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A MINI-REVIEW ON THE EFFECTS OF EXERCISING AND OBSESITY IN PARKINSON'S DISEASE

Daniel TIMOFTE[1], Andrei CIOBICA[2], Cezar HONCERIU[2], Florin TROFIN[2], Alin CIOBICA[3,4,*], Dumitru COJOCARU[2,4]

[1]"Gr. T. Popa" University of Medicine and Pharmacy, 16 Universitatii Street, 700115, Iasi, Romania

[2]"Alexandru Ioan Cuza" University, Bd. Carol I, nr. 11, Iasi, 700506, Romania

[3]Department of Research, Faculty of Biology, "Alexandru Ioan Cuza" University, Bd. Carol I, nr. 11, Iasi, 700506, Romania

[4] Academy of Romanian Scientists, 54 Splaiul Independentei 050094, Bucharest, Romania

* Corresponding author: Alin CIOBICA email: alin.ciobica@uaic.ro

Abstract

Recent knowledge is supporting physical activity as an important preventive factor against the onset of neurological disorders such as Parkinson's disease, even stating that physical exercising is crucial for the maintenance or for slowing down the decline of optimal functional ability levels in these patients, as we will go to detail in the present mini-review. Moreover, even if lately there is a relatively large amount of epidemiological data suggesting that physical activity can have protective functions in the context of Parkinson's disease development, currently there is not sufficient information to enable a precise description for the best exercise regimen for patients with Parkinson's disease. In this way, it seems that it is advisable to combine aerobic exercises with other activities that are beneficial for the neuromuscular system (e.g., strength/power training and stretching), balance function and the performance of motor coordination. Moreover, the development of coordination associated with the stimulation of psychomotor capacity seems particularly relevant for PD subjects, considering the specificity of their pathology involving movement command and control processes.

Key words*:* Parkinson's disease, exercising, neuromuscular system.

Exercising and Parkinson's disease pathology

Neurodegenerative disorders such as Parkinson disease (PD) represent a major medical concern for health professionals and national healthcare societies (Hritcu et al., 2008). This disorder results from progressive neuronal dysfunction and neuronal cell death leading to progressive disability and eventual death

(Ciobica et al., 2012). Classical signs and symptoms specific to this disorder include motor problems, cognitive impairment, behavioural disturbances, and systemic or genetic abnormalities (Foyet et al., 2011, Balmus et al., 2016).

Unfortunately, there is no cure and few cost-effective drug agents for treating people with Parkinson disease (Olanov et al., 2009; Evans et al., 2011). In this way, recent advances in understanding the pathogenic mechanisms responsible for each disorder may aid in the identification and development of cost-effective disease-modifying agents in the future. However, cost-effective treatments, with disease-modifying properties and symptomatic benefits are required in the short term.

Moreover, modern knowledge are supporting physical activity as an important preventive factor against the onset of neurological disorders such Alzheimer's disease (AD) and Parkinson's disease, even stating that physical exercising is crucial for the maintenance or for slowing down the decline of optimal functional ability levels in patients with neuropsychiatric modifications (Honceriu et al., 2016; Sandu et al., 2014, Ciobica et al., 2016), as we will going to detail in the present mini-review, by insisting on PD pathology.

However, currently there is insufficient information to enable a precise definition of the best exercise regimen for patients with AD or PD.

In addition, aerobic exercise is increasingly recommended by therapists because of its role in relation to angiogenesis, as well as the liberation of neurotrophic factors (increases in cerebral blood flow and cerebral plasticity). In fact, as we will insist later on, aerobic exercise is a necessary part of the treatment for AD or PD, but aerobic exercise alone is probably not the best activity. In this way, strength/power training, Tai Chi, balance/coordination, and other types of physical exercises also contribute to reconditioning, maintaining, and improving the cognitive and motor functions of AD and PD subjects.

In fact, there is a relatively large amount of epidemiological data suggesting that physical activity can somehow prevent the development of Parkinson's disease (PD) (Alonso et al., 2011).

In this way, some studies found that the risk of developing this disease appeared to be inversely associated with the amount of physical activity practiced throughout life (Chen et al., 2005, Xu et al., 2010).

Still, it has to be mentioned that a possible important limitation of these observational studies is that subjects predisposed to develop PD may naturally tend to avoid physical activity prior to the onset of the clinical symptoms of the disease. Furthermore, the protective effect of physical exercises against this pathology appears to be particularly large when practiced at young-to-middle adulthood (i.e., around 35-39 years old) and at the end of life. Thus, Xu et al. suggested that people who practice cardiovascular exercises during these two periods of their life have a 40% lower risk of PD, as compared to people who remained inactive during the same periods (Xu et al., 2010).

Moreover, in a study involving 48,574 men and 77,254 women, Chen et al. found that the direct relationship between the amount of physical activity and the risk of developing PD was only significant in men (Chen et al., 2005).

In addition, strength training has been shown in recent years to be beneficial for people with Parkinson disease.

Still, consensus regarding its utility for these disorders nevertheless remains contentious among healthcare professionals. In this way, increased clarity is required, especially in regards to the type and magnitude of effects, as well as the response differences to strength training between individuals with Parkinson disease.

In fact, in many studies strength training has been shown to improve the muscle strength and walking speed of PD patients which are not severely affected by the disease (Hass et al., 2012 , Lima et al., 2013).

Also, accumulating evidence are suggesting that strength training is a useful therapy for addressing many of the clinical features which are present in individuals with neurodegenerative disorders (Falvo et al., 2008, Hindle et al., 2013).

By definition, strength training refers to an intervention in which participants train a muscle or group of muscles against an external resistance (Esco et al., 2013). Whereas evidence suggests that lower limb strength training (i.e., leg press, knee extension, and knee flexion) is beneficial for individuals with Parkinson disease and multiple sclerosis (Shulman et al., 2013, Schilling et al., 2010), consensus regarding the effects, magnitude of those effects and disease-dependent responses remain contentious.

By contrast, the therapeutic utility of strength training is well recognized in the elderly (Nelson et al., 2007), individuals with mild cognitive impairment and in those that have suffered a stroke. In this way, health benefits associated with strength training in elderly individuals include improvements in strength (Fiatarone et al., 1990), cardiorespiratory capacity (Pereira et al., 2012), mood (Pereira et al., 2013), cognition (Cassilhas et al., 2007) and health-related quality of life (Levinger et al., 2007).

Moreover, in individuals who have suffered a stroke, strength training has been found to improve muscular strength, upper and lower limb function and performance on functional tasks (Ada et al., 2006). Improvements in selective attention, conflict resolution, associative memory and regional patterns of functional brain activity have also been observed after strength training in seniors with mild cognitive impairment (Nagamatsu et al., 2012).

Regarding the specific effect that resistance training has on patients suffering from PD, three randomized (Shulman et al., 2013; Corcos et al., 2013, Sage et al., 2011) and one nonrandomized controlled trial (Dibble et al., 2009) evaluated the effect of strength training on clinical disease progression using the Unified Parkinson Disease Rating Scale Version 3.

In this way, Corcos et al. in 2013 reported a significant improvement on the Unified Parkinson Disease Rating Scale Version 3 in the intervention group (7.4 point decrease), but not in the control group after 24 months of strength training. In addition, Shulman et al. in another study in 2013 similarly reported a significant improvement on the motor subscale of the Unified Parkinson Disease Rating Scale Version 3 in the strength training group. Furthermore, Sage et al (Sage et al., 2011) found a significant improvement on the Unified Parkinson Disease Rating Scale Version 3 in the strength training group. In contrast, Dibble et al. in 2009 found no improvement on the Unified Parkinson Disease Rating Scale Version 3 in the intervention group after strength training.

In addition, other studies concentrated on the effect that strength training has on specific areas that are affected by PD. Three randomized (Shulman et al., 2013, Prodoehl et al., 2015, Paul et al., 2014) and 3 nonrandomized controlled trials (Schilling et al., 2010, Hass et al., 2012, Dibble et al., 2006) evaluated the effect of strength training on mobility in individuals with Parkinson disease. Mobility in these studies was assessed using the 10 meter timed walk test, 6 minute walk test, 50 feet walk test and timed up and go.

Moreover, one study by Paul et al. in 2014 did not report significant changes in mobility after strength training. In contrast, Prodoehl et al. and Shulman et al. found significant improvements in mobility as a result of strength training. In addition, the 3 nonrandomized controlled trials (Esco et al., 2013, Sabapathy et al., 2011, Fimland et al., 2010) that reported on mobility as an outcome also documented improvements in this matter.

Regarding the effect on balance, two randomized (Prodoehl et al., 2015, Paul et al., 2014) and 2 nonrandomized controlled trials (Schilling et al., 2010, Sabapathy et al., 2011) examined the effect of strength training on balance outcomes in Parkinson disease. In this way, balance was evaluated by using the single leg stance, choice stepping task, berg balance scale, functional reach test, 5 times sit to stand test, and the activities-specific balance confidence scale.

Moreover, Paul et al did not find a significant improvement in balance as a result of strength training, while Prodoehl et al. reported in contrast a significant improvement in balance after strength training. Still, both nonrandomized controlled trials (Schilling et al., 2010, Sabapathy et al., 2011) were unable to find a significant improvement in balance after strength training.

Another randomized trial (Corcos et al., 2013) examined the effect of strength training on functional capacity, assessing functional capacity by using the modified Physical Performance Test and reporting no significant changes after strength training in the intervention compared to the control group.

Another area of interest in any cognitive impairment is the quality of life of the patients. In this way, two randomized (Shulman et al., 2013; Corcos et al., 2013) and 1 nonrandomized controlled trial (Dibble et al., 2006) evaluated the effect of strength training on quality of life. The quality of life was assessed in all 3 trials using the 39-Item Parkinson Disease Questionnaire. Both randomized controlled trials (Falvo et al., 2008, Hindle et al., 2013) did not report a significant improvement in quality of life after strength training. By contrast only Dibble et al. reported a significant improvement in quality of life in the intervention group after strength training.

Also, another randomized controlled trial (Shulman et al., 2013) evaluated the effect of strength training on mood in Parkinson disease, but found no significant changes in mood after strength training using the Beck Depression Inventory.

In addition, no significant change in fatigue after strength training in a strength training intervention group or high- and low-intensity treadmill intervention groups was found in one randomized controlled trial (Ada et al., 2006), as they used the 16-item Parkinson Fatigue Scale for measuring the fatigue in PD patients.

Moreover, we have to mention that another two randomized controlled trials (Hindle et al., 2013, Medina-Perez et al., 2014) evaluated the effect of strength training on falls in people with Parkinson disease, with falls being assessed by using two scales, the New Freezing of Gait Questionnaire and Falls Efficacy Scale. Still, no trial reported a significant effect on falls outcomes after strength training.

Also, in regards to the muscle volume, one nonrandomized controlled trial (Dibble et al., 2006) evaluated the effect of strength training on quadriceps muscle volume in Parkinson disease. As expected, their results showed a clear and significant increase in quadriceps muscle volume, by using magnetic resonance imaging after strength training in the intervention group only.

Same aspects were also demonstrated in animal models of Parkinson's disease, including by our group of research, which reported in a preliminary study that physical exercising seems to reduce anxiety, depression and memory deficits (Ciobica et al., 2015) associated with a 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced rat model of PD (Ababei et al., 2015). In fact, we mostly want it to see if induced physical exercising in an MPTP-induced rat model of PD (20 mg/kg i.p.), will result in any changes in memory (as tested in Y maze), anxiety (as tested in elevated-plus-maze) and depression-like behaviour (forced-swim-test), as compared to a non-exercised control group of rats which also received MPTP, as the exercising was performed on an adapted treadmill, for 2 weeks (3 series of 5 minutes/day).

Thus, our mostly unpublished results showed an increased time spent by the rats in the open arms of the elevated-plus-maze at in the group of exercised MPTP group, together with a significant decrease of stretching behaviour and increased head dipping, as compared to non-exercised MPTP group, factors which suggested an anxiolytic-like manifestation. In addition, spontaneous alternation in Y maze (index for immediate memory), and swim time (anti-depressive index) in forced swim test were increased in the exercised rats with an MPTP-induced model of PD (Ciobica et al., 2015).

In the same context, we could mention here the fact that oxidative stress status could be another key player in the positive roles exerted sometimes by the various exercising performing, considering for example that our group previously demonstrated the importance of vitamin C and oxidative stress in general in both exercising rats or human patients (Trofin et al., 2014, 2017), by using original or general oxidative stress markers determinations (Cojocaru et al., 2005, 2007, 2010). Of course, this could be also correlated with increased oxidative stress status in most of the neuropsychiatric disorders (Ciobica et al., 2011, Padurariu et al., 2013, Stefanescu et al., 2012, Bild et al., 2013), including in Parkinson's disease (Hritcu et al., 2011; 2013), as we previously mentioned in this mini-report.

Thus, it seems that strength training is having a positive effect on disease progression in people with Parkinson disease (Unified Parkinson Disease Rating Scale-Version 3). Interestingly, improvements in disease progression were observed also in a cohort with mild-to-advanced disability that were not on medication, suggesting that strength training alone may be capable of positively impacting on disease progression in individuals at all stages of Parkinson disease. In this way, it seems that this positive effect of strength training on disease progression may have been mediated by favourable central changes. For instance, recent evidence showed that repetitive force generation increases neuronal activation in the basal ganglia, thalamus, parietal cortex, cerebellum and motor cortex (Ehrsson et al., 2000).

Furthermore, emerging evidences have shown that exercise interventions can increase regional brain volume and structural connectivity in patients with Parkinson disease and other neurodegenerative disorders (Sehm et al., 2014), suggesting fundamental implications of these aspects in the neuropathology of Parkinson’s disease.

Conclusions

Recent knowledge is supporting physical activity as an important preventive factor against the onset of neurological disorders such as Parkinson's disease, even stating that physical exercising is crucial for the maintenance or for slowing down the decline of optimal functional ability levels in these patients. Moreover, even if lately there is a relatively large amount of epidemiological data suggesting that physical activity can have protective functions in the context of Parkinson's disease development, currently there is not sufficient information to enable a precise description for the best exercise regimen for patients with Parkinson’s disease. Still, it seems that it is advisable to combine aerobic exercises with other activities that are beneficial for the neuromuscular system (e.g., strength/power training and stretching), balance function, and the performance of motor coordination. Even more, the development of coordination associated with the stimulation of psychomotor capacity seems particularly relevant for PD subjects, considering the specificity of their pathology involving movement command and control processes.

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