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DUAL-TASK EXERCISE AS A THERAPY FOR EXECUTIVE MOTOR FUNCTION IN PARKINSON'S DISEASE

original paper
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ABSTRACT
Purpose. To evaluate the effects of aerobic exercise with dual-task on the motor function in patients with Parkinson's disease.
Methods. Clinically evaluated by the Unified Parkinson's Disease Rating Scale – III and the Senior Fitness Test battery, 20 patients with Parkinson's disease were randomly divided into a control and an experimental group, with the latter performing a 4-week program of water-walking in a deep pool while executing dual-tasks. Evaluations were made before and after 4 weeks in both groups.
Results. Patients with Parkinson's disease revealed significant improvements in pre-/post-exercise motor function, with a moderate effect ($p < 0.001$; $d = 0.44$). Bradykinesia ($p < 0.001$) and agility ($p < 0.001$) exhibited significant changes individually.
Conclusions. Regular exercise combined with executive challenge such as dual-task may counteract the advanced motor symptoms of Parkinson's disease neurodegeneration.
Key words: dual-task exercise, aerobic exercise, executive function, motor control, Parkinson's disease

Introduction

Parkinson's disease (PD) is a neurodegenerative disorder that affects 10–14 new individuals per 100,000 people a year in the world, according to WHO. Usually manifested after the 5th decade of a life, PD is primarily expressed by the motor symptoms of hypokinesia (partial loss of muscle movements), bradykinesia (slowness of movements), rigidity, and resting tremor [1]. Such movement disorders rise as a consequence of a progressive neuronal loss in sub-thalamic nuclei, importantly involved in the central control of voluntary movement [2]. The disease's severity is described in stages of advance that represent the degree of motor impairment, with special attention to patient's balance, speed of movements and gait [1]. Clinically, the patients can be assessed within 5 stages of motor impairment, as recommended by the Movement Disorders Society – Hoehn and Yahr stating scale (Figure 1).

Modified Hoehn and Yahr scale

1.0: Unilateral involvement only
1.5: Unilateral and axial involvement
2.0: Bilateral involvement without impairment of balance
2.5: Mild bilateral disease with recovery on pull test
3.0: Mild to moderate bilateral disease; some postural instability; physically independent
4.0: Severe disability; still able to walk or stand unassisted
5.0: Wheelchair bound or bedridden unless aided

Figure 1. Hoehn and Yahr recommended scale for Parkinson's disease staging [16]

PD slowly evolves in time, with the lesions in the central nervous system initiating quite before the first symptoms, which makes it possible to take decades for the disease to be fully visible and reveal the whole symp-

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tomatic picture. The disease course starts from intraneuronal lesions, continually progressing in severity throughout the encephalon, in predictable patterns [3, 4]. Patients with PD may live long periods with the disease and supposedly have had it in a 'blind' phase for even more time than after diagnosis [5].

Currently, PD treatment focuses on the recovery of the dopaminergic transmission depletion caused by the loss of dopamine-deliver neuronal tissue, but the drug efficacy is not fully satisfying and may lead the patient to accumulation of new motor disturbances as a side effect [6]. Therefore, the search for new opportunities to improve the patients' status or to reduce their symptoms is an actual challenge.

Voluntary movements require a more advanced strategy of executive control than externally generated stimuli, involving integrated cognitive functions [7]. Therefore, cognitive-motor interference based therapies, referred to as dual-task (DT) ones – when two tasks are performed and simultaneously interact within primary motor cortex – have been well required for patients with motor impairment. Such methodology has shown to provoke significant adaptive changes in the executive processing of patients with PD [8]. For instance, great costs of cognition have been evidenced in individuals with PD while performing DT whereas their inefficiency to walk during a DT was associated with losses in specific domains of executive functions [9].

Exercising, instead, physiologically impacts on the metabolic profile of individuals with and without disease, thus improving the trophic support necessary for neuroplasticity [10], as it has been observed in brain areas specifically related to the executive function [11, 12]. Moreover, a symptomatic relief pronounced by exercise in individuals with PD is attributed to an enhance of dopaminergic transmission in the same circuitry as those assessed by medication [13]. Additionally, DT strategies have also been successfully approached in people with PD in order to recover functional capacities [14].

As current pharmacological and surgical approaches are poorly effective in the control of motor symptoms in PD [15], the appropriate exercise would potentially suit as a complementary therapy for the recovery and preservation of the patients' motor functions, even for those in advanced stages of the disease. In this study, patients with PD were submitted to a water-walking DT exercise program in order to check the effect of a 4-week program on their executive motor function.

Material and methods

Participants

The total of 20 patients with PD (stages 2–3 on the Hoehn and Yahr scale), aged 59–73 years, with a medical permission to exercise were recruited from the Neurology Department of University Hospital Onofre Lopes at the Rio Grande do Norte state, Brazil. The subjects were randomly divided into equal groups (10 individuals each). The experimental group (EG) was enrolled in a 4-week aerobic exercise program with 30-min sessions of water-walking with DT, while the control group (CG) remained in a sedentary routine during the same period. The exclusion criteria involved inability to walk independently, as well as lack of completion of at least 85% of the exercise program.

Assessment procedures

The subjects were briefed on the procedures and objectives of the exercise program, and completed demographic and psychometric questionnaires referring to executive function and fitness evaluations. All tests were conducted in phase ON of medication, that is between 20 and 40 min after the latest dose of levodopa. The executive function and fitness evaluations comprised the Unified Parkinson's Disease Rating Scale (UPDRS), part III, which incorporates elements from the existing motor control scales compiled into one [16]; and the Senior Fitness Test (SFT), referring to a non-laboratory battery of tasks used to assess the physical valences of strength and agility [17]. All the physical tests were applied 4 days both before and after the exercising period.

Water-walking program

The EG underwent a 2-week adaptation phase in a 120-cm deep pool, 25/12.5 m sidelong, with the water controlled for pH and chlorine, and of natural temperature (28–32°). The subjects had to wear a Colet Power EVA floater for safety. Heart rate (HR) and blood pressure (BP) were recorded before and after all sessions.

The adaptive phase consisted of 3 goals: (1) to walk along the entire width (12 m) of the pool without any help; (2) to walk all the length (25 m) of the pool without help; (3) to walk along the four corners of the pool without help. These stages could require more than 1 session. During this phase, Borg scale of perceived exertion was introduced for subjective control of intensity.

In the exercising phase, the subjects had a 10-min warm-up (free water-walking), then they were positioned at the longitudinal side of the pool (12.5 m) and, at the evaluator's signal, they started walking along the length of the pool (25 m) as fast as possible, from one side to another, during 30 min. To stimulate speed during the walk, they were given the mission of carrying the biggest number of 'flags' from one side of the pool to the other. In addition to this walking, one motor task – meaning new movements to be executed either with the arms or legs, or the whole body – was requested from the subjects at the frequency of 1/min, summing up to 15 different motor tasks plus 15 min of free water-walking each session. Data from Borg scale were collected every 10 min per session. All the sessions were terminated with 10 min of cooling down and stretching exercises. The motor tasks added to the water-walking were previously tested and recorded, and then executed in a systematic sequence.

Statistical analysis

Normality and homogeneity of variances were verified by the Shapiro-Wilk and Levene's tests, respectively. Parametric variable data are presented as mean and standard deviation, and nonparametric data as median and interquartile range. Data from the SFT were normalized by logarithmic transformation. The independent *t*-test was used to compare parametric variables, and the Mann-Whitney U-test for non-parametric analysis. ANOVA split-plot (2 × 2) with Bonferroni's *post hoc* were applied for inter- and intragroup comparison of all dependent variables. Size effect was calculated by partial eta squared (η^2_p) to indicate the proportion of variance in the dependent variable explained by the independent variable, and Cohen's *d*. The statistical procedures were carried out with the SPSS 22.0 software (Statistical Package for Social Sciences, Chicago, USA). The significance level was set at $p < 0.05$ for all tests.

Ethical approval

The research related to human use has been complied with all the relevant national regulations and institutional policies, has followed the tenets of the Declaration of Helsinki, and has been approved by the authors' institutional review board or an equivalent committee.

This study, registered as U1111-1191-0247, has been approved by the Institutional Human Research Ethics Committee in accordance with Resolution No. 466/2012 of the Brazilian National Health Council and the Code of Ethics of the World Medical Association's Declaration of Helsinki – N.°46205815.1.0000.5537.

Informed consent

Informed consent has been obtained from all individuals included in this study.

Results

After excluding the patients who did not accomplish at least 85% of the program, the final number of subjects in the EG was 7. The general data for both groups are shown in Table 1. No significant difference was observed for the perceived effort between sessions (Borg scale).

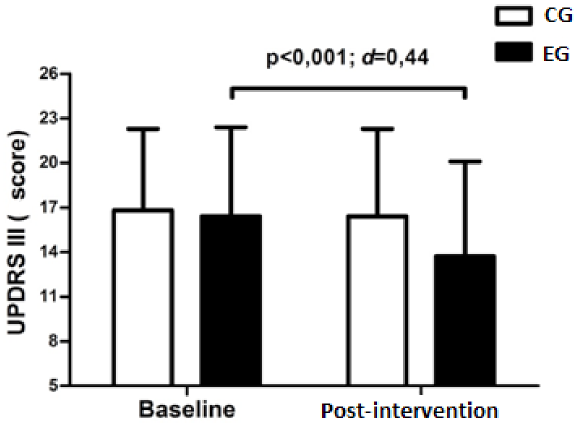
Repeated measures ANOVA presented a significant time effect for systolic ($p = 0.04$) and diastolic ($p = 0.02$) BP with an effect revealed for the EG ($d = 0.36$). A significant time × group interaction ($F(1, 10) = 33.75$, $p < 0.001$, $\eta^2_p = 0.771$) was shown with a significant time effect ($F(1, 10) = 61.12$, $p < 0.001$, $\eta^2_p = 0.859$) for UPDRS III. The *post hoc* Bonferroni test revealed a significant difference in executive motor functions between the pre- and post-intervention only for the EG ($p < 0.001$, $d = 0.44$) (Figure 2). The most relevant differences observed among items of UPDRS III observed at the pre- and post-exercise assessment occurred for bradykinesia ($p < 0.001$), lower limb agility ($p < 0.001$), and postural stability ($p < 0.05$).

For the STF (Figure 3), repeated measures ANOVA showed no significant time × group interaction ($F(1, 10) = 1.81$, $p = 0.209$, $\eta^2_p = 0.153$), as well as no effect of time ($F(1, 10) = 1.81$, $p = 0.209$, $\eta^2_p = 0.153$) for the lower limbs strength (Figure 3A). For the upper limbs strength, there was no time × group interaction ($F(1, 10) = 3.51$, $p = 0.090$, $\eta^2_p = 0.260$) but there was

Table 1. Characteristics of the control group and experimental group. Data are presented as means and *SD* for parametric, and median and interquartile range for non-parametric analyses

	Control group (n = 10)	Experimental group (n = 7)	*p* value
Sex (male/female)	8/2	5/2	
Age (years)	66.4 ± 6.1	65.0 ± 5.4	0.684
Stature (m)	1.67 ± 0.06	1.62 ± 0.10	0.287
Body mass (kg)	64.5 ± 5.4	65.6 ± 13.1	0.861
BMI (kg/m^2)	23.0 ± 1.0	25.0 ± 3.1	0.202
TD (years)	10.8 ± 5.9	12.3 ± 6.2	0.685
Hoehn and Yarh (score)*	3.0 ± 0.8	3.0 ± 1.0	0.558
MoCA (score)	20.4 ± 1.7	21.1 ± 5.3	0.770

BMI – body mass index, TD – time since diagnosis, Hoehn and Yarh – disease severity scale of Hoehn and Yarh, MoCA – Montreal cognitive assessment
* non-parametric variable



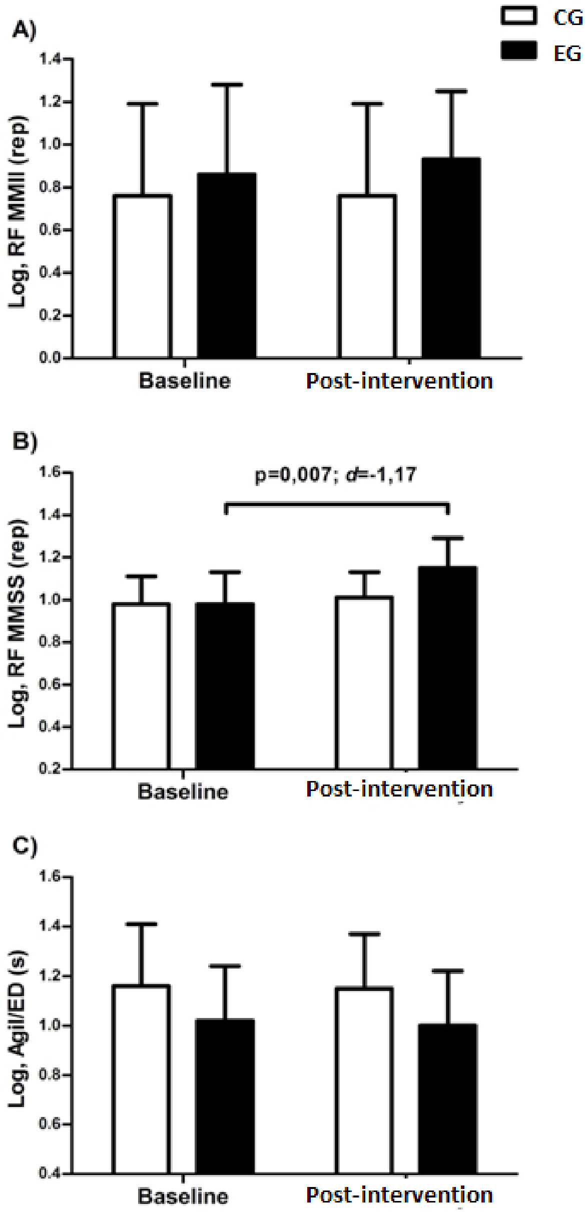
CG – control group, EG – experimental group,
UPDRS III – Unified Parkinson's Disease Rating Scale, part II

Figure 2. The effects of 4 weeks of aerobic exercise with cognitive interference on the motor function of patients with PD. Control group: n = 5, experimental group: n = 7, UPDRS III: clinician-scored monitored motor evaluation scale

a significant effect of time (F(1, 10) = 6.27, p = 0.031, η^2_p = 0.385). The *post hoc* Bonferroni test revealed a significant difference between the pre- and post-intervention status only for EG (p = 0.007, d = –1.17) (Figure 3B). Similar to the lower limbs, the variable of agility / dynamic balance did not show time × group interaction (F(1, 10) = 0.01, p = 0.928, η^2_p = 0.001) or an effect of time (F(1, 10) = 0.41, p = 0.535, η^2_p = 0.040) (Figure 3C).

Discussion

Regular exercise evokes changes in many levels of a human organism that ultimately display in the individuals profile; so it was observed in individuals' BP after exercising. The positive change found in the resting levels of BP of the patients submitted to exercise is attributed to an improvement in their fitness conditions as an adaptive exercise response required for the production of energy with a smaller load of heart function [18]. The water-walking showed to be as effective as a solo walking when it refers to the motor function and balance gains. The aerobic exercise combined with a cognitive stimulation effectively evoked positive changes in the clinical parameters of motor function in the subjects with advanced symptoms of PD. Furthermore, although the self-selected speed and the water resistance featured by this model of exercise may have represented a limitation in the gains of strength, they did show to be of a great advantage for the activation of the processes of central control of the motor action provided by the incremental tasks [19].



CG – control group, EG – experimental group, RF MMII – lower limb strength, RF MMSS – upper limb strength, Agil/ED – agility/dynamics

Figure 3. Effect of 4 weeks of aerobic exercise with cognitive interference on lower (A) and upper (B) limb strength, and agility / dynamic balance (C) of patients with moderate Parkinson's disease. Control group: n = 5, experimental group: n = 7

The usage of DT approaches to improve the motor function of patients with PD has been explored for a few decades. A motor-cognitive interference that occurs in the brain owing to an overlap of tasks generated by such a technique is revealed to yield a positive impact on the specific spatiotemporal domains of velocity and step planning, as well as on domains of balance and cognition. Therefore, DT challenges may evoke important changes in patients with PD at executive levels [20]. For instance, the participants' gait has been noticed to improve in balance, with the risk of fall decreasing in number [21].

Water-based aerobic exercise has already shown to be effective for the improvement of functional mobility in patients with PD in the earliest stages [22]. In the present study, it has been demonstrated that patients at a more advanced stage of disability can execute an exercise training program, thus being able to yield gains in the executive motor function and the strength levels. The aquatic environment designed for the exercise provided an indispensable scope for the accomplishment of the aerobic training combined with cognitive stimulation, in a way that is suitable for the effective practice in individuals at elevated levels of motor disability. After the exercise, a positive change was detected in the clinical profile of the patients' motor function, as expressed by a battery of motor tasks evaluated by a neurologist (UPDRS III), and also in the parameters of fitness conditions as strength and BP.

Our results indicate that the exercise benefits related to the executive control of the patients must have been potentiated by the increment of DT. Further, gains of strength can indeed be pronounced by patients in severe stages of PD, although a limited number of studies have addressed exercise to this population, to whom alternative therapies are of a greater importance.

Considered as the major contributor for the motor disability faced by patients with PD, bradykinesia was the most responsive symptom affected by the exercise program. This likely occurred owing to an exercise-induced increase in muscle activity that triggers a series of cellular and molecular processes which ultimately elevate the oxidative and excitatory neuromuscular capability. These changes may counteract the compensatory mechanisms of cortical developed hyperconnectivity in patients with PD in stages of sub-thalamic nuclei degeneration that impedes proper movement [23]. Additionally, the exercise-related increases in epinephrine and norepinephrine raise these neurotransmitters supply and uptake by the central nervous system, positively impacting on the sub-thalamic circuits of neurotransmission and so the effectiveness of rapid movement [24].

Aerobic exercise has been shown to play an important role in neuroplasticity. Interestingly, the exercise can induce adaptive neurophysiological responses as much as the coordination stimulus can induce changes in the information processing with respect of energy expenditure and cognitive demands, where the latter is more crucial for potentiation of molecular and cellular processes involved in neuroplasticity [25]. The water-walking with DT proposed in this study is thus suggested to improve motor performance in PD by the incorporation of goal-based motor skills learning to an automatic exercise, enhancing the cognitive engagement. Combining goal-based tasks with aerobic training may have increased the exercise effect, thus becoming possible to reach the executive motor control improvement not only to the walking skill itself, but also in a wider spectrum of motor functions as measured by UPDRS III [26].

Whereas exercise effects on executive function in PD has previously been associated with the exercise frequency and volume [2], in our study, the increment of DT during aerobic stimulation is believed to be the crucial factor for the achievement of such executive gains in a relatively shorter period comparing with programs supplying only exercise, even to less compromised individuals [27, 28].

The water-walking with DT enabled the participants with a strong motor disadvantage to restore a range of movements hitherto compromised by the severity of the disease. The amplified repertory of movement provided by the DT and made especially possible by the aquatic environment was essential for the motor gains, with the advantage of the exercise adaptations, as blood perfusion in central areas, oxygen delivery, and neurotrophic transport, which are necessary for the support of neuronal circuits.

Conclusions

Aerobic exercise with DT is effective to improve general motor function and fitness conditions in patients with PD even on severe stages of disease in a short period of time.

Limitations

The access to individuals with movement disorders makes administration of long-term exercise protocols a challenge. Side effects of supplementary medication may occur during the process as a confusing bias.

Disclosure statement
No author has any financial interest or received any financial benefit from this research.

Conflict of interest
The authors state no conflict of interest.

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