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REVIEW

Effects of physical exercise on myelin sheath regeneration: A systematic review and meta-analysis

Effets de l'exercice physique sur la régénération de la gaine de myéline : une revue systématique et une méta-analyse

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Summary
Objectives. — This study aimed to verify the effects of physical exercise (PE) on myelin sheath regeneration (MSR).
News. — The databases searched were MedLine/PubMed, Lilacs, and Scielo. Articles not related to the effects of PE on MSR, concentration of proteins and other factors linked to myelin regeneration, and studies that used medicine concomitantly with PE were defined as exclusion criteria. After removing duplicates, applying exclusion criteria, and checking the reference lists, 21 studies were added to this review and divided in two groups: i) articles assessing the effect of PE on permissiveness of environment in central nervous system to MSR and ii) articles assessing the effect of PE on regeneration of myelin sheath components. The random effect model was used to the meta-analysis of myelin sheath thickness (MST) and G ratio because Cochran's Q test showed high heterogeneity. In the first group, low-intensity physical training was the most common PE adopted among the interventions and resulted in improvement of permissiveness on central nervous system environment. The studies in the second group, low-to-moderate PE

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was the most prevalent protocol adopted among interventions. Additionally, this type of training enhanced MST and maturation. Regarding to meta-analysis, PE was associated with the MST [0.11 (0.05—0.17) μm, $P < 0.001$] and G ratio [−0.04 (−0.06 − −0.02), $P = 0.009$], although the high ($I^2 = 77.1\%$) and moderate ($I^2 = 65.0\%$) heterogeneity, respectively.
Conclusion. — The results suggest that moderate continuous exercise could potentially enhance MSR and improve concentration of myelination-related proteins and as a result, its practice is encouraged to both prevent and treat demyelination.

MOTS CLÉS
Gaine de myéline ;
Activité physique ;
Exercice ;
Santé ;
Plasticité neuronale ;
Cerveau

Résumé
Objectifs. — Cette étude visait à vérifier les effets de l'exercice physique (PE) sur la régénération de la gaine de myéline (MSR).
Informations. — Les bases de données recherchées étaient MedLine/PubMed, Lilas et Scielo. Les articles non liés aux effets de l'EP sur MSR, la concentration de protéines et d'autres facteurs liés à la régénération de la myéline, et les études qui ont utilisé des médicaments en même temps que les PE ont été définis comme des critères d'exclusion. Après avoir supprimé les doublons, en appliquant les critères d'exclusion et en vérifiant les listes de référence, 21 études ont été ajoutées à cette revue et divisées en deux groupes : i) articles évaluant l'effet de PE sur la permissivité de l'environnement dans le système nerveux central à MSR et ii) évaluation des articles sur l'effet de l'EP sur la régénération des composants de la gaine de myéline. Le modèle d'effet aléatoire a été utilisé pour la méta-analyse de l'épaisseur de la gaine de myéline (MST) et du ratio G car le test Q de Cochrane présentait une hétérogénéité élevée. Dans le premier groupe, la formation physique de faible intensité a été l'adoption de l'EP plus fréquent parmi les interventions et a entraîné une amélioration de la permissivité sur l'environnement du système nerveux central. Les études dans le deuxième groupe, PE à faible à modérée ont été le protocole le plus répandu adopté parmi les interventions. En outre, ce type de formation a amélioré le MST et la maturation. En ce qui concerne la méta-analyse, le PE a été associé au MST [0,11 (0,05—0,17) μm, $p < 0,001$] et le ratio G [−0,04 (−0,06—−0,02), $p = 0,009$], bien que le haut (I2 = 77,1 %) et une hétérogénéité modérée (I2 = 65,0 %), respectivement.
Conclusion. — Les résultats suggèrent que l'exercice continu modéré pourrait améliorer la MSR et améliorer la concentration des protéines liées à la myélinisation et, par conséquent, sa pratique est encouragée à la fois pour prévenir et traiter la démyélinisation.

1. Introduction

Myelin sheath is a lipid-protein substance, which wraps axons and acts as an electrical insulator to facilitate electrical conduction in axons [1,2]. Moreover, it is produced from Schwann cells in the peripheral nervous system (PNS) and from oligodendroglial cells in the central nervous system (CNS) [1]. Furthermore, those axons with large myelin sheaths, and consequently large diameter, conduct impulses more rapidly than small nonmyelinated fibers [3]. On the other hand, damage or destruction of myelin along myelinated nerve fibers results in nervous system dysfunction known as demyelinating diseases. These are characterized by formation of plaques, lowering nerve impulses velocity, and chronic inflammation, as it happens with multiple sclerosis (MS) [2,4]. In this sense, it is estimated that MS affected around 400,000 people in United States and about 2.5 million worldwide in 2012 [5].

However, the etiology of this disease is unknown. Recently, studies have identified some genetic factors which may lead to an immune response and damage to the myelin sheath, myelinating cells, and axons [5]. Nevertheless, there has been evidence showing that about 70% of identical twins are discordant for MS, suggesting that environmental and other unknown factors are likely to contribute to disease susceptibility [6]. In addition, progressive demyelination in CNS may facilitate inflammation at demyelinated areas [4], muscle weakness, fatigue, spasticity, and other sensory and cognitive dysfunctions, which may lead to a decrease in physical activity (PA) levels [7]. This fact could explain the small level of PA of people with MS when compared to general population [8—10].

In addition to having an unknown etiology, most of demyelinating diseases have their treatment unknown as well [5]. Studies have reported that specific myelin components, such as myelin-associated glycoprotein (MAG) and Nogo-A, both expressed by oligodendrocytes, act as the major source of inhibition for growing neurites after CNS injury [11,12]. Besides, several pieces of evidence have been shown on the beneficial effect of PA on axonal growth

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