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EFEITOS DO TREINAMENTO RESISTIDO UNILATERAL *VERSUS* BILATERAL A CURTO PRAZO NO CONTROLE MOTOR E NA FORÇA EM INDIVÍDUOS COM A DOENÇA DE PARKINSON, UM ENSAIO CLÍNICO RANDOMIZADO

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‘’*Veni, Vidi, Vici*‘’

General Júlio César

RESUMO EXPANDIDO

EFEITOS DO TREINAMENTO RESISTIDO UNILATERAL *VERSUS* BILATERAL A CURTO PRAZO NO CONTROLE MOTOR E NA FORÇA EM INDIVÍDUOS COM A DOENÇA DE PARKINSON, UM ENSAIO CLÍNICO RANDOMIZADO

Sacha Clael Rodrigues Rêgo

Introdução: As pessoas com a doença de Parkinson geralmente possuem um maior acometimento em um lado do corpo. Hipotetiza-se que o treinamento resistido unilateral possa provocar mudanças no controle motor e na força no lado mais afetado pela doença, quando comparado ao treinamento resistido bilateral. **Objetivo:** Verificar os efeitos dos treinamentos resistidos unilateral versus bilateral no controle motor e na força em indivíduos com a DP. **Materiais e Métodos:** A amostra foi composta por 17 indivíduos diagnosticados com a DP, divididos de forma aleatória, em grupo de treinamento unilateral [(GTU), n = 9] e grupo de treinamento bilateral [(GTB), n = 8]. Foram realizadas 24 sessões de treinamento resistido. As seis primeiras sessões de treino foram voltadas à familiarização do treinamento. Antes (T0), durante (T12) e após (T24) a intervenção foram coletados dados do controle motor fino, utilizando-se os testes Nine-Hole Peg e o Box and Blocks; dados da força de membros superiores por meio do dinamômetro de preensão palmar e da força de membros inferiores por meio do dinamômetro isocinético, todos os testes foram feitos unilateralmente. Para a análise estatística dos dados foi utilizado uma ANOVA de Friedman [3 (TEMPO) x 4 (GRUPO)] bem como os testes de Mann-Whitney U e Wilcoxon. **Resultados:** O pico de torque a 60°/s do lado direito no momento T12, no GTU foi significativamente maior que no GTB. O pico de torque do lado direito foi significativamente menor no momento T24 em relação aos momentos T12 e T0 no GTU. **Conclusão:** O TR unilateral a curto prazo não se mostrou eficiente para provocar mudanças no controle motor e na força no membro mais acometido pela doença por meio do *cross-education* e nem diminuiu o déficit bilateral.

Palavras-chave: Cross-education, déficit bilateral, isocinético, preensão palmar, preensão manual, nine-hole peg, box and blocks, lado acometido.

Introdução

A Doença de Parkinson (DP) é uma doença neurodegenerativa, caracterizada pela deterioração progressiva da substância negra no mesencéfalo que causa diminuição na produção de dopamina (1). Devido a essa diminuição as pessoas com a DP podem apresentar déficits motores na marcha, postura e equilíbrio, dos quais pode-se citar a bradicinesia, a hipocinesia, o *freezing* da marcha, a rigidez, os tremores e a instabilidade postural (2).

Visando a atenuação dos sintomas motores é utilizado o fármaco Levodopa (3), porém o uso prolongado promove déficits motores como a discinesia (4). Devido a tais efeitos medicamentosos e objetivando o auxílio no tratamento da DP, essa população tem buscado terapias complementares ao uso da medicação (5), e uma delas é o treinamento resistido (TR). O TR atua como tratamento coadjuvante, promovendo a melhora no controle do movimento, retarda a progressão da doença e melhora à resposta medicamentosa (6).

No que concerne a DP, esta inicia-se em um dos lados do corpo, permanecendo este como o lado mais afetado durante todo o curso da doença (6), tal situação reflete no controle motor e na força muscular dos indivíduos. Devido a estas conjunturas é necessário uma metodologia de treino adequada para não agravar tal desequilíbrio.

Suspeita-se que a realização do TR de forma bilateral possa agravar o membro mais acometido da doença, pois a contração bilateral de membros homólogos compromete a capacidade de produção de força máxima, esse fenômeno é chamado de déficit bilateral e ocorre quando a força voluntária máxima bilateral é menor que a soma das forças unilaterais dos membros direito e esquerdo contraídos isoladamente (7).

Uma alternativa para a situação supracitada seria a execução dos exercícios de forma unilateral, pois hipotetiza-se que possa ocorrer uma melhora no lado mais acometido pela doença, devido a uma ação chamada *cross-education* (8). Tal fenômeno sugere a melhora no membro não treinado devido as adaptações neurais (8). Assim, o objetivo do presente estudo é verificar se o TR realizado de forma unilateral a curto prazo poderia provocar mudanças no controle motor e na força no membro mais acometido de pessoas com a DP devido ao *cross-education*, diminuindo o déficit bilateral comparado ao TR realizado de forma bilateral.

Materiais e Métodos

A amostra foi composta por 17 indivíduos diagnosticados com a DP, divididos de forma aleatória, em grupo de treinamento unilateral [(GTU), n = 9] e grupo de treinamento bilateral [(GTB), n = 8]. Foram realizadas 24 sessões de treinamento resistido. As seis primeiras sessões de treino foram voltadas à familiarização bem como à adaptação ao treinamento.

Antes (T0), durante (T12) e após (T24) a intervenção foram coletados dados do controle motor fino, utilizando-se os testes Nine-Hole Peg (9) e o Box and Block (10); dados da força de membros superiores por meio do dinamômetro de preensão palmar (11) e da força de membros inferiores por meio do dinamômetro isocinético (12), todos os testes foram executados unilateralmente. Visando a análise de dados, somente o lado mais acometido pela doença foi utilizado para os resultados finais, assim o GTU e o GTB foram subdivididos em 4 grupos, lado superior ou inferior afetado mais o tipo de TR realizado. Para a análise estatística dos dados foi utilizado uma ANOVA de Friedman [3 (TEMPO) x 4 (GRUPO)] bem como os testes de Mann-Whitney U e Wilcoxon.

Resultados

O pico de torque a 60°/s do lado direito no momento T12, no GTU foi significativamente maior que no GTB. O pico de torque do lado direito foi significativamente menor no momento T24 em relação aos momentos T12 e T0 no GTU.

Discussão

O GTU obteve um maior pico de torque a 60°/s no lado direito quando comparado ao GTB no momento T12, tal resultado pode ser explicado pelo principio da especificidade do treinamento (13), pois a avaliação no isocinético foi realizada de forma unilateral, logo o GTU teria vantagem em relação ao GTB por ter treinado de forma unilateral. Outrossim, o declínio de força durante contrações bilaterais é acompanhado por um declínio na ativação do giro pré-central (14) e este é danificado pela DP (15), portanto o GTB tem menor estímulo do giro pré-central.

O decréscimo do pico de torque do lado direito no GTU pode ser explicado devido aos relatos dos indivíduos, pois não se sentiam bem ao serem avaliados no dinamômetro isocinético, várias reclamações com relação ao equipamento foram feitas para o pesquisador.

Conclusão

O TR unilateral a curto prazo não se mostrou eficiente para provocar mudanças no controle motor e na força no membro mais acometido pela doença por meio do *cross-education* e nem diminuiu o déficit bilateral.

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LIST OF ABBREVIATIONS AND ACRONYMS

PD Parkinson's Disease

RT Resistance Training

BT Bilateral Training

BFD Bilateral Force Deficit

UT Unilateral Training

BPD Bilateral Performance Deficit

T0 Pre Intervention

T12 Inter Intervention

T24 Post Intervention

UnB University of Brasilia

MMSE Mini Mental State Examination

GTU Unilateral Resistance Training Group

GTB Bilateral Resistance Training Group

9H 9-Hole Peg Test

BB Box and Blocks Test

HGS Handgrip Strength Test

PT Peak Torque

PT/BW Relative Peak Torque

TTPT Time to Peak Torque

ACT Acceleration Time

BD Bilateral Deficit

BDSA Bilateral Deficit Corrected by the Most Affected Side

BFDSA Bilateral Force Deficit Corrected by the Most Affected Side

BPDSA Bilateral Performance Deficit Corrected by the Most Affected Side

IPAQ International Physical Activity Questionnaire

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1. INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disease characterized by progressive deterioration of the substantia nigra in the midbrain causing a decrease in dopamine production (1). This reduction in dopamine results in a GABA mediated tonic inhibition of the thalamus which in turn reduces the excitation of the thalamus on cortical projection areas. Which in turn, is manifested as alteration in somatic motor activities commonly observed in patients with PD (2).

Dopamine is responsible for preparation, initiation, and execution of movements. The depletion of dopamine by lesions or drugs, or dopamine receptor blockade, results in changes in neuronal activity in the striatum, the globus pallidus, and the motor cortex (3). Changes in neuronal activity may alter movements and motor control generated by neural circuits of the brain and the spinal cord, disturbances in functioning of the globus pallidus may compromise sending of excitatory signals from the subthalamic nucleus (2).

Due to these brain changes, people with PD may have motor symptoms that include hypokinesia, tremor, rigidity and postural instability that causes mobility loss and dependence to perform activities of daily life (4). Also, the onset of motor symptoms in PD is typically unilateral, with the side of onset often remaining more affected throughout the course of the disease (5). Levodopa is the standard of treatment for the symptoms of PD, however with its prolonged use greater fluctuations periods of the medication benefits, called ‘’off moments’’, might be observed, as well as troublesome side effects such as dyskinesias (6).

Because of motor impairments caused by long term use of Levodopa medication, at least 40% of people with PD use one or more forms of alternative therapy to complement or help standard treatments (7). One of these treatments is physical exercise that improves physical functioning and health-related quality of life, and may slow disease progression (5). Among physical exercise types, resistance training (RT) has been shown to significantly improve muscle strength, gait initiation, and gait speed (8).

There are several methodologies applied to RT and one of them is bilateral training (BT). BT is the simultaneous muscular contraction of homologous members (9), but this methodology generates a phenomenon called bilateral force deficit (BFD). BFD is when the force produced during simultaneous maximal contraction of both limbs is lower than the sum of the forces produced by the left and the right limbs separately (10).

This phenomenon occurs because activity of the motor cortex in one hemisphere reduces the maximum motor outflow of homologous parts of the opposite hemisphere, possibly through transcallosal inhibitory connections (11). BFD is established in different population types (e.g., young, middle-aged and elderlies), in different muscle groups, (e.g., lower and upper extremities), and in different types of muscular contractions (e.g., isometric and dynamic) (12).

As a result, is suspected that BT can further aggravate the difference between sides of the disease and increase the BFD. Moreover, PD affects middle-aged to elderly people (5), these populations have reduced neuromuscular activation because of the aging process, they begin to have a decrease in the muscular fibers, mainly those of fast-twitch (13), and decreased activation of fast motor units have been found to be associated with greater BFD (14), which lends further support to the hypothesis mentioned above.

One solution for such situations would be to use the methodology of unilateral training (UT). UT can reduce BFD and maybe improve the most affected side through the cross-education concept (15). This concept suggests that during voluntary activation of a single limb there is a crossover effect of the neural drive occurring at either the motor cortex, pyramidal tract, or somewhere in the spinal cord (16). This crossover effect can increase corticospinal excitability and generate neural plasticity, promoting changes in interhemispheric interactions, such changes may contribute to motor acquisitions, such as intermanual transfer and improve motor function of the most affected side (17).

Besides that, the cross-education of muscular strength bears some similarity to the cross-education of motor skills (18), which can improve motor control on the most affected side by the disease, this difference in motor skills between sides will be called ‘bilateral performance deficit (BPD)’. However, it is yet to be known how RT performed unilaterally would alter motor control and strength in people with PD. We hypothesize that unilateral RT will improve the most affected side, and reduce BFD and BPD.

2. OVERALL OBJECTIVE

PURPOSE

To verify if the unilateral RT on short-term could lead to changes on motor control and strength on the most affected limb of people with PD.

SPECIFIC AIMS

1. To check if the unilateral RT on short-term can generate the phenomenon cross-education for motor control and strength in people with PD
2. To test BFD and BPD between unilateral and bilateral RT
3. To investigate if unilateral RT is better than bilateral RT to improve strength and motor control on the most affected side in people with PD.

3. LITERATURE REVIEW

3.1. PD Pathophysiology

PD is characterized as a disorder of movement consisting of tremor, rigidity, elements of bradykinesia (slowness of movement), hypokinesia (reduced movement), akinesia (loss of movement), and postural abnormalities. PD consists of pigmented brain stem nuclei degeneration, including the dopaminergic substantia nigra pars compacta, with the presence of Lewy bodies in remaining nerve cells (19).

The cause of PD is unknown and is likely to be multifactorial. There is evidence that disease onset is result of an interaction of genetic factors, environmental neurotoxins, oxidative stress, and mitochondrial abnormalities. Symptoms usually appear after the age of 50 years, but the young are not exempt. Incidence is greater in men. The characteristic tremor affects about 70% of patients. Sensations of numbness or pain without demonstrable sensory loss often are described. Muscles may be referred to as painful and tender and limbs may be said to be weak or stiff. Difficulty with handwriting, or inability to undertake repetitive sequential tasks such as cleaning the teeth are some complaints. Fatigue is a common complaint, as is depression and a vague sensation that the patient has slowed down and life has become weary. Unexplained weight loss may be prominent (19).

PD produces damage beyond the *substantia nigra*. Other areas of damage include the substantia innominata, locus coeruleus, and dorsal vagal nucleus. The United Kingdom Parkinson's Disease Society Brain Bank proposed formal diagnostic criteria for PD, which consist of bradykinesia identification, plus one of the disease’s motor symptoms, and three criteria of positive support. Diagnostic criteria can be divided into 3 groups according to Table 1 (20).

The basal nuclei (ganglia), located at the brain base, are part of circuits that make up a complex network. One among these circuits, the motor circuit, is in charge of motor acts of planning and sequencing. In PD, projections from motor areas to the striatum are altered because of decrease on dopamine. Changes on neural conduction in the corticostriatal pathway lead to a derangements sequence in the others basal ganglia pathways, generating dysfunction on motor responses (21).

The basal nuclei are nuclear masses of gray matter derived from the embryonic colliculus of the telencephalon, forming subcortical structures, which comprise several interconnected nuclei in the telencephalon, mesencephalon, and diencephalon. These nuclei are the caudate, the putamen and the accumbens, which constitute the striatum; the pallid globe, divided into external (lateral) and internal (medial) segments; the subthalamic nucleus, located in the diencephalon, and the substantia nigra in mesencephalic nucleus, divided into part compact and part reticulated (2).

Non-motor manifestations of PD are divided into neuropsychiatric (depression, anxiety, apathy, and hallucinations), sleep disorders (rapid-eye-movement sleep behavior disorder, excessive daytime somnolence, and insomnia), fatigue (central and peripheral), sensory (pain, olfactory disturbance, and visual disturbance), autonomic dysfunction (bladder urgency, sexual dysfunction, and orthostatic hypotension) and gastrointestinal symptoms (dribbling of saliva, dysphagia, constipation, nausea, reflux, and vomiting) (22).

Table 1. Positive and negative criteria for PD diagnosis.

Criteria for PD diagnosis	- Bradykinesia (and at least one of the following symptoms):
	- Muscular rigidity;
	- Rest tremo (4-6 Hz);
	- Postural instability not caused by primary visual, vestibular, cerebellar, or proprioceptive dysfunction.
Exclusion criteria for PD	- History of repeated strokes with stepwise progression of Parkinsonian features;
	- History of repeated head injury;
	- History of definite encephalitis;
	- Oculogyric crises;
	- Neuroleptic treatment at onset of symptoms;
	- More than one affected relative;
	- Sustained remission;
	- Strictly unilateral features after three years;
	- Supranuclear gaze palsy;
	- Cerebellar signs;
	- Early severe autonomic involvement;
	- Early severe dementia with disturbances of memory, language and praxis;
	- Babinski sign;
	- Presence of a cerebral tumour or communicating hydrocephalus on CT scan;
	- Negative response to large doses of levodopa;
	- MPTP exposure.
Supportive prospective positive criteria for PD, 3 or more required for diagnosis of definite PD.	- Unilateral onset;
	- Rest tremor present;
	- Progressive disorder;
	- Persistent asymmetry affecting the side of onset most;
	- Excellent response (70–100%) to levodopa;
	- Severe levodopa-induced chorea;
	- Levodopa response for 5 years or more;
	- Clinical course of 10 years or more.

3.2. Motor control

Voluntary movements originate in the cortex. Information is ‘sent’ to the muscles via the spinal cord. Simultaneously, information about impending movement is also sent to the cerebellum and the basal ganglia. They play a role in error correction and modulation of movement. When a part of the basal ganglia, i.e, the central nervous system degenerates, the modulatory capacity of the basal ganglia is adversely affected. This is partly caused by excessive inhibition of the thalamus mediated by GABAergic signaling, eventually resulting in impairment in gross and fine movement (2).

The upper frontal cortex is responsible for bilateral movements, such as holding an object with both hands. However, in some people with PD this part of the frontal cortex has also been shown to degenerate (23). Given that this area works with the pre-motor area to generate movements responsible for the general posture and fine motor control, with its degeneration, it is likely that muscles receive weak transmissions and performance of motor tasks is compromised (24).

The cord gray matter is the integrative area for the cord reflexes. Sensory signals enter the cord almost entirely through the sensory (posterior) roots. After entering the cord, every sensory signal travels to two separate destinations: (1) One branch of the sensory nerve terminates almost immediately in the gray matter of the cord and elicits local segmental cord reflexes and other local effects. (2) Another branch transmits signals to higher levels of the nervous system—to higher levels in the cord itself, to the brain stem, or even to the cerebral cortex, Each segment of the spinal cord (at the level of each spinal nerve) has several million neurons in its gray matter (24).

The brain stem consists of the medulla, pons, and mesencephalon, it is an extension of the spinal cord upward into the cranial cavity because it contains motor and sensory nuclei that perform motor and sensory functions for the face and head regions in the same way that the spinal cord performs these functions from the neck down. Besides it provides many special control functions, such as the following as control of respiration, control of the cardiovascular system, partial control of gastrointestinal function, control of many stereotyped movements of the body, control of equilibrium and eye movements (24).

The cerebellum plays a major role in the timing of motor activities and in rapid, smooth progression from one muscle movement to the next. It also helps to control the intensity of muscle contraction when the muscle load changes and controls the necessary instantaneous interplay between agonist and antagonist muscle groups (24).

The basal ganglia help to plan and control complex patterns of muscle movement, controlling relative intensities of the separate movements, directions of movements, and sequencing of multiple successive and parallel movements for achieving specific complicated motor goals (24).

Movement disorders comprise a large variety of motor manifestations, not all of which are necessarily due to dysfunction of the basal ganglia, some dysfunction may be associated with nonmotor manifestations such as attention deficit and depression (1).

Progressive degeneration of neurons in the *pars compacta* of the *substantia nigra* leads to dysfunction of neuronal circuits that include the basal ganglia and motor cortical areas. The degenerative changes behaviorally manifest as significant movement abnormalities. These movement abnormalities in turn cause major disruptions that range from an individual's quality of life to society- wide economics. (25).

Exercises can reduce motor impairments in people with PD, Caglar et al. (26) verified that after a constant practice of exercises the scores in a motor control test, the Nine-Hole Peg test, significantly reduced within group and between the control group. This within group reduction may be a possible indicator for BPD reduction.

3.3. Resistance Training

Anti-Parkinsonian medication is the standard treatment for PD, but some medications lose their efficacy over time and are associated with motor complications such as dyskinesias (27). Therefore, there is a need for alternate therapies that remain effective and are not accompanied by troublesome side effects. PE is one such option. PE is a non-drug, adjunct treatment that has been extensively studied in patients with PD that has been shown to improve motor symptoms in patients with PD (4).

For people with PD, exercise has reported benefits for controlling motor and non-motor symptoms, recent research suggests that optimally prescribed PE following diagnosis may alter neurophysiological processes, possibly slowing symptom progression (28).

Muscular strength is an important component for physical activity and to perform tasks of daily living (29). Orcioli-Silva et al. (4) used a multimodal exercise program (strength, balance and coordination) on people with PD (n = 14), individuals were separated into groups by gender and disease severity. After 6 months of intervention both groups improved coordination and strength, and patients who had bilateral involvement had significant strength gains.

But it is important to know what RT type is most beneficial for people with PD, UT or BT, because, simultaneous muscular contraction of homologous members generates BFD, whereupon the force produced during simultaneous maximal contraction of both limbs is lower than the sum of the forces produced by the left and right limbs separately (10).

BT is when both limbs are used in unison to contract the muscles, which creates force, and subsequently moves a given load. UT is when each limb works independently of the other to create the desired movement. However, as with any attempt to classify exercise-based movement patterns, there will always be exercises that do not necessarily fit neatly into a classification scheme (30).

Hakkinen et al. (31) evaluated two groups, one that performed UT and one that performed BT for 24 training sessions, unilaterally and bilaterally in knee extension and found that people who performed UT had better results in unilateral evaluation, and those who performed BT had better results in bilateral evaluation in healthy middle-aged and elderly men and women, supporting the principle of specificity.

Beyer et al. (16) evaluated two groups of healthy young individuals after 12 training sessions. One group performed UT and the second group was a control group. They found differences between groups in leg extension in dominant and nondominant leg, but no difference was found within unilateral group, in healthy young people.

Different from Hakkinen et al. (31) and Beyer et al. (16) who found difference between methodologies, Speirs et al. (32) found no difference between UT and BT after 10 training sessions in unilateral and bilateral evaluations in academy rugby players. However, these authors compared only in relation to strength and not in relation to change percentage.

Using bilateral index formula, ‘‘100 x [bilateral force/(right unilateral force + left unilateral force)] – 100’’ (33), Botton at al. (34) found no difference between UT and BT in young women in knee extension with the same 24 training sessions. Similarly, Taniguchi (35, 36) found no difference between UT and BT on HGS and leg extension in healthy young people after 18 training sessions. However, with a different formula, Schantz et al. (37) found bilateral evaluation was significant higher than unilateral evaluation in a single session evaluation in isometry of knee extensors in healthy young people.

Beurskens et al. (12) evaluated lower limb strength in two different ways, unilaterally and bilaterally, in healthy elderly, RT group (n = 19), balance training group

(n = 14), and control group (n = 20), both groups resistance and balance had significant improvements on isometric peak torque (PT) in both legs.

There are other formulas for the BFD calculation, as proposed by Maly et al. (38) that interpret the BFD as a difference between dominant and non-dominant sides, and another proposed by Xaverova et al. (39) that interpret the BFD as an asymmetric difference between limbs.

A review by Shi Zhou notes an improvement up to 77% of strength on homologous contralateral limb with UT, and up to 104% with electrostimulation. The minimum time to observe significant changes in strength was 4 weeks. They found that both genders have benefits, but the studies have been done on individuals who suffered some type of injury and / or less experience on RT (40).

The effects of UT on motor control in people with PD are scarce, but the literature has shown an improvement on motor control assessed by the Unified Parkinson's Disease Rating Scale part 3, in a RT program combined with aerobic, balance and flexibility (41).

Hester et al. (42) found that after 12 training sessions in a single knee in young and older people, they had their untrained limb increased in strength, peak velocity and acceleration when compared with control groups. This effect is also observed in children. Othman et al. (43) found that after 24 training sessions in a single leg, participants showed increased strength in the untrained limb, as well as non-local untrained muscles in the upper limb.

A recent meta-analysis has confirmed the existence of a CE effect in healthy subjects, namely that UT leads to statistically significant but moderate gains of strength in the contralateral untrained limb (44).

The BFD exists for both large and small muscle groups in a variety of movement patterns, in both males and females, in older individuals, and also in subjects with motor disorders (45). This phenomenon also occurs in fine motor tasks (46), which we will call in this work of BPD.

Until now, Paasuke et al. (47) were the only ones that researched BFD in people with PD, and they found that women with PD have greater BFD than those of age- and sex-matched controls in one single evaluation using bilateral index as formula. They also found that women with PD had longer chair-rise time and lower maximal rate of vertical-ground-reaction-force development while rising from a chair. It is speculated that BFD directly affects activities of daily living.

For people with PD is unknown the effects of unilateral RT and whether this training type could cause cross-education, improving the most affected by the disease on motor control and strength.

4. MATERIALS AND METHODS

4.1. Study Type

The study design is randomized, prospective (48) clinical trial (49), with pre (T0), inter (T12) and post-intervention (T24) data collection. Where T0 is the measure pre intervention, T12 is after 12 training sessions and T24 is after 24 training sessions.

4.2. Sample

Individuals with a confirmed diagnosis of PD were recruited in the Federal District and surroundings, using the convenience sampling technique. The recruitment happened through a public call in social networks, in centers of movement disorders treatment, in Parkinson's Association of Brasília, and neurological clinics, in the second half of 2017. Additionally, participants enrolled in the *Viva Ativo* (Physical Exercise Program for Individuals with Parkinson's Disease) of the University of Brasilia (UnB) were also recruited to participate in the current study. No power analysis was performed. Below are the list of inclusion/exclusion criteria for participation in the study.

INCLUSION CRITERIA

1. Clinical diagnosis of PD by neurologist or physician according to the United Kingdom Parkinson's Disease Society Brain Bank criteria (20)
2. Modified Hoehn and Yahr Scale classification between stages 1 and 3
3. No cognitive impairment as assessed by the Mini Mental State Examination (MMSE). The cut-off points for inclusion were > 24 points for literate individuals and > 19 for non-literate individuals
4. Controlled hypertension (<150/90 mmHg)
5. Do not have extreme obesity (>40 Kg/m^2)
6. Do not have a heart pacemaker

7. Do not have amputation of upper or lower limbs
8. Male and female volunteers from Federal District
9. Individuals between 40 and 80 years who do not have health problems and / or disabilities that prevent them from completing the test batteries and training program or who may have their problems aggravated due to participation in the program
10. Availability to participate on activities proposed by researcher

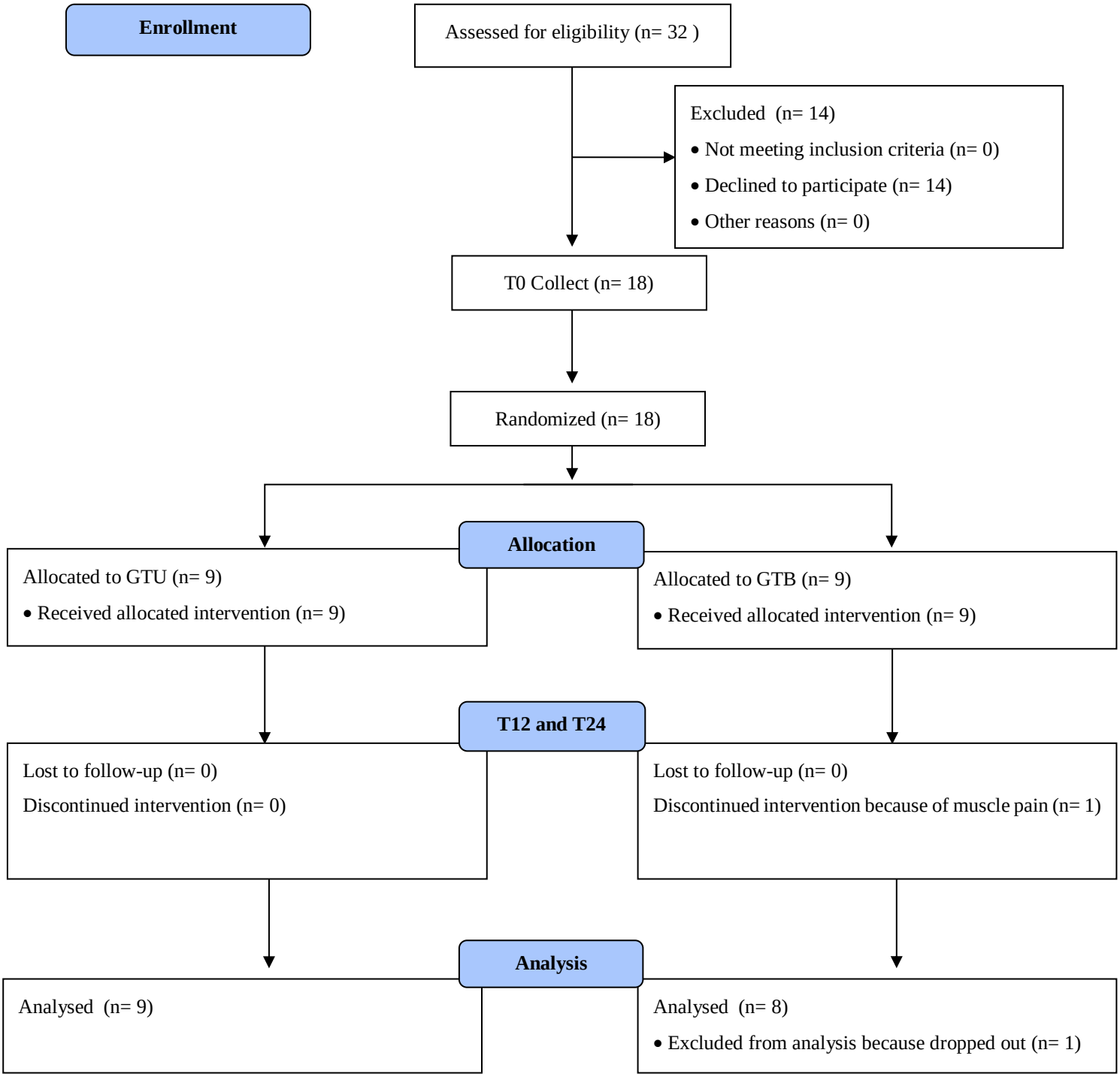
EXCLUSION CRITERIA

1. Any kind of trauma that prevents participation in the study
2. Inability to perform any of the tests that are part of the research study
3. Individuals who may voluntarily want to stop their participation in research
4. Individuals who do not have availability to participate in the research activities.

Of the 32 individuals that were initially recruited, 14 were excluded as they did not meet the inclusion/exclusion criteria (Figure 1). The sample consisted of 18 individuals randomly allocated to two groups, Unilateral Resistance Training Group (GTU), n = 9, and Bilateral Resistance Training Group (GTB), n = 9. The simple randomization was performed in the Statistical Package for the Social Sciences software version 24.0 for windows by the principal investigator. One participant from the GTB dropped out of the study in the second week as the participant was unable to perform the proposed activities due to muscle pain.

Before randomization, variables related to motor control and strength were collected, only at T0. This was followed by participation in their respective training programs.

Figure 1. CONSORT Flow Diagram.



Source: Self authorship.

4.3. Ethical aspects

The study was approved by the ethics committee of the UnB with number CAAE: 79851717.2.0000.0030.

Each participant received, read, and signed a consent form, previously authorized by the ethics committee of the University of Brasília, according to guidelines and norms regulating research involving humans and resolution nº. 196/96 of the National Health Council (Appendix A).

5. PROCEDURES

5.1. Place

The lower limb strength assessment was performed at the Strength Training Laboratory at the Faculty of Physical Education at UnB. All other evaluations were carried out in the *Viva Ativo* research group room at the UnB Olympic Center, room 15A. Training sessions were performed in the weight room at the UnB Olympic Center. Both data collection and intervention activities occurred in the morning and in the afternoon.

Individuals were instructed to wear light clothing and sneakers during assessments and training sessions. In order to maintain procedural fidelity, all the evaluators involved in study participated in training sessions that emphasized the correct form, safety, and protocol of each test/evaluation tool used.

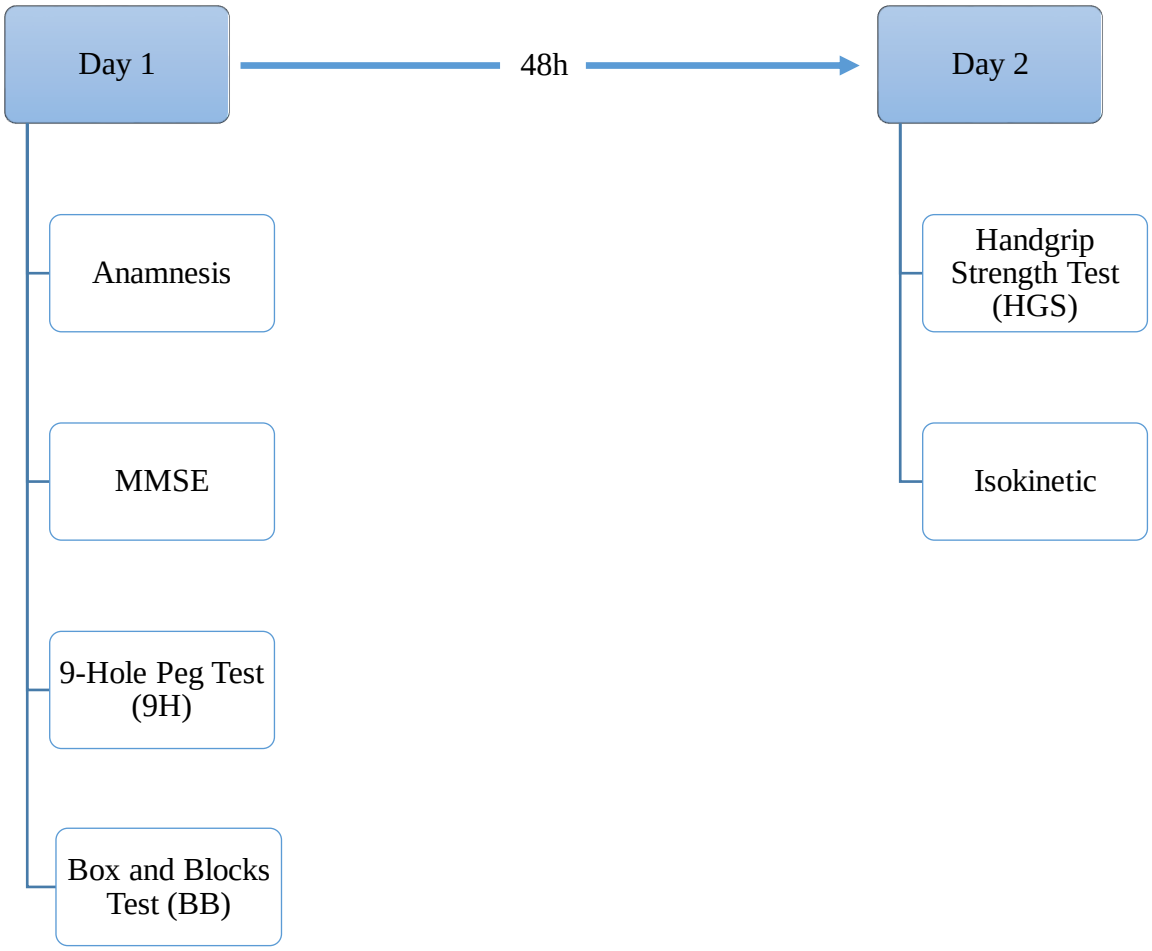
5.2. Medication

All tests and training sessions were performed with the patients in "on" medication, at peak medication effect.

5.3. Evaluation Instruments

The evaluations were divided into two days with an interval of 48 hours (Figure 2) because of the medication effect. On the first day anamnesis, MMSE, and motor control were evaluated. On the second day, upper and lower limbs strength were evaluated.

Figure 2. Test's chart.



Source: Self authorship.

5.3.1. Anamnesis

The anamnesis questions were answered by each individual or responsible family member, in order to obtain the personal data and the general clinical conditions (Appendix B). The International Physical Activity Questionnaire (IPAQ) (Annex A) short-form and the modified Hoehn and Yahr scale were part in the anamnesis.

The IPAQ measure assesses the types of intensity of physical activity and sitting time that people do as part of their daily lives are considered to estimate total physical activity (50). The modified Hoehn and Yahr scale provide a general estimate of clinical function in people with PD, combining functional deficits and objective signs (51).

5.3.2. Cognitive Function Evaluation

MMSE was used to screen for mild cognitive impairment of participants (Annex B). This instrument is composed of seven categories: orientation to time, orientation to place, record of three words, attention and calculation, recall of the three words, language, and visual-constructive praxia (52). The criterion for inclusion in the study was established as a score > 24 points. As the test is influenced by educational level, inclusion scores were adjusted to > 19 points for illiterate individuals (53).

5.3.3. Motor Control Evaluation

9H Test

Participants performed 1 trial for each hand. Trials were performed first with the dominant hand and then with the nondominant hand. Prior to the trials, familiarization was performed with each hand, first with the dominant hand followed by the nondominant hand. Table and chair distance from the pegboard were adjusted individually for each subject based on comfort. Trials were completed one after the other with a brief rest, no more than 30 seconds, in between trials.

Instructions were as follows, “On this test, I want you to pick up the pegs one at a time, using one hand only, and put them into the holes as quickly as you can in any order until all the holes are filled. Then, without pausing, remove the pegs one at a time and return them to the container as quickly as you can. You will have do this one time with each hand’’. The evaluator starts the timer when the participant picks up the first peg and stops the timer when the participant releases the last peg in container (Figure 3). The score is the task time of each hand (54).

Figure 3. 9-Hole Peg Test.

Source: Self authorship.

BB Test

Participants performed 1 trial with each hand. Trials were performed first with the dominant hand and then with the nondominant hand. Prior to the trials, the evaluator demonstrated the test by transporting 3 cubes with each hand. This was followed by the familiarization trials. Familiarization trials were performed with each hand for 15 seconds starting with the dominant hand. Table and chair distance from the box were adjusted individually for each subject based on comfort. Trials were completed one after the other with a brief rest, no more than 30 seconds, in between trials.

Instructions were as follows, “On this test, I want you to pick up the blocks one at a time, using one hand only, and move it to the other side of the box as quickly as you can in any order until I say stop. You will have to do this one time with each hand’’. The evaluator starts the timer when the individual picks up the first cube and stops the timer

60 seconds later (Figure 4). The score is the blocks numbers passed to the other side of the box (55).

Figure 4. Box and Blocks Test.

Source: Self authorship.

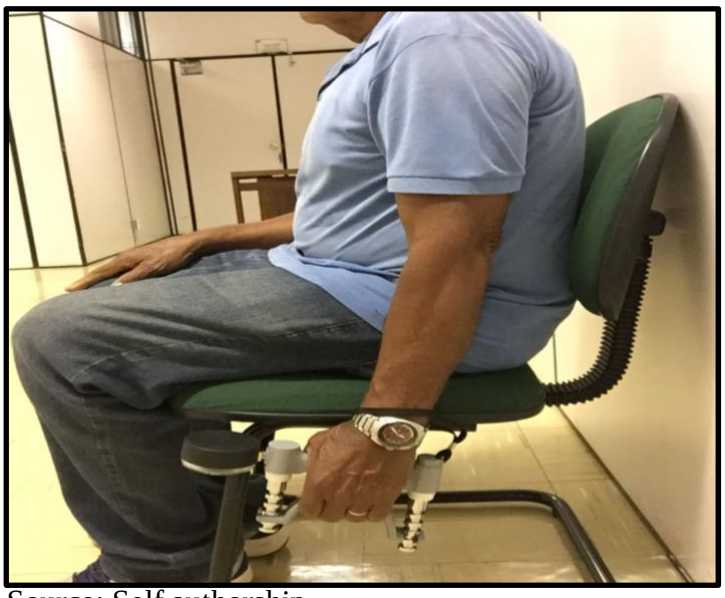
5.3.4. Strength Evaluation

HGS Test

To measure upper limbs strength, the Jamar® dynamometer was used with the protocol adapted from the American Society of Hand Therapists (56). Participants performed 3 trials with each hand. Subjects chose the hand to start the test and then the hands were alternated in subsequent trials. Prior to the trials, familiarization was performed with each hand by performing a submaximal squeeze.

Participants were seated in an armless chair with shoulder adducted and neutrally rotated, elbow in full extension, forearm and wrist in a neutral position. Rest between trials was 60 seconds. Instructions were as follows, “On this test, I want you to hold the handle and squeeze as hard as you can’’. At the evaluator's command the volunteer tightens the dynamometer for 5 seconds (figure 5). The highest value among all trials in both hands was used as the score.

Figure 5. Handgrip Strength Test.



Source: Self authorship.

Quadriceps Strength Test

To measure lower limbs strength, the isokinetic Biodex Sytem 3 (Biodex Medical Sytem, New York, USA) dynamometer was used with the protocol adapted from Malicka et al. (57). All warm-ups and trials had 60 seconds of rest interval, and was performed only in concentric phase. Participants performed 2 trials for each leg. The protocol was counterbalanced (Figure 6).

Warm-up: 1 set of 10 repetitions at 180º/s as follows, was ordered for the volunteer to do one maximum contraction, and then it was ordered to do 9 more contractions between 50% and 60% of the maximal effort.

Test: 2 sets of 4 repetitions at 60º/s and 2 more sets of 4 repetitions at 180º/s.

Instructions were as follows, “On this test, I want you to kick as hard and fast as you can’’. The trial with the highest value at each speed was used to determine the following outcomes: absolute peak torque (PT), relative peak torque (PT/BW), time to PT (TTPT), and acceleration time (ACT). The velocities were chosen due to one of the

PD symptoms, which is reduction of the total strength and this is reduced also with movement speed increase (58).

Figure 6. Isokinetic.

Source: Self authorship.

5.4. Data Analysis

All statistical analysis related to strength and motor control outcomes were performed based only on the side (left or right) and part of the body (upper or lower) most affected. For example, if an individual has the most affected upper limber as the right and the most affected lower limb as the left, this individual will just be part of statistical analyses for upper limb right outcomes and for lower limb left outcomes. Consequently, all analyses are comparisons of most affected limb for each group.

5.4.1. Calculation of bilateral deficit and bilateral deficit corrected by the most affected side.

To calculate the bilateral deficit (BD) and bilateral deficit corrected by the most affected side (BDSA) two formulas were used (39). They are described in detail below. To calculate the BFD the following equation was used

$$\left(\frac{\text{Higher Force - Lower Force}}{\text{Higher Force}}\right) \times 100$$

Using the same mathematical principle as above, the BPD was calculated. BPD was used for motor control tests. The above equation was adapted as follows:

$$\left(\frac{\text{Higher value - Lower value}}{\text{Higher value}}\right) \times 100$$

Because the 9H is a timed test, the shorter the time the higher the score, the formula above was inverted only for this test.

To calculate the bilateral force deficit corrected by the most affected side (BFDSA) and bilateral performance deficit corrected by the most affected side (BPDSA) the following equations was used:

$$\left(\frac{\text{Most affected side - Less affected side}}{\text{Most affected side}}\right) \times 100$$

6. INTERVENTION

The GTU performed unilateral RT, while the GTB performed bilateral RT. The duration for each intervention was 8 weeks with a total of 24 RT sessions. Training sessions were performed three times a week in the morning or afternoon and lasting no more than 60 minutes. The 18 participants were divided into 4 schedules, each group had a morning and afternoon training schedule and the participants chose the best time to train.

The periodization was performed as follows, three times a week, Mondays, Wednesdays and Fridays. First day training of upper limbs (Training A), second day training of lower limbs (Training B), third day Training A and so on until the end of the intervention.

Prior to intervention period, 11 UnB student volunteers were trained one week on correct execution of each training exercise, as well as on safety rules and assistance to be applied during the sessions. These volunteers were present throughout the training period, 8 in the morning and 3 in the afternoon, aiming for greater safety and orientation of individuals with PD.

The training protocol consisted of the exercises in Table 2 and all exercises were performed with machines.

Table 2. Exercises performed in the intervention.

GTU	GTB
Pulldown articulated supinated unilateral	Pulldown articulated supinated bilateral
Row seated neutral unilateral	Row seated neutral bilateral
Chest press articulated unilateral	Chest press articulated bilateral
Chest press inclined articulated unilateral	Chest press inclined articulated bilateral
Inclined leg press unilateral	Inclined leg press bilateral
Leg extension unilateral	Leg extension bilateral
Lying leg curl unilateral	Lying leg curl bilateral
Seated leg curl unilateral	Seated leg curl bilateral

6.1. Familiarization

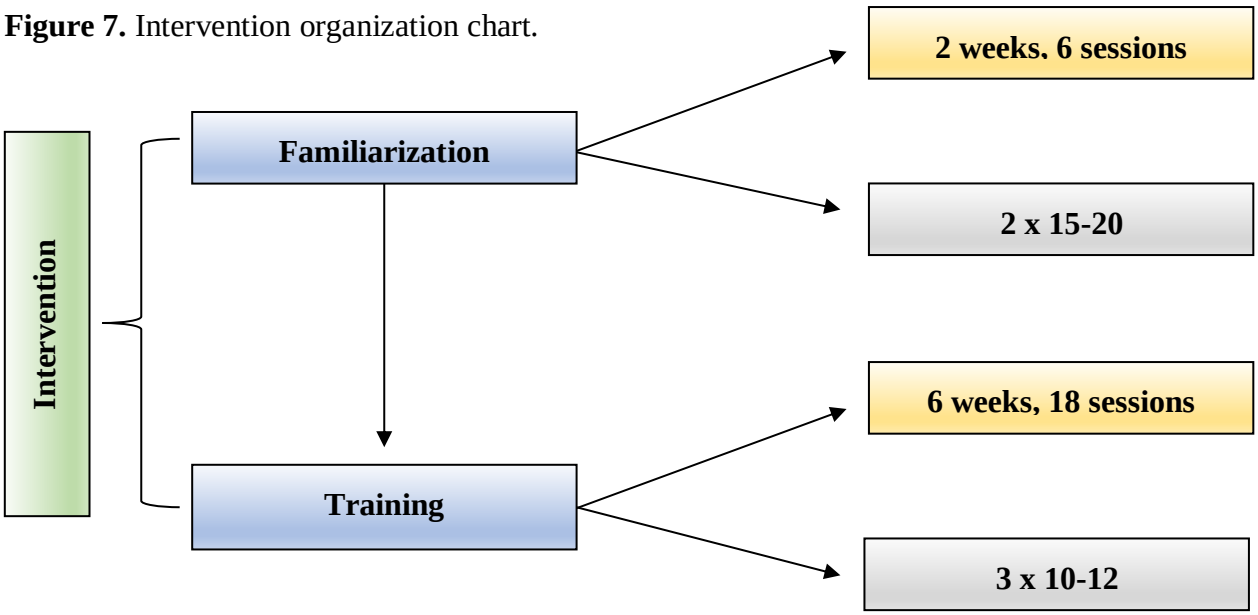
In the first two weeks the GTU and GTB went through a familiarization and adaptation period to the training program and the machines used. During this period, proper accomplishment of movements and learning of training were prioritized, besides promoting physiological adaptations. The exercises performed were the same as the training period (Table 1), but with a lower training volume. This phase consisted of 2 sets of 15 to 20 repetition maximum with 60 seconds recovery interval between sets (Figure 7), adapted from Gallo and Ewing (59).

6.2. Training

In the following 6 weeks GTU and GTB performed training program with progressive load characteristics. The volunteers performed 3 sets of 10 to 12 repetition maximum with 60 seconds recovery interval between sets (Figure 7), adapted from Gallo and Ewing (59). The load progression system was determined by the individual's ability

to overcome 12 repetition maximum, and when this occurred 1 kilogram was added to the previous load.

Figure 7. Intervention organization chart.



Source: Self authorship.

7. STATISTICAL ANALYSIS

For sample characterization, descriptive statistics were performed with mean and standard deviation for quantitative variables, and simple frequency for qualitative variables. To verify data normality the Shapiro-Wilk test was used.

Friedman's ANOVA was used to determine if there were differences within groups across the three time-points. The Wilcoxon signed rank test was used to determine where this difference occurred within each group (i.e., T0 vs T12 or T0 vs T24). The Mann Whitney U was used to determine difference between groups at a specific time point. Every test was adjusted by most affected side. The Bonfferroni correction was employed for multiple pairwise comparisons and the significance level adopted was $p \leq 0.05$. The Statistical Package for Social Sciences version 24.0 for iOS was used for data analysis.

8. RESULTS

The characterization data of 17 individuals who performed all program stages are described in table 3.

Table 3. Sample characterization.

	GTU (n = 9)			GTB (n = 8)		
	Mean		SD	Mean		SD
Age (years)	65.56	±	6.46	67.75	±	9.45
Height (meters)	1.73	±	0.08	1.64	±	0.12
Weight (kilograms)	74.96	±	12.49	69.00	±	15.52
Gender (f)						
Men	8			4		
Women	1			4		
Modified Hoehn & Yard (f)						
Level 1	1			1		
Level 1.5	1			2		
Level 2	3			3		
Level 2.5	3			0		
Level 3	1			2		
Upper Limb Dominance (f)						
Right	9			7		
Left	0			1		
Lower Limb Dominance (f)						
Right	9			7		
Left	0			1		
Upper Limb Affected (f)						
Right	6			4		
Left	3			3		
Do not exist	0			1		
Lower Limb Affected (f)						
Right	5			4		
Left	2			3		
Do not exist	2			1		
IPAQ (f)						
Very active	6			5		
Active	3			2		
Irregularly active	0			1		
Sedentary	0			0		

GTU = Unilateral Resistance Training Group; GTB = Bilateral Resistance Training Group; SD = standard deviation; f = frequency; IPAQ = International Physical Activity Questionnaire.

Table 4 shows means and standard deviations for the various outcomes used to evaluate upper limbs before, inter, and after training period. There are no difference between groups and within groups in upper limb tests on the most affected side. Lower limb results are shown in Table 5, there are difference between groups in moment T12 on right side in PT, and there are differences within groups in GTU in moments T24 to T12 and T24 to T0.

Table 6 shows the difference between groups and within groups on BPD and BFD on most affected side, there are difference on Friedman's ANOVA but not on Wilcoxon neither Mann-Whitney U. Table 7 shows difference between groups and within groups on BFDSA and BPDSA on affected side, there are no difference between groups and within groups in BPDSA and BFDSA on the most affected side.

Table 4. Means and standard deviations in upper limb tests on the most affected side.

	GTU			GTB		
	T0	**T12**	**T24**	**T0**	**T12**	**T24**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
9H_R (seconds)	33.84 ± 9.04	37.48 ± 18.32	32.00 ± 6.53	28.72 ± 7.28	30.86 ± 12.66	24.70 ± 6.10
9H_L (seconds)	30.54 ± 12.44	30.40 ± 5.72	30.55 ± 6.43	28.75 ± 9.27	30.91 ± 6.23	31.02 ± 6.25
BB_R (blocks)	40.25 ± 8.46	42.50 ± 8.34	43.50 ± 9.03	41.33 ± 15.50	38.67 ± 9.60	55.00 ± 9.53
BB_L (blocks)	38.67 ± 6.65	37.67 ± 10.78	42.67 ± 14.57	47.25 ± 8.18	45.25 ± 5.73	46.00 ± 4.08
HGS_R (kgf)	29.00 ± 8.04	32.50 ± 9.00	29.50 ± 10.14	26.00 ± 6.55	28.67 ± 8.02	27.67 ± 10.50
HGS_L (kgf)	35.33 ± 5.85	36.00 ± 4.00	36.67 ± 5.13	30.25 ± 10.65	31.75 ± 9.74	32.00 ± 12.72

GTU = Unilateral Resistance Training Group; GTB = Bilateral Resistance Training Group; T0 = Pre Intervention; T12 = Inter Intervention; T24 = Post Intervention; SD = Standard Deviation; 9H = 9-Hole Peg Test; BB = Box and Blocks Test; HGS = Handgrip Strength Test; R = right; L = left; kgf = kilograms-force.

Table 5. Means and standard deviations in lower limb tests on the most affected side.

	GTU			GTB		
	T0	**T12**	**T24**	**T0**	**T12**	**T24**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
60_PT_R (Nm)	136.22 ± 31.40	133.22 ± 33.60*	127.80 ± 33.12#†	83.85 ± 25.04	77.30 ± 19.11	78.82 ± 21.74
60_PT_L (Nm)	133.85 ± 78.98	144.95 ± 81.81	143.50 ± 84.42	102.15 ± 37.56	131.50 ± 71.58	104.25 ± 31.00
180_PT_R (Nm)	89.40 ± 21.60	87.92 ± 22.52	85.40 ± 21.73	56.30 ± 20.70	48.20 ± 12.93	48.02 ± 11.74
180_PT_L (Nm)	93.90 ± 57.69	101.45 ± 54.37	93.65 ± 56.63	96.20 ± 56.79	90.73 ± 54.99	67.83 ± 17.60

GTU = Unilateral Resistance Training Group; GTB = Bilateral Resistance Training Group; T0 = Pre Intervention; T12 = Inter Intervention; T24 = Post Intervention; SD = Standard Deviation; PT = Peak Torque; 60 = 60º/s; 180 = 180º/s; R = right; L = left; Nm = Newton meter; * = difference between groups in moment T12; # = difference within groups in moments T0 and T24; † = difference within groups in moments T12 and T24.

Table 6. Means and standard deviations in BPD and BFD on the most affected side.

	GTU			GTB		
	T0	**T12**	**T24**	**T0**	**T12**	**T24**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
9H_BPD_R (%)	-5.56 ± 4.81	-20.35 ± 26.84	-23.70 ± 12.54	-28.21 ± 25.84	-13.20 ± 13.01	-14.70 ± 14.88
9H_BPD_L (%)	-12.24 ± 10.78	-14.04 ± 15.26	-13.80 ± 11.33	-23.17 ± 12.86	-16.28 ± 15.27	-18.18 ± 11.57
BB_BPD_R (%)	21.39 ± 6.49	7.01 ± 6.16	6.72 ± 5.79[§]	9.75 ± 5.24	13.05 ± 11.48	5.55 ± 6.73
BB_BPD_L (%)	5.98 ± 3.36	12.82 ± 7.13	1.14 ± 1.99	6.89 ± 6.84	5.14 ± 5.11	9.00 ± 6.83
HGS_BFD_R (%)	9.88 ± 9.09	4.98 ± 5.78	11.56 ± 13.57	9.72 ± 8.46	4.72 ± 4.11	15.38 ± 11.99
HGS_BFD_L (%)	9.30 ± 3.58	8.33 ± 4.81	6.29 ± 4.59	9.14 ± 8.39	12.91 ± 5.88	9.36 ± 6.64
60_PT_BFD_R (%)	6.21 ± 6.53	7.57 ± 4.96	9.73 ± 9.37	9.15 ± 7.25	6.80 ± 2.20	10.57 ± 3.95
60_PT_BFD_L (%)	16.40 ± 6.79	13.09 ± 0.65	14.13 ± 4.64	32.23 ± 28.10	24.19 ± 25.38	21.21 ± 19.97
180_PT_BFD_R (%)	4.43 ± 4.65	9.13 ± 8.75	9.20 ± 8.03	11.37 ± 11.65	9.50 ± 10.78	10.75 ± 6.69
180_PT_BFD_L (%)	17.44 ± 1.57	6.71 ± 7.28	14.37 ± 1.36	27.95 ± 18.58	25.60 ± 26.52	15.60 ± 10.30

GTU = Unilateral Resistance Training Group; GTB = Bilateral Resistance Training Group; T0 = Pre Intervention; T12 = Inter Intervention; T24 = Post Intervention; SD = Standard Deviation; BFD = Bilateral Force Deficit; BPD = Bilateral Performance Deficit; 9H = 9-Hole Peg Test; BB = Box and Blocks Test; HGS = Handgrip Strength Test; PT = Peak Torque; 60 = 60º/s; 180 = 180º/s; R = right; L = left; % = percentage; [§] = Difference on Friedman's ANOVA but not on Wilcoxon neither Mann-Whitney U.

Table 7. Means and standard deviations in BPDSA and BFDSA on the most affected side.

	GTU			GTB		
	T0	**T12**	**T24**	**T0**	**T12**	**T24**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
9H_BPDSA_R (%)	5.12 ± 4.30	5.32 ± 22.89	-7.62 ± 26.36	-9.38 ± 38.84	-6.09 ± 19.05	-6.32 ± 21.75
9H_BPDSA_L (%)	-2.99 ± 17.46	10.93 ± 12.02	0.76 ± 17.61	6.76 ± 23.18	11.75 ± 12.39	14.77 ± 8.41
BB_BPDSA_R (%)	-9.87 ± 26.88	3.37 ± 9.54	2.05 ± 9.53	0.12 ± 13.40	-13.68 ± 19.86	4.51 ± 7.81
BB_BPDSA_L (%)	-6.45 ± 3.74	-15.25 ± 9.89	1.14 ± 1.99	5.66 ± 8.22	-1.07 ± 8.52	-1.19 ± 14.45
HGS_BFDSA_R (%)	-8.05 ± 15.39	3.16 ± 7.31	-15.28 ± 19.33	-11.39 ± 9.92	-5.08 ± 4.42	-19.92 ± 18.45
HGS_BFDSA_L (%)	-10.37 ± 4.41	-7.40 ± 8.82	-3.55 ± 8.92	0.44 ± 13.86	5.80 ± 15.19	0.26 ± 13.45
60_PT_BFDSA_R (%)	-0.02 ± 10.48	-4.26 ± 9.75	-9.30 ± 14.70	-1.88 ± 15.18	-5.32 ± 6.32	-0.80 ± 13.79
60_PT_BFDSA_L (%)	-7.66 ± 27.23	-0.45 ± 19.81	2.62 ± 20.92	-83.26 ± 100.13	-36.81 ± 68.01	-49.76 ± 60.74
180_PT_BFDSA_R (%)	-3.23 ± 6.63	-6.79 ± 15.19	-5.49 ± 14.61	-4.33 ± 21.03	-7.99 ± 18.12	-2.62 ± 14.90
180_PT_BFDSA_L (%)	-3.22 ± 27.66	5.13 ± 9.51	-0.07 ± 21.79	-20.65 ± 65.90	-35.89 ± 80.03	-6.08 ± 25.56

GTU = Unilateral Resistance Training Group; GTB = Bilateral Resistance Training Group; T0 = Pre Intervention; T12 = Inter Intervention; T24 = Post Intervention; SD = Standard Deviation; BFDSA = Bilateral Force Deficit Corrected by the Most Affected Side; BPDSA = Bilateral Performance Deficit Corrected by the Most Affected Side; 9H = 9-Hole Peg Test; BB = Box and Blocks Test; HGS = Handgrip Strength Test; PT = Peak Torque; 60 = 60º/s; 180 = 180º/s; R = right; L = left; % = percentage.

9. DISCUSSION

The training protocol worked on components related to strength development aiming to verify which methodology could decrease the deficits and improve the most affected side. Two findings were significant. First, PT significantly improved in the GTU relative to the GTB at time T12, when the right lower limb was the most affected lower limb. Second, BB_BPD_R in GTU at time T24 significantly declined relative to baseline, while there was no significant decline in the GTB group.

Regarding to the first finding, one possible explanation is that bilateral contractions reduce activation in the precentral gyrus (60) and maybe this can occur on the most affected limb too. It is known that degenerative changes in the precentral gyrus are observed in people with PD (61). When this is coupled with inter-callosal inhibition (62), bilateral contractions are likely to be reduced in patients with PD. Another possible reason for the higher values in PT in GTU compare to GTB at time T12 is training specificity (63). To elaborate, RT for the GTU group was done unilaterally and so was the evaluation using the isokinetic dynamometer and therefore training and evaluation was similar. As a result participants from GTU would have an advantage over those from the GTB. Besides that, the individuals did not feel comfortable with evaluations in the isokinetic dynamometer, several complaints regarding to the assessment were reported to the researcher.

Regarding to the second finding, we found that BPD declined with training only in the GTU group and not in the GTB group in BB test. This suggests that UT may be better than BT in reducing the BPD. Maximal unilateral muscular contractions, can bring about plastic changes in the precentral gyrus such that the efferent drive to the muscle can be increased (60). It is also likely that unilateral training might reduce the inter-callosal inhibition thereby facilitating a reduction in BPD.

One reason that we did not find any other significant differences between the GTU and GTB might be related to the fact that subjects who previously performed some PE were not excluded. Almost all participants practiced some form of PE, which may have caused a ceiling effect (64), that is, the subjects were unable to achieve better results in the evaluations after the intervention because they had already adapted. It was not possible to exclude these participants as this might have reduced our sample size.

Another possible reason is that perhaps that the duration of the study was too short for patients with PD. The time required for an adaptation to manifest itself subsequent to

PE is a phenomenon known as lag time (32). While previous studies have shown improvement in healthy elderly with the duration used in the current study (65). Also PD causes hypometabolism in the temporal area of the brain (62), this area is linked to learning and memory (2). This duration might have been too short for patients with PD in order to bring about specific adaptations to RT. A related reason for a lack of significant findings is that BD is related to fiber type. Decreased activation of fast motor units have been found to be associated with greater BD (14). Given, it is know that in patients with PD have a lower percentage of fast-twitch fibers (66), and given the short duration of the study, it is likely that these factors influenced the non-alteration in almost BD and BDSA.

In order for cross-education to improve performance of the most affected limb, adaptations are required to occur in the motor and the somatosensory cortexes with the participation of the temporal lobe (67). In patients with PD temporal lobe degeneration has been observed (68), which may further explain the lack of improvement of the most affected limb following GTU.

Besides that, during unilateral movements, there are increases in activity in the supplementary motor area and cingulate motor area. These structures have dense structural white matter that connects within the homologous zone in the opposite cerebral hemisphere (69). Again degeneration of the white matter has been observed in patients with PD (70), which could compromise unilateral movements. This factor may have also influenced the results of the most affected limb.

Exercises that involve movement at multiple joints may be more susceptible to a BFD than exercises that involve movement at a single joint (71), if the strength outcomes were performed on multi-joint equipment the BFD results could be different.

In relation to physiological factors PE activates AMPK, which it is responsible for activation of PGC-1 alpha. One of the roles of PGC-1 alpha is in the transformation of fast-twitch fibers to slow-twitch fibers (29), and as previously mentioned decrease activation of fast motor units are associated with greater BD (14). Perhaps power training would be more appropriate for people with PD. Moreover, higher concentrations of Tau protein are found in people with PD (72), these proteins are associated with motor problems in animal models (73), perhaps such effects occur in people with PD too. Aerobic exercise can reduce total Tau protein in animal models (74), probably this occurs in people with PD too. It appears that the best exercise regimen is a multimodal regimen that includes RT and aerobic exercise in patients with PD.

A surprising finding is that the difference in BD for upper limbs was significant but not for lower limbs. We expected that if one side would improve, it would improve in its entirety, not only a part, superior or inferior. However, the literature reported that the dominant limb has an influence on the BD of upper limbs but not for lower limbs (75). Only one of our subjects was left-hand dominant. Therefore, this might justify the lack of a significant finding in the lower limb but a significant finding in the upper limb.

There are a few limitations associated with the present study. The first limitation is the small sample size which reduces the statistical power and reduces the generalizability of our findings. The second limitation is the short duration of the intervention. Some of the central and peripheral changes that accompany UT might require a longer training period in people with PD because these are the exact structures that are affected by the degenerative disease process. The third limitation is the lack of neurophysiological outcomes like MRI to localize brain changes that accompany UT. In order to localize the area of the nervous system affected, direct investigation into neural control differences between the upper and lower body must be further elucidated. The fourth limitation is non-split between men and women to be randomized, that resulted on the GTU has only one woman, which probably affected the strength results. Future studies that assess UT as an intervention to improve function in patients with PD should employ a larger sample size, longer training durations, and include neurophysiological outcomes to identify brain adaptations.

10. CONCLUSION

Short-term unilateral resistance training was not efficient to induce changes on motor control and strength on the most affected limb by the disease as a result of cross-education, nor did it decrease the bilateral deficit.

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12. APPENDIX

Appendix A. Ethics committee

UNIVERSIDADE DE BRASÍLIA

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Termo de Consentimento Livre e Esclarecido - TCLE

Convidamos o(a) Senhor(a) a participar **voluntariamente** do projeto de pesquisa " EFEITOS DOS TREINAMENTOS RESISTIDOS UNILATERAL *VERSUS* BILATERAL NO CONTROLE MOTOR E NA FORÇA EM INDIVÍDUOS COM A DOENÇA DE PARKINSON ", sob responsabilidade do pesquisador Sacha Clael Rodrigues Rêgo.

O objetivo desta pesquisa é verificar os efeitos dos treinamentos resistidos unilateral versus bilateral no desempenho de tarefas motoras e na força em indivíduos com a doença de Parkinson. O intuito da pesquisa é promover um maior conhecimento sobre os sintomas motores da doença de Parkinson, melhorar a qualidade de vida e a capacidade funcional.

O(a) senhor(a) receberá todos os esclarecimentos necessários antes e no decorrer da pesquisa e lhe asseguramos que seu nome não aparecerá sendo mantido o mais rigoroso sigilo pela omissão total de quaisquer informações que permitam identificá-lo(a).

A sua participação se dará por meio dos seguintes testes: uma avaliação da condição clínica geral (anamnese) e do estado cognitivo por meio de um questionário chamado Mini Exame do Estado Mental (MEEM). A força de preensão manual será avaliada por um dinamômetro hidráulico de preensão manual e a força muscular será avaliada por um dinamômetro isocinético, além disso serão realizados testes funcionais e de coordenação motora. O(a) Senhor(a) poderá sentir um leve desconforto muscular ao

realizar o teste no dinamômetro isocinético, pois será pedido que o(a) senhor(a) produza o máximo de força possível. Os testes serão realizados no Laboratório de Pesquisa em Treinamento de Força situado na Faculdade de Educação Física da Universidade de Brasília e na sala 15A no Centro Olímpico da Universidade de Brasília. Além dos testes mencionados anteriormente, haverá um período de intervenção na Sala de Musculação do Centro Olímpico da Universidade de Brasília. O(a) senhor(a) será avaliado no momento pré-intervenção e no momento pós-intervenção.

Esta pesquisa será realizada no período de 21/03/2018 até 23/05/2018. Tendo três sessões semanais de intervenção, em um total de 24 sessões, com duração entre 30 a 60 minutos.

Para realização dos testes bem como o período de intervenção, será combinado datas e horários com o(a) senhor(a). Para a realização dos testes pré-intervenção e pós-intervenção em ambas as fases, o(a) senhor(a) terá que ir em dois dias não consecutivos, pela manhã ou pela tarde no local, na data e no horário combinados posteriormente, tais testes tem um tempo estimado de 60 a 80 minutos para sua realização. Para a realização dos pós-testes é necessária uma frequência mínima de 75% de presença nas intervenções.

Os riscos físicos decorrentes de sua participação na pesquisa são leves desconfortos musculares devido a sobrecarga de peso que será imposta pelos exercícios e pelos testes que exigem força máxima. Esse risco será minimizado com o uso de uma periodização de treino aliada a uma progressão de cargas adequadas, bem como o objetivo do próprio período de familiarização ao treinamento ser evitar possíveis desconfortos decorrentes do treinamento, além dos intervalos de recuperação entre séries de 60 segundos como consta na literatura. Caso algo fora do previsto aconteça o médico do Centro Olímpico será acionado imediatamente para realizar o atendimento, e se necessário será solicitado uma ambulância para levar o(a) senhor(a) à um hospital ou centro de saúde mais perto do CO/FEF. Além disso teremos voluntários do curso de Educação Física da Universidade de Brasília que passarão por um período de treinamento visando a segurança e aumento de conhecimento para melhor atende-lo(a) durante as fases da pesquisa bem como a utilização de uma Escala Subjetiva de Esforço. Se você aceitar participar, estará contribuindo para uma melhor avaliação motora, um melhor acompanhamento da progressão dos sintomas motores e a possibilidade de direcionar um treinamento específico para pessoas com a doença de Parkinson. Desta forma estaremos auxiliando os profissionais de saúde na avaliação, tratamento e acompanhamento da progressão da doença de Parkinson.

Os riscos psíquico, moral, intelectual e/ou social decorrentes de sua participação na pesquisa são não conseguir realizar as tarefas motoras propostas ou responder de forma assertiva o questionário. Para minimizar tais riscos, os questionários e testes motores serão aplicados de forma individual por um avaliador previamente treinado, em uma sala reservada, tornando um ambiente tranquilo e seguro para o(a) senhor(a), no qual somente o avaliador e o(a) senhor(a) saberão as respostas e pontuação dos testes e questionários. Além disso o aplicador será treinado para fazer as perguntas de forma mais leve possível, buscando gerar um ambiente de descontração e não insistirá em perguntas que o(a) senhor(a) demonstre algum desconforto.

O(a) Senhor(a) pode se recusar a responder (ou participar de qualquer procedimento) qualquer questão que lhe traga constrangimento, podendo desistir de participar da pesquisa em qualquer momento sem nenhum prejuízo para o(a) senhor(a). Sua participação é voluntária, isto é, não há pagamento por sua colaboração.

Todas as despesas que você (você e seu acompanhante, quando necessário) tiver (tiverem) relacionadas diretamente ao projeto de pesquisa (tais como, passagem para o local da pesquisa, alimentação no local da pesquisa ou exames para realização da pesquisa) serão cobertas pelo pesquisador responsável.

Caso haja algum dano direto ou indireto decorrente de sua participação na pesquisa, você deverá buscar ser indenizado, obedecendo-se as disposições legais vigentes no Brasil.

Os resultados da pesquisa serão divulgados na Faculdade de Educação Física da Universidade de Brasília podendo ser publicados posteriormente. Os dados e materiais serão utilizados somente para esta pesquisa e ficarão sob a guarda do pesquisador por um período de cinco anos, após isso serão destruídos.

Após o término da pesquisa, o(a) senhor(a) irá receber um relatório constando todas as informações fornecidas pelos questionários, testes funcionais, controle motor e de força, bem como a disponibilidade do pesquisador para eventuais dúvidas. Caso um tipo de treinamento seja comprovadamente melhor que o outro, o(a) senhor(a) terá o direito de usufruir de tal treinamento nos mesmos períodos que o outro grupo.

Se o(a) Senhor(a) tiver qualquer dúvida em relação à pesquisa, por favor telefone para: Pesquisador responsável, Sacha Clael Rodrigues Rêgo, telefone (61) 98383-7418 ou no e-mail: *sachaclael@hotmail.com* e Profª Drª Lídia Bezerra Aguiar, (orientadora) telefone (61) 99995-8907 e-mail:*lidia.bezerra@gmail.com*. Ambos os telefones podem receber ligações a cobrar.

Este projeto foi aprovado pelo Comitê de Ética em Pesquisa da Faculdade de Ciências da Saúde (CEP/FS) da Universidade de Brasília. O CEP é composto por profissionais de diferentes áreas cuja função é defender os interesses dos participantes da pesquisa em sua integridade e dignidade e contribuir no desenvolvimento da pesquisa dentro de padrões éticos. As dúvidas com relação à assinatura do TCLE ou os direitos do participante da pesquisa podem ser esclarecidos pelo telefone (61) 3107-1947 ou do e-mail cepfs@unb.br ou cepfsunb@gmail.com, horário de atendimento de 10:00hs às 12:00hs e de 13:30hs às 15:30hs, de segunda a sexta-feira. O CEP/FS se localiza na Faculdade de Ciências da Saúde, Campus Universitário Darcy Ribeiro, Universidade de Brasília, Asa Norte.

Caso concorde em participar, pedimos que assine este documento que foi elaborado em duas vias, uma ficará com o pesquisador responsável e a outra com o Senhor (a).

_____

Nome / assinatura

_____

Pesquisador Responsável

Nome e assinatura

Brasília, ___ de _____de _____.

Appendix B. Datasheets used for data collection

Universidade de Brasília
Faculdade de Educação Física

viva ativo

NOME:_____ID:_____

Estado Civil:_____ Sexo: ( ) M ( ) F Escolaridade:_____

Contato:_____

Emergência:_____

Idade:_____

Endereço:_____

Possui Plano de Saúde? ( ) Sim ( ) Não Convênio/Número:_____

Problema de saúde? _____

Medicamentos que usa:_____

Data da Avaliação:___/___/_____

Peso Corporal:_____Kg Altura:_____cm

MS Afetado:_____ MI Afetado: _____

AVALIAÇÕES LABORATÓRIOS:
( ) ISOCINÉTICO

AVALIAÇÕES FUNCIONAIS:
( ) JAMAR
( ) NINE-HOLE PEG
( ) BOX AND BLOCKS

AVALIAÇÕES QUESTIONÁRIOS E PONTUAÇÃO:
( ) MEEM - _____
( ) H&Y - _____
( ) IPAQ

viva ativo

Universidade de Brasília
Faculdade de Educação Física

Nome:_____ **Data:**___/____/____

JAMAR COTOVELO ESTENDIDO - MÃO DIREITA

1ª tentativa	2ª tentativa	3ª tentativa	Maior Valor

JAMAR COTOVELO ESTENDIDO - MÃO ESQUERDA

1ª tentativa	2ª tentativa	3ª tentativa	Maior Valor

9H - MÃO DIREITA

Tempo

9H - MÃO ESQUERDA

Tempo

BB - MÃO DIREITA

Nº Blocos

BB - MÃO ESQUERDA

Nº Blocos

viva ativo

XXXXX

UNILATERAL

DIREITO

Nome	Séries	Repetições	I.R.	Carga
Puxada alta articulada supinada	4	10 – 12	60s	
Remada sentada neutra máquina	4	10 – 12	60s	
Supino reto articulado	4	10 – 12	60s	
Supino inclinado articulado	4	10 – 12	60s	
Leg press 45°	4	10 – 12	60s	
Cadeira extensora	4	10 – 12	60s	
Mesa flexora	4	10 – 12	60s	
Cadeira flexora	4	10 – 12	60s	

ESQUERDO

Nome	Séries	Repetições	I.R.	Carga
Puxada alta articulada supinada	4	10 – 12	60s	
Remada sentada neutra máquina	4	10 – 12	60s	
Supino reto articulado	4	10 – 12	60s	
Supino inclinado articulado	4	10 – 12	60s	
Leg press 45°	4	10 – 12	60s	
Cadeira extensora	4	10 – 12	60s	
Mesa flexora	4	10 – 12	60s	
Cadeira flexora	4	10 – 12	60s	

viva ativo

XXXXX

BILATERAL

Nome	Séries	Repetições	I.R.	Carga
Puxada alta articulada supinada	4	10 – 12	60s	
Remada sentada neutra máquina	4	10 – 12	60s	
Supino reto articulado	4	10 – 12	60s	
Supino inclinado articulado	4	10 – 12	60s	
Leg press 45°	4	10 – 12	60s	
Cadeira extensora	4	10 – 12	60s	
Mesa flexora	4	10 – 12	60s	
Cadeira flexora	4	10 – 12	60s	

Nome	Séries	Repetições	I.R.	Carga
Puxada alta articulada supinada	4	10 – 12	60s	
Remada sentada neutra máquina	4	10 – 12	60s	
Supino reto articulado	4	10 – 12	60s	
Supino inclinado articulado	4	10 – 12	60s	
Leg press 45°	4	10 – 12	60s	
Cadeira extensora	4	10 – 12	60s	
Mesa flexora	4	10 – 12	60s	
Cadeira flexora	4	10 – 12	60s	

13. ANNEX

Annex A. International Physical Activity Questionnaire

QUESTIONÁRIO INTERNACIONAL DE ATIVIDADE FÍSICA – VERSÃO CURTA -

Nome:_____
Data: _____/ _____ / _____ **Idade :** _____ **Sexo: F ( ) M ( )**

Nós estamos interessados em saber que tipos de atividade física as pessoas fazem como parte do seu dia a dia. Este projeto faz parte de um grande estudo que está sendo feito em diferentes países ao redor do mundo. Suas respostas nos ajudarão a entender que tão ativos nós somos em relação à pessoas de outros países. As perguntas estão relacionadas ao tempo que você gasta fazendo atividade física na **ÚLTIMA** semana. As perguntas incluem as atividades que você faz no trabalho, para ir de um lugar a outro, por lazer, por esporte, por exercício ou como parte das suas atividades em casa ou no jardim. Suas respostas são MUITO importantes. Por favor responda cada questão mesmo que considere que não seja ativo. Obrigado pela sua participação !

Para responder as questões lembre que:
- atividades físicas **VIGOROSAS** são aquelas que precisam de um grande esforço físico e que fazem respirar MUITO mais forte que o normal
- atividades físicas **MODERADAS** são aquelas que precisam de algum esforço físico e que fazem respirar UM POUCO mais forte que o normal

Para responder as perguntas pense somente nas atividades que você realiza **por pelo menos 10 minutos contínuos** de cada vez.

1a Em quantos dias da última semana você **CAMINHOU** por pelo menos 10 minutos contínuos em casa ou no trabalho, como forma de transporte para ir de um lugar para outro, por lazer, por prazer ou como forma de exercício?

dias _____ por **SEMANA** ( ) Nenhum

1b Nos dias em que você caminhou por pelo menos 10 minutos contínuos quanto tempo no total você gastou caminhando **por dia**?

horas: _____ Minutos: _____

2a. Em quantos dias da última semana, você realizou atividades **MODERADAS** por pelo menos 10 minutos contínuos, como por exemplo pedalar leve na bicicleta, nadar, dançar, fazer ginástica aeróbica leve, jogar vôlei recreativo, carregar pesos leves, fazer serviços domésticos na casa, no quintal ou no jardim como varrer, aspirar, cuidar do jardim, ou qualquer atividade que fez aumentar **moderadamente** sua respiração ou batimentos do coração **(POR FAVOR NÃO INCLUA CAMINHADA)**

dias _____ por **SEMANA** ( ) Nenhum

2b. Nos dias em que você fez essas atividades moderadas por pelo menos 10 minutos contínuos, quanto tempo no total você gastou fazendo essas atividades **por dia**?

horas: _____ Minutos: _____

3a Em quantos dias da última semana, você realizou atividades **VIGOROSAS** por pelo menos 10 minutos contínuos, como por exemplo correr, fazer ginástica aeróbica, jogar futebol, pedalar rápido na bicicleta, jogar basquete, fazer serviços domésticos pesados em casa, no quintal ou cavoucar no jardim, carregar pesos elevados ou qualquer atividade que fez aumentar **MUITO** sua respiração ou batimentos do coração.

dias _____ por **SEMANA** ( ) Nenhum

3b Nos dias em que você fez essas atividades vigorosas por pelo menos 10 minutos contínuos quanto tempo no total você gastou fazendo essas atividades **por dia**?

horas: _____ Minutos: _____

Estas últimas questões são sobre o tempo que você permanece sentado todo dia, no trabalho, na escola ou faculdade, em casa e durante seu tempo livre. Isto inclui o tempo sentado estudando, sentado enquanto descansa, fazendo lição de casa visitando um amigo, lendo, sentado ou deitado assistindo TV. Não inclua o tempo gasto sentando durante o transporte em ônibus, trem, metrô ou carro.

4a. Quanto tempo no total você gasta sentado durante um **dia de semana**?
_____horas ____minutos
4b. Quanto tempo no total você gasta sentado durante em um **dia de final de semana**?
_____horas ____minutos

PERGUNTA SOMENTE PARA O ESTADO DE SÃO PAULO

5. Você já ouviu falar do Programa Agita São Paulo? ( ) Sim ( ) Não
6.. Você sabe o objetivo do Programa? ( ) Sim ( ) Não

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INFORMAÇÕES ANÁLISE, CLASSIFICAÇÃO E COMPARAÇÃO DE RESULTADOS NO BRASIL
Tel-Fax: – 011-42298980 ou 42299643. E-mail: celafiscs@celafiscs.com.br
Home Page: www.celafiscs.com.br IPAQ Internacional: www.ipaq.ki.se

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Annex B. Mini Mental Status Exam

Universidade de Brasília
Faculdade de Educação Física

viva alivo

Nome:_____ **Data:**___/____/____

MINI EXAME DO ESTADO MENTAL

Orientação Temporal Espacial

1. Qual é o dia?

	Pt. Obtido	Pt. Máx
Da semana?		1
Do mês?		1
Mês?		1
Ano?		1
Hora aproximada		1

2. Onde estamos?

	Pt. Obtido	Pt. Máx
Local?		1
Instituição (casa, rua?		1
Bairro?		1
Cidade?		1
Estado?		1

Registros

3. Mencione 3 palavras levando 1 segundo para cada uma. Peça ao paciente para repetir as 3 palavas que você mencionou. Estabeleça um ponto para cada resposta correta.

– VASO – CARRO – TIJOLO –

Pt. Obtido	Pt. Máx
	3

Atenção é cálculo

4. Sete seriado:**(100-7=93-7=86-7=79-7=72-7=65)**
Ou soletrar a palavra **MUNDO** de trás para frente.

Estabeleça um ponto para cada resposta correta. Interrompa após cinco respostas.

Pt. Obtido	Pt. Máx
	5

Lembranças (memória de evocação)

5. Pergunte o nome das 3 palavras aprendidas na questão 2. Estabeleça um ponto para cada resposta correta.

Pt. Obtido	Pt. Máx
	3

Linguagem

6. Aponte para um lápis e um relógio (caso não haja relógio, aponte para a mesa). Faça o voluntário dizer o nome desses objetos conforme você os aponta.

Pt. Obtido	Pt. Máx
	2

7. Faça o voluntário repetir
"NEM AQUI, NEM ALI, NEM LÁ"

Pt. Obtido	Pt. Máx
	1

8. Faça o voluntário seguir o comando de 3 estágios:
"PEGUE O PAPEL"
"DOBRE O PAPEL AO MEIO"
"COLOQUE O PAPEL NA MESA COM A MÃO DIREITA"

Pt. Obtido	Pt. Máx
	3

9. Faça o voluntário ler e obedecer o comando:
"FECHE OS OLHOS"

Pt. Obtido	Pt. Máx
	1

10. Faça o voluntário escrever uma frase. (A frase deve conter um sujeito e um objeto e fazer sentido).
(Ignore erros de ortografia ao marcar o ponto).

Pt. Obtido	Pt. Máx
	1

11. Faça o voluntário copiar o desenho da folha.
Estabeleça m ponto se todos os lados e ângulos forem preservados e se os lados da interseção formarem um quadrilátero.

Pt. Obtido	Pt. Máx
	1

ESCREVA UMA FRASE

COPIE O DESENHO