fatigue can be extremely debilitating and bring on an episode itself [4, 21]. Research done by Ulrik Dalgas for the for the Neurodegenerative Disease Management noted, "Although exercise training may induce a transient worsening of symptoms in some MS patients, it is generally considered safe and does not increase the risk of relapses" [4, 20]. One study found that given the right regimen, patients were actually able to reduce self-reported fatigue [10, 11, 19]. Overall,Dalgas has found exercise to be a "safe and potent nonpharmacological intervention in MS, with beneficial effects on both functional capacity and the brain" [5]. Another less intense form of exercise are activities such as Pilates or yoga [8, 14, 17]. Strengthening of stabilizing muscles improved their balance and coordination [21]. This is important since patients are prone to falls due to an inability to balance.

4. Summary and Practical Applications

Through this literature review, it can be concluded that a leading treatment to reduce the progression of multiple sclerosis is physical exercise. Years ago, findings were limited and the perspective was physical exercise may exacerbate the patients' conditions. Extensive research in the past eight years since then has proven otherwise. Each patient is effected differently, so an individualized exercise plan should be prescribed to have optimal improvements [13]. There are many varieties that can be incorporated into a daily routine to

allow more accommodations for limitations patients may have. It is recommended to do aerobic exercise at low to moderate intensity for at least 30 minutes 2-3 times per week for those who have mild to moderate disability [20]. Considering the many positive benefits that exercise has to offer as a form in the management for MS symptoms, practitioners should indeed start incorporating it as a standard form of treatment with or without the accompany of other treatments. Drugs may or may not have any improvement for the patient and often can cause side effects. Exercise is a low cost, versatile alternative to those drugs.

More research needs to go into finding the proper intensity and duration level to get optimal benefits. Further studies can also focus on the specific causes beyond the broad concept of degeneration of the myelin sheath that leads to loss of cognitive function. Since BDNF plays such a major role in building neurons, more studies should be conducted to determine how it interacts in MS patients and ways to increase its activity. Other future studies should look at finding ways to accommodate the severely disabled patients who are vulnerable to becoming disoriented and fatigued during physical exercise in order to get them to have the same benefits as moderately impaired patients.

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