

Metabolic syndrome in individuals suffering from multiple sclerosis: Why we should not blame the patients

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Abstract

Multiple sclerosis (MS) is a progressive inflammatory disease of the central nervous system that normally leads to impairment and persistent disability at a rather early age. The observation that physical stress can lead to the onset of reversible neurological symptoms has in the past led to patients being discouraged from doing sports. We investigated the current status of research and conclude that this advice may be as incorrect for a majority of MS patients as recent recommendation which encourage individuals with MS to engage in all kinds of physical activity.

Analysis

The occurrence of reversible neurological symptoms during physical exertion was first described by a German scientist in the 19th century.¹⁸ It was not until years later that it was shown that the symptoms were not caused by exercise itself, but by an increase in body temperature during strenuous activity.¹⁷ This results in a temperature-dependent conduction blockade of partially demyelinated nerve pathways, which is considered to be the causative factor. The incidence of this phenomenon varies with the intensity and type of exertion and occurs in 30% to 65% of patients with MS. The duration of symptoms is highly variable. Sensory disturbances under physical activity are short-lived in the majority of affected individuals, and mild cooling can help many patients out of such symptom worsening.⁹

In addition to the actual functional limitations caused by the disease, the degree of disability is by a growing number of researchers believed to be determined due to secondary damage caused by physical inactivity. According to recent studies, MS patients are less physically active and more likely to suffer from obesity, type 2 diabetes, osteoporosis, or cardiovascular sequelae.^{4,5} It is unclear, however, whether these symptoms will persist for long periods of time. However, it is still a completely open question if these findings are just a correlation or a valid causal effect. Just because recent studies indicate that competitive sports are not necessarily and in any case harmful for young MS patients, one should not make the mistake of recommending any sport per se for MS patients.

Physicians who interpret symptoms of metabolic syndrome or cardiovascular damage in their MS patients as a result of abstinence from sports are straying into the realm of mental shortcuts. There may be statistical correlations in some papers, but no reputable study has yet produced causal evidence that MS patients are to blame for other diseases as a result of physical laziness. We know from patients with narcolepsy that they are more likely to be overweight than healthy people. However, in the case of narcolepsy, obesity with all its consequences is primarily caused by damage to structures responsible for both the disturbance of vigilance as well as metabolic

processes that lead to obesity.¹⁹⁻²² This is a fairly recent finding, and many narcoleptics have been blamed for their obesity by physicians who did not ask for causal evidence because stereotypes and pseudo-logic fit too well. So far, no one has any proof that a similar phenomenon is at work in MS, or not. There is an unjustifiable lack of data on this so far, so that the impression that MS patients have metabolic problems due to less physical activity cannot be accepted as scientifically proven, at least a causality can still not be claimed. To actively avoid sports and thus be responsible for symptoms of metabolic syndrome, etc., is disrespectful towards patients suffering from one of the most devastating diseases known by neurology. Those who do so are potentially exposing MS patients to negative stress and a nocebo effect that can be as harmful as lack of physical activity.^{23,24}

What does seem to be true, however, is the recurring claim that exercise-loving MS patients were once discouraged from moderate exercise because of the temperature aspect mentioned earlier. For example, surveys show that one in five to seven MS patients still fear that physical activity is harmful to them. So far, there is no evidence of a negative influence of moderate exercise on the course of the disease. On the contrary, evidence suggests that regular moderate exercise might be able to contribute to the reduction to functional limitations in some patients. A meta-analysis of the Cochrane Center concludes that positive effects of regular and moderate activity in MS patients can be confirmed. Furthermore, moderate exercise seems to have a positive effect on the quality of life in MS patients. But what is “regular” and “moderate” in a specific case? Furthermore, moderate exercise seems to have a positive effect on the quality of life in MS patients.¹⁻⁸ Careful physical activity has direct effects on the immune system. Strong physical exertion leads to an increased susceptibility to infections in the following weeks. For example, a study done with participants of the Los Angeles Marathon showed an increase in the rate of infections from ~2% to ~13% in the following weeks. In contrast, studies demonstrate the protective effect of moderate exercise; for example, the risk of respiratory tract infection is reduced by up to ~30% in trained individuals compared to untrained subjects.¹¹⁻¹⁴ Depending on the duration and intensity of exercise, there is a significant increase in lymphocyte numbers in the peripheral blood during activity (primarily T cells, but also B cells and killer cells). In the recovery phase, however, an immunosuppression lasting up to 24 h is observed: lymphocyte numbers in peripheral blood fall below baseline levels, the proliferative immune response of lymphocytes to a mitogenic stimulus is impaired, and the cytotoxic function of important defense cells is inhibited. Furthermore, a decrease in anti-body secretion by plasma cells could be shown. While previous studies on the influence of exercise on the immune system have generally focused on the consequences of the changes for the defense against infections, the observation that physical exertion can lead to a shift in the balance of type 1 (Th1) to type 2 (Th2) T-helper cells, for example, underscores the potential importance of immune-modulating physical activity for autoimmune processes. An imbalance of Th1/Th2 differentiation might play a role as a pathogenetic factor in MS. Regular moderate exercise could lead to a temporary improvement of the Th1/Th2 balance in MS patients.¹⁵⁻¹⁸ Studies on the influence of

sport on the immune system are surprisingly rare and so far mostly limited to healthy subjects. Only a few studies, each with a small number of cases, have dealt with autoimmune diseases such as MS. An interesting observation was made by Heesen and colleagues.²⁵ They investigated the influence of acute physical exertion on mitogen-induced cytokine secretion (IFN γ , TNF α , IL-10) of trained and untrained MS patients, as well as healthy volunteers in ex vivo experiments. While the cytokine response of trained MS patients resembled that of healthy subjects, there was a clear trend toward attenuated cytokine release in untrained MS patients. This is only one possible indication of a longer-term effect of exercise on the immune system in MS, which underlines the call for detailed studies on the influence of exercise on autoimmune diseases.^{25,26} In animal models, which have very limited applicability to humans, it has been shown that physical activity supports neurogenesis and can promote learning processes by enhancing neuronal plasticity. In practice, physical fitness also seems to counteract the loss of cognitive abilities in MS patients and to promote the recruitment of compensatory centers during cognitive tests. An activity-associated release of neurotrophic factors is discussed as a causal factor. The factor best studied in this context is the brain-derived neurotrophic factor. It has neuroprotective properties and promotes neurogenesis and neuronal plasticity. In the laboratory, increased BDNF levels were measured after moderate exercise in both healthy individuals and patients with MS. However, the extent to which exercise can also influence BDNF expression in immune cells is currently unclear.²⁶

Discussion

While there now seems to be evidence that total abstinence from exercise and physical activity is no longer indicated in MS, evidence is accumulating that moderate activity, such as yoga and activating physical therapy, can be of benefit for patients with MS. Increasing voices, however, advising MS patients to engage in virtually any type of exercise still owe a proof that they do more good than harm with this advice. In addition, multiple sclerosis is an extremely multifaceted disease whose course varies greatly from patient to patient. It is essential to take this fundamental factor into account before providing any lifestyle recommendations.^{9,10,15,16}

Conclusion

A certain positive influence of moderate physical activity on the clinical course of MS seems to exist. Furthermore, immunomodulating and thus course-modifying effects of exercise are at least conceivable, but far from proven. Further studies to evaluate an influence of physical activity on the immunopathogenesis of the disease are necessary and would give MS patients as well as their physicians more certainty.

Conflicts of interest

None.

Illustrations

From the manufacturers, all labels removed.

Ethical standards and patient's rights

This paper is in accordance with the Declaration of Helsinki.

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