Chapter 1

Physical Exercise as a Complementary Treatment for Parkinson's Disease: State of the Art and Future Directions

Renato Sobral Monteiro-Junior[1,2,3*], Ana Elisa Montalvão Braga[2], Luiz Felipe da Silva Figueiredo[2], Maria de Fátima Matos Maia[1]

[1]Department of Physical Education and Sport, Universidade Estadual de Montes Claros, Brazil
[2]Neuroscience Laboratory of Exercise (LaNEx – UERJ/UFRJ), Brazil
[3]Universidade Federal Fluminense, Niterói, Brazil

[*]**Corresponding Author:** Renato Sobral Monteiro-Junior, Department of Physical Education and Sport, Universidade Estadual de Montes Claros, Montes Claros, Minas Gerais, Brazil, Tel: +5521976622715; Email: monteirojuniorms@gmail.com

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Abstract

Treatments for Parkinson's disease (PD) as drug therapy, surgery and others are expensive. Physical exercise has been able to improve many aspects related to PD. People who are more physically fit have the risk of developing PD 33% lower than sedentary individuals. Physical exercise stimulates many neurobiological mechanisms in the brain. In this chapter we show how physical exercise can help healthy professionals and patients to manage PD.

Introduction

Pharmacologic therapy is currently the most common treatment, but not the only one for the control of Parkinson's Disease (PD). Other methods, such as pallidotomy and transcranial stimulation (magnetic or direct current) have been used [1-3]. However, the cost of purchasing the drugs or the above methods can be high, in addition to troublesome depending on the intervention caused the patient. In this context, less costly strategies and more pleasurable intervention is needed. One such strategy is the use of physical exercise, which studies have shown good prospects in their use [4].

People who are more physically fit have the risk of developing PD 33% lower than sedentary individuals [5]. Depending on the time of life and the intensity of the exercise, the protective effect against the disease may be even higher, reaching 38% [6]. The aerobic exercise and strength are the most investigated and show results of improvement in motor and cognitive functions, as well

as overall quality of life [7,8]. So to consider exercise as a PD treatment helper method, is somewhat motivating because the exercise programs are low cost and can effect positively in changing the lives of patients with PD.

This chapter will show some topics about neurobiological mechanisms of physical exercise, and will discuss practical applications.

Effects of Physical Exercise On PD

Both aerobic exercise and strength seems to result in improved motor and cognitive functions in addition to the quality of life in individuals with PD. However, in addition to the physiological effects, strength training appears to result in greater benefit for patients with the disease due to functional aspects related to the activities of everyday life. Bloomer et al. [7] investigated the impact of eight weeks of resistance training, done twice a week, on oxidative stress and antioxidant factors of 18 subjects divided into two groups. Although not identified differences in the activity of antioxidant enzymes, the group that performed strength training showed significant reductions between 15-16% in serum oxidative stress biomarkers (H_2O_2, malondialdehyde, among others), while the control group showed increase of up to 14% on these markers. Importantly, this reduction occurred in a relatively short training period (eight weeks), with weekly frequency

twice. This shows the positive outlook of rapid physiological adaptation to strength training, indicating an optimal dose-response relationship. In addition, individuals with PD who perform high-intensity strength training in addition to a balance training showed better responses to the control of body stability while maintaining performance even during a period of one month of detraining [9]. These findings support the notion that the effects obtained with such training setting is maintained for some time, even with the interruption of activity. Such benefits can be related to neurobiological changes due to exercise especially neurogenesis [10] and an increase in the synthesis of neurotransmitters, such as dopamine [11]. It is possible that these results are associated with neuroprotection [6], already mentioned earlier in this chapter.

How can Physical Exercise Modulate Neurobiological Mechanisms?

The reduction in oxidative stress seems to play a key role in the reduction of progression of Parkinson's disease. It can minimize the cyclical effect of neuro-degeneration in the substantia nigra controlled by microgliocytes. Sharply exercise induces oxidative stress by increasing ROS production. These responses have been described in both athletes [12,13] as in patients with Parkinson's disease and in healthy individuals [14]. However, it should be considered that these studies [12-14] used as methodo-

logical approaches strenuous exercise. This fact has important implications since activities with low intensities do not appear to alter the balance between ROS production and action of antioxidants [15]. Moreover, it should also be considered that the nutritional status can affect the antioxidant mechanism [15], thus the results presented in the study should be interpreted with caution. Also, it is important to remember that the human body adapts only under stimulus conditions, such as stress.

In relation to chronic responses, physical exercise can stimulate production of neuro-protective factors that optimize antioxidant mechanisms, thus slowing the progression of Parkinson's disease [16]. Previous studies have reported improvements of parameters related to oxidative stress both in humans [7] as in rats [17] undergoing strength training and aerobic respectively. In a study conducted in rats with induced Parkinson, aerobic training promoted increase of antioxidant enzymes (superoxide dismutase and catalase) and reduced oxidative damage in lipids and proteins [17]. This phenomena can be enhanced when combined with the production of trophic factors stimulated by exercise. Trophic factors are proteins and hormones that act on cell division and growth. The best known substances are: nerve growth factor derived from the brain (BDNF), growth factor similar to insulin (IGF-1), and vascular endothelial growth factor (VEGF) , neurotrophin-3 (NT3), neurotrophin-4 (NT4), growth

factor of fibroblasts (FGF-2), growth factor glial cell line (GDNF), growth factor nerve (NGF), among others [18-20]. These mechanisms are important in maintaining survival of neurons as well as their proliferation. The trophic factors are "fertilizer" to the brain, causing neurons to improve their operation. Thus, the modulation of the synthesis and release of neurotransmitters, the amount of protein carriers and the number of membrane receptors [21] may increase. Thus, according to the above phenomena in the central nervous system, exercise should be considered as a treatment that help,manage symptoms related to mental disorders, as in PD.

Trophic factors stimulated by exercise are known for their action in specific cells. Thus, for each function, certain cells undergo neurotrophic effect that will generate appropriate responses. The best-known phenomena resulting from the signaling processes of trophic factors for neurons depending on the exercise and that may result in improvement of symptoms of PD are neurogenesis, synaptogenesis and angiogenesis [22-24]. One might suppose that, through these mechanisms a reorganization of neuronal circuits would occur, making the most propitious neuronal morphology to a healthy development. For example, regeneration of axons damaged by disease, increased dendritic branching, decreasing the distance between the pre neurons and postsynaptic [25].

New Perspective

New methods have been introduced in the treatment of PD. Recent one of these methods is virtual rehabilitation (VR). This treatment uses an interface patient-computer where required motion for interaction with virtual environment in real time. Currently, the advances in technology allow us to use several kinds of devices for this treatment such as: head-mounted glasses, computers, electronic games, among others. These devices can generate two or three dimensional virtual environment, causing different types of immersion [26].

Currently, the evolution of electronic games is generating many possibilities for clinical settings. The use of electronic games with virtual reality and movements simultaneously is known as exergame (see reference 30). Lee et al. [27] showed an improvement of postural balance, activities of daily living and depressive symptoms of patients with PD after a treatment composed by virtual reality dance exercise. Mirelman et al [28] have seen that virtual reality exercises can be included in treatments to improve gait and cognitive functions and reduce fall risk in patients with PD. Besides research needs to advance in this field, health professionals should be ready to open their mind for this new method of treatment.

Practical Applications

Currently there are practical considerations for exercise prescription for people with PD.Aerobic training is recommended activity in cycle ergometer and support body with a weekly frequency of three to five times. The intensity of aerobic training should be progressive in accordance with the initial level of fitness of the individual, ranging as follows: Phase 1 < 40% of Reserve Heart Rate (RHR) or VO_2 of Reserve (VO_2R) (Borg CR10 = 2, light); Phase 2 < 60% RHR or VO_2R (Borg CR10 = 3, moderate); and Phase 3 > 60% RHR or VO_2R (Borg CR10 > 4, relatively high). As already mentioned, the progression of the intensity will depend on the level of trainability of the subject beyond the stage of the disease. It notes that the familiarization exercise is necessary because the motor symptoms of PD hinder the realization of the activities. Therefore, to ensure the safety of the individual, increased intensity (especially if the exercise is performed on a treadmill) is recommended only when security is evident [29].

With regard to strength training, the recommendations prioritize the strengthening of the lower limbs, with weekly frequency of two to three times, with intensities of 40-50% 1maximum repetitions (MR) (light) and 60-80% 1MR (moderate / high), taking into consideration the conditions of the patient, as described above. In addition to aerobic training and strength, functional exercises, especially those involving balance and gait are also indicated

[29]. Exercises for increase motor function and mobility, cognitive abilities, activities of daily living, falls prevention and quality of life are needed. One hour of exercise per day is sufficient to generate the beneficial responses mentioned in this text.

Conclusion

Physical exercise can trigger acute or chronically important biological phenomena for the treatment of Parkinson's disease. The physiological adaptations as a result of regular training can increase production of neuroprotective factors, providing better response to oxidative stress and maintaining neuronal health as well as physical and functional benefits. An exercise program systematized, including aerobic activity, strength training and functional tasks are recommended to treat the disease and improving independence and quality of life.

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