CHRONIC RESPONSES OF PHYSICAL AND IMAGERY TRAINING ON PARKINSON'S DISEASE

RESPOSTAS CRÔNICAS DO TREINAMENTO FÍSICO E DE IMAGÉTICA NA DOENÇA DE PARKINSON

RESPUESTAS CRÓNICAS DEL ENTRENAMIENTO FÍSICO Y DE IMAGÉTICA EN LA ENFERMEDAD DE PARKINSON

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ABSTRACT

Introduction: Physical and motor imagery training is known to induce positive results in the quality of life of patients with neurodegenerative diseases. However, it is not known which effects are achievable when both types of training are combined. Objective: This study aimed to investigate the effects of a combination of physical and imagery training on neurotrophin levels, the perception of body dimensions and activities of daily living (ADL) in individuals with Parkinson's disease (PD). Methods: Over an 8-week period, thirteen subjects underwent one hour of aerobic training in combination with twice-weekly imagery training (MIT). The following parameters were measured: brain-derived neurotrophic factor (BDNF) serum levels, level of dependence for activities of daily living (ADLs – Basic [ABDL] and Instrumental [AIDL]), perception of body dimensions and hand laterality test. Results: Physical training combined with MIT increased serum BDNF levels in a non-statistically significant manner by 128.08% (88.81 ± 111.83 pg/ml versus 202.56 ± 183.43 pg/ml, p= 0.068). Delta BDNF showed a mean variation of 218.05 ± 547.55% (ES = 1.04). Perception of body dimensions and hand recognition reaction time both improved, but not in a non-statistically significant manner. ADLs (9.52% in ABDLs and 17.76% in AIDLs) improved in a statistically significant manner. Conclusion: Despite the small number of subjects, study limitations, and the fact that most results were non-statistically significant, the results obtained here indicate clinical improvement associated with the neurotrophic action of BDNF on the perception of body dimensions and the functional capacity of Parkinson's disease subjects. ***Level of evidence II, Therapeutic studies–Investigation of treatment results.***

Keywords: Aging; Neurodegenerative diseases; Central Nervous System; Imagination; Exercise.

RESUMO

Introdução: Sabe-se que o treinamento físico e de imagética motora induz a resultados positivos na qualidade de vida dos pacientes com doenças neurodegenerativas. Entretanto, não se sabe quais efeitos são possíveis de se obter quando ambos tipos de treinamento são combinados. Objetivo: O presente estudo teve como objetivo investigar os efeitos de uma combinação de treinamento físico e de imagética sobre os níveis neurotróficos, percepção das dimensões corporais e atividades da vida diária (AVD) em indivíduos com doença de Parkinson (DP). Métodos: Durante um período de oito semanas, 13 indivíduos realizaram uma hora de treinamento aeróbico em combinação com um treinamento de imagética motora (MIT) duas vezes por semana. Foram mensurados os seguintes parâmetros: níveis séricos do fator neurotrófico derivado do cérebro (BDNF), nível de dependência para atividades de vida diária (AVD - Básico [ABDL] e instrumental [AIDL]), percepção das dimensões corporais e teste de lateralidade da mão. Resultados: O treinamento físico combinado ao MIT aumentou os níveis séricos de BDNF de um modo não estatisticamente significativo em 128,08% (88,81 ± 111,83 pg/ml versus 202,56 ± 183,43 pg/ml, p = 0,068). O delta BDNF apresentou uma variação média de 218,05 ± 547,55% (ES = 1,04). A percepção das dimensões corporais e o tempo de reação para o reconhecimento da mão melhoraram, porém, não de um modo significativo estatisticamente. As AVDs (9,52% nas ABDL's e 17,76% nas AIDLs) melhoraram de um modo significativo estatisticamente. Conclusão: Apesar do pequeno número de indivíduos, limitações do estudo e ao fato de que a maioria dos resultados não era estatisticamente significativo, os resultados aqui obtidos indicam uma melhora clínica associada à ação neurotrófica do BDNF na percepção das dimensões corporais e na capacidade funcional de indivíduos com doença de Parkinson. ***Nível de evidência II, Estudos terapêuticos–Investigação dos resultados do tratamento.***

Descritores: *Envelhecimento; Doenças neurodegenerativas; Sistema nervoso central; Imaginação; Exercício.*

RESUMEN

Introducción: Se sabe que el entrenamiento físico y de imagética motora induce a resultados positivos en la calidad de vida de los pacientes con enfermedades neurodegenerativas. Entretanto, no se sabe qué efectos son posibles de obtenerse cuando ambos tipos de entrenamiento son combinados. Objetivo: El presente estudio tuvo como objetivo investigar los efectos de una combinación de entrenamiento físico y de imagética sobre los niveles neurotróficos, la percepción de las dimensiones corporales y las actividades de la vida diaria (AVD) en individuos con enfermedad de Parkinson (EP). Métodos: Durante un período de ocho semanas, 13 individuos realizaron una hora de entrenamiento aeróbico en combinación con un entrenamiento de imagética motora (MIT) dos veces por semana. Se midieron los siguientes parámetros: niveles séricos del factor neurotrófico derivado del cerebro (BDNF), nivel de dependencia para las actividades de la vida diaria (AVD - Básico [ABDL] e Instrumental [AIDL]), percepción de las dimensiones corporales y test de lateralidad de la mano. Resultados: El entrenamiento físico combinado al MIT aumentó los niveles séricos de BDNF de un modo no estadísticamente significativo en 128,08% (88,81 ± 111,83 pg/ml versus 202,56 ± 183,43 pg/ml, p = 0,068). El delta BDNF mostró una variación promedio de 218,05 ± 547,55% (ES = 1,04).

La percepción de las dimensiones corporales y el tiempo de reacción para el reconocimiento de la mano mejoraron, aunque no de un modo estadísticamente significativo. Las AVD (9,52% en las ABDL y 17,76% en AIDL) mejoraron de un modo estadísticamente significativo. Conclusión: A pesar del pequeño número de sujetos, limitaciones del estudio y el hecho de que la mayoría de los resultados no era estadísticamente significativos, los resultados obtenidos aquí indican una mejora clínica asociada a la acción neurotrófica del BDNF en la percepción de las dimensiones corporales y la capacidad funcional de individuos con enfermedad de Parkinson. ***Nivel de evidencia II, Estudios terapéuticos–Investigación de los resultados del tratamiento.***

Descriptores: *Envejecimiento; Enfermedades neurodegenerativas; Sistema nervioso central; Imaginación; Ejercicio.*

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INTRODUCTION

Population aging has been discussed on a large scale due to structural and physiological changes.[1,2] In this context, Parkinson's disease (PD) stands out as the second most prevalent neurodegenerative disease in the elderly population worldwide. Its progression is accompanied by loss of motor independence and reduction of approximately 60% of dopaminergic neurons in the late stage.[3]

There is increasing evidence that various cognitive and perceptual abilities are impaired in idiopathic PD, and conventional treatment of dopaminergic drugs has limitations.[4]

One of the strategies used to stimulate neuronal plasticity is physical training, whose benefits are associated with increased levels of neurotrophins such as brain-derived neurotrophic factor (BDNF), physical and cognitive functions, and improvement of depressive symptoms.[5-7]

However, some individuals may present limitations for physical activities and one way to overcome this difficulty is through the practice of motor imagery (MIT). MIT is described as the state of an action in its specific environment that uses the same internal motor representations as the movements performed physically at a specific neural level. The practice of MIT is a complement to physical practice, since the hypothesis is that patients receiving this treatment, in addition to physical training, demonstrate greater gains over those who receive only physical practice. Rienzo et al[8] mention that the association of MIT with physical training may be efficient for the treatment of PD, since mental activity through physical activity may be able to establish new neural connections, leading to neuronal plasticity, in addition to preservation of body perception, making it important for motor planning. The implementation of this combined treatment regimen allows prolonging the practice time with low risk and low cost.[9]

All of this leads us to assume that physical training associated with MIT may be able to improve serum BDNF levels, daily life activities (ADLs), and body dimensional perception. Thus, the objective of this study was to investigate the effects of the association between physical exercise and MIT on neurotrophin levels, perception of body dimensions and ADL in elderly with PD.

METHODS

This study was approved by the Human Research Ethics Committee under number 1,738,264. All participants signed the informed consent form.

The sample consisted of 13 subjects (male, age 60.63 ± 14.45 years), with an average diagnosis time of 9.38 ± 5.85 years and continuous treatment of 2.92 ± 3.19 years. All subjects were right-handed, predominantly PD on the left side. The volunteers continued the prescribed treatment, with common (despite differentiated dosages) use of levodopa (dopaminergic agonist antiparkinsonic drug with action in the CNS).

The volunteers were classified according to the degree of disability determined by the Hoehn and Yahr[10] scale, and participants with PD degree II and III were included. (Table 1) The Mental State Mini-Exam Questionnaire (MMSE) was applied, composed of six groups of questions,[11] allowing to track the cognitive losses by means of punctuation.

Participants diagnosed with other diseases such as dementia, cerebral vascular disease, spinal cord injury, amputated limb, systemic arterial hypertension, uncontrolled diabetes mellitus, orthopedic injury that made the experiment impossible to perform, aphasia, and inability to follow two controls at the same time were excluded from the study at the time of screening.

Participants underwent physical-cognitive training during the afternoon, associating MIT aerobic[12-16] and explicit (external-visual) and implicit (internal-kinesthetic).

Experimental Design

The research protocol was composed of three stages. (Figure 1)

Table 1. Hoehn & Yahr Scale (1967) - stages and symptoms of Parkinson's Disease.

Stages	Symptoms
1	Has unilateral symptoms
2	It presents bilateral symptoms, without prejudice to the balance
3	Postural commitment: reflected in physical independence
4	Severe disability, but still able to walk or stand without assistance
5	Wheelchair or bedridden

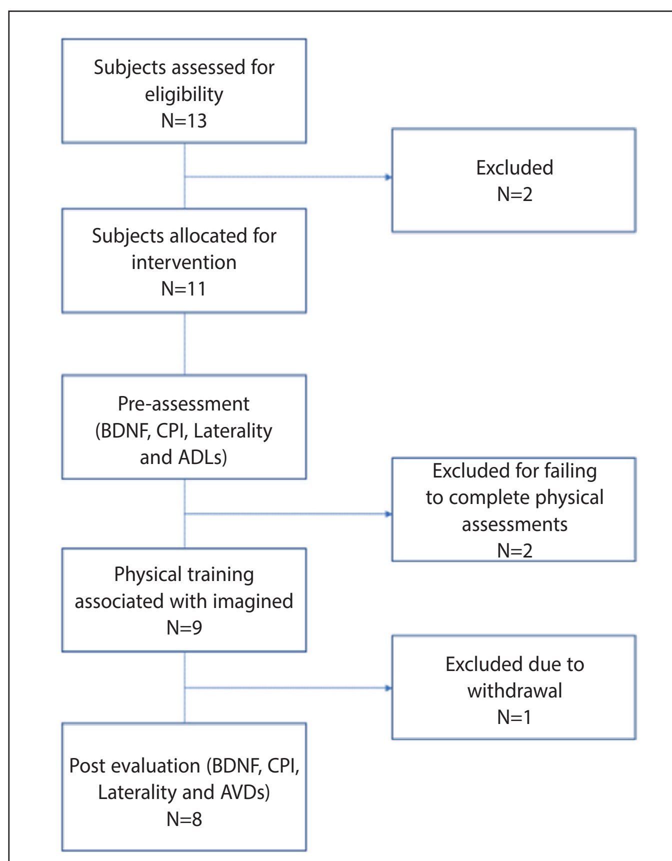

Figure 1. Outline of the study design, showing enrollment and participation of subjects at each stage.

Aerobic training protocol

Aerobic training was chosen because it was recognized for improving gait and for inducing neuroplasticity in several models.[12,14,17,18] The training was carried out on a treadmill (Johnson Jet3000® brand) and intensity controlled by the Polar® heart rate monitor (model RS 800 CXSD).

After familiarization, all were submitted to a training period of 8 weeks (2x/week, 40 minutes and 50-70% HRmax).

Motor imagery training

The MIT session followed the physical training, seeking to optimize performance in imaginary practice, since physical exercise itself triggers alterations in regional blood perfusion, favoring oxygenation of the underlying motor circuits, which contributes to changes in the cerebral connectivity associated with synaptogenesis.[14]

MIT training lasted approximately 12 to 15 minutes, distributed in:

- 3 minutes: initial concentration with instrumental music, the subject being verbally oriented by the professional to perceive their articulations and members;
- 7 minutes: imaginary practice, the subject being verbally oriented to imagine himself practicing the movements involved in the work activities of everyday life;
- 2 minutes: the return of images (video projection) recorded in physical training (real), referring to the running on a treadmill;
- 2 minutes: final relaxation.

During this training, detailed verbal instructions of the MIT exercises were given for both visual and kinesthetic aspects, seeking to use descriptions of the movements to be performed in a manner compatible with the actual movement.

In each session, different groups of daily activities were worked out.

Time congruence tests were used to address the accuracy of MIT content. Participants were instructed to perform the MIT of a sequential motor task. At some point in the coach-controlled process, the trainees were stopped and asked to verbally describe the content of MIT at the evaluator's breakpoint. The accuracy of MIT was also evaluated after completion of the imagined actions. MIT and physical practice involve common motor planning strategies, so the time needed to complete the two tasks was similar.[8]

There is no detailed protocol of training with motor imaging, so we prescribe MIT according to the available evidence in the literature.[9,19-22]

Serum BDNF quantification

Blood samples were collected aseptically in Vacutainer tubes (10 ml) with anticoagulant and kept at 4°C for no more than 2 hours of collection of blood, and centrifuged at 3000 rpm for 15 minutes and stored at -80°C until analysis. This material was collected in two moments: before the beginning and after the interventions. Serum BDNF levels were determined using the commercial kit enzyme immunoassay available for BDNF (Human BDNF Duo Set Elisa) by the Elisa method.

Microtiter plates (96 flat bottom wells) were coated for 24 hours with samples diluted 1:2 and the standard curve in the range of 2.8 to 500 pg BDNF. The plates were washed four times with wash buffer, the anti-BDNF antibodies being added and incubated for 2 hours at room temperature. After washing, a second incubation was added with peroxidase-conjugated antibodies for 2 hours at room temperature. After addition of streptavidin, substrate and prepared solution, the amount of BDNF was determined (absorbance at 450 nm). Absorbance values obtained after reading in a spectrophotometer at 450 nm were converted to pg / mL after elaboration of the standard curve with known concentrations of BDNF (R = 0.99).

Dependency Questionnaire for ADLs

Basic activities (ABDL) were evaluated based on the Katz Index,[23] while instrumental activities (AIDL) were measured based on the Lawton Scale.[24]

We investigated six self-care activities (feeding, bathing, dressing, going to the bathroom, lying down and getting up from bed and / or chair and controlling urination and / or evacuation functions) and eight instrumental activities (telephone, clothes, preparing meals, taking medicines, shopping, transporting / transporting and taking care of money). In cases where the respondent reported that he did not perform a particular activity in his daily life, he was invited to think of a similarly experienced situation or, if he preferred, to attempt to perform the activity without the help of a third party and respond later, according to the result.

The score of the dependence degree scale based on the Katz Index is done by summing the number of activities in which the individual is dependent, on a scale of 0 to 6, where 0 = independent and 6 = dependent on all functions. In the Lawton-Brody index, the score used was 0 (dependent) to 8 (independent) for women and 0-5 for men. Thus, the higher the score obtained, the greater is the degree of dependence of the subject to perform the daily activities.

Body Dimensional Perception Test

The perception of the body dimension was evaluated through the Image Marking Procedure (IMP), later relating the results to laterality. In this test, individuals were scored on the following regions of the body: right and left acromioclavicular joints, right and left waist curves, and large trochanters of the right and left femur. The subjects were blindfolded and placed in orthostatic position in front of a white wall. The distance from the subject to the wall was determined by the length of the upper limb of the semi-flexed subject so that his hand reached the wall. The subjects were instructed, through verbal instructions, to imagine that the wall was a mirror. To mark the perceived dimension, the marked points were touched and the individuals pointed to the wall before them, the projection of each point touched. To determine the actual measure, the evaluator positioned the subject near the wall to mark the points touched by the use of a ruler.

The Body Perception Index (BIS) was applied to verify the asymmetries. Next, the formula is applied: perceived size (average of the 3 perceived dimensions) divided by the actual size multiplied by 100 (perceived size / real size x 100), whose result is given in percentage values. The classification was made according to the following criteria: subjects who perceived between 99.4% and 112.3% were considered adequate body perception; values below 99.4% were classified as hypo-skeletal and those above 112.3% are hyperschemical.[25] (Table 2)

Laterality test

To recognize the hand in different positions, the subject makes the mental movement to identify the presented hand.[26] In order to evaluate the hand recognition ability, a laterality test was applied using the "E-Prime" software (Standart 2.0 version developed by Cohen et al., Version for Windows, Psychology software and tools, Inc.). time spent to recognize whether the hand displayed in a photo and at different angles is the right or the left. The "E-Prime" was programmed to display scanned photos of the right and left hands

Table 2. Categorization of general body perception index (BPIg) based on the criteria of Segheto et al. (2012).

Classification	Percentage of classification
Hypo schematic	<99.4
Normal schematic	99.4-112,3
Hiper schematic	>112.3

in different positions: 0 °, 90 ° lateral, 90 ° medial and 180 ° with the palm facing up or down randomly. Participants recognized which hand was being displayed by pressing a corresponding button, being "Q" when the hand shown was left and "P" when it was to the right. The parameter used for laterality analysis was the time spent (milliseconds) for hand recognition.[27]

Statistical analysis

The descriptive data were presented with mean and standard deviation (SD). The Levene test was used to verify equality of variance and normality. The analysis between pre-post moments was done through paired Student's t-test. The correlation between the deltas (%) of the quantitative variables was evaluated by the Pearson correlation test. The Cohen effect size calculation (ES = difference between pre- and post-intervention divided by SD pre-intervention) was used to assess the magnitude of BDNF changes and other parameters. ES values were determined from very small (0.01-0.19), small (0.20-0.49), moderate (0.50-0.79), large (0.80-1,19) and very large (1.20 <). Data analysis was performed using the statistical program SPSS (Statistical Package for Social Science version 21.0) and the significance level adopted was $p \leq 0.05$.

RESULTS

Of the thirteen subjects recruited for this study, eight volunteers completed all study procedures. (Figure 1)

BDNF measurement

Serum levels of resting BDNF increased by 128.08% between pre and post-training (88.81 ± 111.83 pg / ml versus 202.56 ± 183.43 pg / ml) [p> 0.05). The delta BDNF change showed an average change of 218.05 ± 547.55%. In addition, the effect size of the intervention was characterized as strong (ES = 1.04). Large response variations were presented at the post-training time. (Figure 2)

Perception of body dimensions

The group presented a hyper-schematic profile (BIP> 112.4%) before the intervention and adequate at the post-training moment. (Table 3) The BPI effect size for waist width showed a strong reduction (ES = -0.85), while the others were only trivial.

Table 4 shows the quantitative analysis of body symmetry (p> 0.05). The calculations of effect sizes on the left side showed a moderate change, while on the right side they were only trivial.

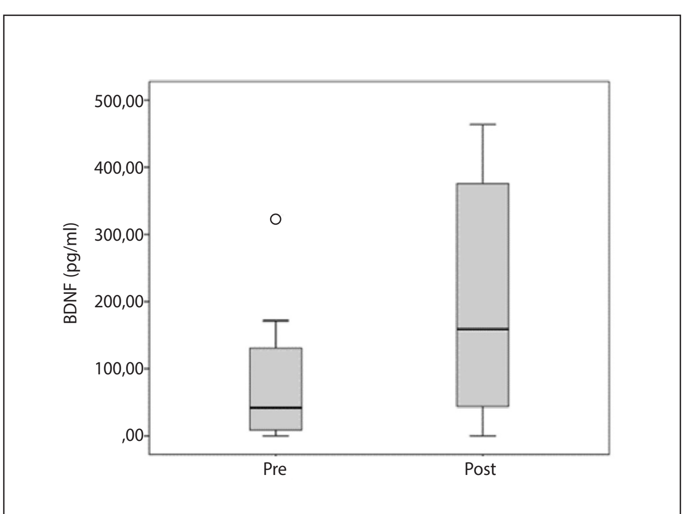

Figure 2. Box-plot of brain-derived neurotrophic factor (BDNF) values between pre-post moments. An outlier is presented in the pre-moment.

Laterally

Comparing reaction times for right and left hand recognition before and after the intervention, there was no significant difference between the values. (Table 5) Effect size was moderate for all parameters.

We observed a shorter reaction time after the intervention in relation to the general time before the intervention, which can be understood as an indicator of clinical improvement. The angle 0° presented the shortest pre-reaction time (1901.69 ± 578.95 ms) for powders (1518.25 ± 388.38 ms), while the 90º L angle presented the highest increase in the mean reaction time (5071,69 ± 4192.38 ms vs 5252.82 ms) 3579.92 ms).

Day to day activities

In the ABDL analysis, there were statistical differences between the pre and post-training moments (p = 0.033). The effect size was moderate (ES = 0.70). (Table 6)

As for the Lawton score (AIDL), there was an increase in the mean score of approximately 17.76%, representing a statistically significant difference (p = 0.018). The effect size was considered strong (ES = 1.10). (Table 7)

Table 3. Mean and standard deviation of general body perception indices (BPI) and height, shoulder, waist and hip segments. *Effect size* (ES).

BPI Measures	Pre (%)	Post (%)	ES
General	112.64 ± 18.15	104.32 ± 14.67	-0.46
Height	96.60 ± 4.54	95.90 ± 3.27	-0.15
Shoulder Width	104.04 ± 24.55	103.77 ± 16.93	-0.01
Waist Width	120.18 ± 23.92	99.81 ± 20.76	-0.85
Hip Width	129.75 ± 33.80	117.81 ± 28.13	-0.35

Table 4. Analysis of the symmetry between right and left sides as a function of the segments, before and after the intervention.

Segments	Right			Left		
	Pre	Post	ES	Pre	Post	ES
Shoulder	102.55±5.02	102.06±3.83	0.10	103.78±6	100.33±3.13	0.57
Waist	104.23±5.74	103.13±2.97	0.19	108.64±6.22	105.51±1.82	0.50
Hips	111.30±6.98	108.99±3.44	0.33	113.71±7.19	108.82±4.04	0.68

ES = effect size.

Table 5. Mean and Standard Deviation of Reaction Time (in milliseconds) for hand recognition Before and After intervention. *Effect size (ES).*

Hands	Pre	Post	Delta (%)	ES	P
Right	3188.08 ± 1235.76	2519.87 ± 758.55	20.96%	0.54	0.13
Left	3441.65 ± 1445.01	2706.19 ± 778.22	21.37%	0.51	0.17
Mean	3314.87 ± 1284.67	2613.03 ± 756.44	21.17%	0.55	0.13

Table 6. Distribution of the subjects regarding classification by the Katz index before and after the intervention.

Classification	n (%)	
	Pre	Post
Total Independence	4 (50.0)	6 (75.0)
Slight dependence	3 (37.5)	2 (25.0)
Moderate dependence	1 (12.5)	0 (0)

Table 7. Mean and standard deviation of the score obtained in the basic activities (ABDL's) with the Katz index and the instrumental activities (AIDL's) with the Lawton index. Effect size (ES).

Tests	Score		*ES*	*P*
	Pre	Post		
ABDLs	5.25 ± 0.71	5.75 ± 0.46	0.70	0.033
AIDLs	5.63 ± 0.91	6.63 ± 0.91	1.10	0.018

DISCUSSION

The present study demonstrated that daily activities were affected by the association of the two types of training. However, as our sample consisted of individuals with PD, we need to analyze the evidence from a more clinical point of view. Increasing BDNF, normalizing body perception indices, improving reaction time without increasing the number of errors, was responsible for improving ADLs and reducing the physical dependence of individuals with PD.

It is known that motor actions, through the association of physical and mental practice, can induce cerebral changes associated to the learning of abilities. Pascual-Leone et al[28] demonstrated that changes in cortical sensory maps are similar to those obtained with physical training. Because mental training has preparatory effects and increases the efficiency of subsequent physical training, it is expected that their combination will produce better results. The mechanisms underlying the effects of exercise on subjects classified as intermediate degree of PD have not yet been elucidated, but animal studies suggest some reflections, such as that increased physical effort allows neuronal activation and dopamine action in the base nuclei. As far as we know, only one study[5] included a direct measure in such outcome, demonstrating an increase in BDNF after high volume physical therapy.[29] In addition, neurotrophins may become useful markers for PD-related neuroplasticity and physical exercise.[18] An emerging body of evidence suggests that exercise triggers various events related to brain plasticity in human PD.[18] Recent evidence indicates a possible role for exercise-induced changes in human DNA methylation between genes and molecular pathways associated with PD, including the positive regulation of exercise-induced neurogenesis and reprogrammed synaptic neurotransmission.

Exercise-induced BDNF activity, whether physical or imagined, as there are similarities in the recruited areas, can put the brain in a state of readiness for plasticity. Reliable evidence in humans indicates that each exercise episode results in a "dose" of BDNF activity and that its magnitude can be increased over time by regular exercise.[15]

The analysis of the specific height of the head, based on the approximation of 100% of perceived real value x, showed that the subjects underestimated, having a probable relation with the kyphotic posture of the parkinsonian individual. A study with subjects after the period of practice of ballroom dancing, we noticed smaller ones, whose hypothesis suggested by the authors is that this result was related to the observation of the feet themselves during the classes.[30]

It is observed that, after the intervention, the group went from hyperskematic to the appropriate state, due to an improvement in dimensional perception of the waist and hip. This finding corroborates with studies that point to this segment as more distorted.[30,31]

Performance gains related to MIT are associated with increased recruitment of motor regions and areas of fronto-parietal mirror neurons and attention control.[32]

We know that there is a relationship between the reaction time for hand recognition and body perception through MIT.[33] This supports the discovery of better acuity of body perception and less reaction time for hand recognition after the intervention.

Functional decline is a predictor of the development of dementia, such as PD.[34] Thus, our results lead us to believe that the intervention favored not only the preservation (AIDL) but also the functional capacity (ABDL) of the volunteers. The addition of MIT training to physical practice seems to promote better motor performance of ADLs and this performance is improved with more physical practice.[35]

CONCLUSION

Through the results presented in this study, we can conclude that the association of physical-cognitive training can improve clinical outcomes associated with neuroplasticity, perception of body dimensions and, more significantly, activities of daily living.

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