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Asymmetry in parkinson's disease and its relationship with strength

Assimetria na doença de parkinson e sua relação com a força

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ABSTRACT

The onset side in Parkinson's disease remains unclear. Furthermore, the motor symptoms are typically unilateral, with the onset side often remaining more affected throughout the disease course. Therefore, as Parkinson's disease is an idiopathic disease, several questions are raised, one of them how the disease affects each person differently. For example, a person can be right-handed for the upper limb and left-footed for the lower limb, which can change strength scores. Thus, the aim of the study was to investigate the differences in muscle strength in people with Parkinson's disease, right-handed for upper limb and right-footed for lower limb, that have one most affected side, right or left side, on the upper and lower body. The sample consisted of 26 individuals diagnosed with Parkinson's disease, right-handed for the upper limb and right-footed for the lower limb. Subjects needed to visit the laboratory one time to assess handgrip and knee extensors strength. There were no differences between sides in upper limbs affected by the disease, and there were no differences between sides in lower limbs affected by the disease, $p > 0.05$. There were no differences in strength between sides of the same body part affected by the disease. To say that people affected on the determined side are weaker than others may be a misconception since Parkinson's disease is idiopathic.

KEYWORDS: handgrip; isokinetic; Hoehn & Yard; handedness; substantia nigra.

INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disease characterized by progressive deterioration of the substantia nigra in the midbrain, which cause a decrease in dopamine production, and the dopamine reduction modifies the somatic motor activities, in addition to decrease muscle strength (Clael, 2018). Regarding the onset of motor symptoms, PD typically demonstrates unilateral impairments, with the side of onset often more affected throughout the disease course (Earhart & Falvo, 2013), causing asymmetry between limbs (Frazzitta, Pezzoli, Bertotti, & Maestri, 2013).

The development of asymmetry can worsen the quality of life of people with PD because it leads to progressive disuse of the most affected limb, inducing increased difficulties in daily living activities and motor tasks (Beretta et al., 2015). Therefore, the quantification of limb asymmetry with the aim of disease treatment is an optimal resource. Once the asymmetry is identified, the health professionals can be more accurate to indicate appropriate treatments, perhaps to improve strength on the most affected limb. Therefore, the isokinetic dynamometer and (Thistle, Hislop, Moffroid, & Lowman, 1967) the handgrip dynamometer are used to quantify muscle strength, and both are recommended for limbs assessments (Fess, 1992). Both types of equipment are considered the gold standard and widely used in the assessment of people with PD (Cano-de-la-Cuerda, Perez-de-Heredia, Miangolarra-Page, Munoz-Hellin, & Fernandez-de-Las-Penas, 2010; Olivola et al., 2018; Alomari, Khalil, Khabour, & Wood, 2018).

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The idiopathic nature of PD raises several questions, such as how the disease affects each person differently. For example, for the upper limb, the disease can affect the right side more, while for the lower limb, PD can affect the left side more. Regarding limb asymmetry, a variety of authors performed studies to investigate upper and lower limb asymmetries; however, some important methodological aspects were not reported, as the dominant side (Frazzitta et al., 2015; Yust-Katz, Tesler, Treves, Melamed, & Djaldetti, 2008). A person can be right-handed for the upper limb and left-footed for the lower limb, in addition, the PD could affect only the right side of this person, upper and lower, which can change the strength scores since the dominant side tend to be the strongest side (Noguchi, Demura, & Aoki, 2009), and a person right-handed for upper limb and left-footed for lower limb would produce less strength on the lower limb test.

Thus, the aim of the study was to investigate the differences in muscle strength in people with PD, right-handed for upper limb and right-footed for lower limb, that have one most affected side, right or left side, on the upper and lower body. We hypothesize that there will be differences between muscle strength of the limbs from the same body part.

METODOLOGY

This is an experimental, analytical study with exploratory, descriptive and explanatory objectives and mixed (quantitative and qualitative) approach.

Participants

Subjects with a confirmed diagnosis of PD and right-handed for upper limb and right-footed for lower limb were recruited. The subjects were selected using the convenience sampling technique. The exclusion criteria were any trauma that prevents participation in the study and the inability to perform any tests part of the research study.

Instruments

Subjects visited the laboratory one time for anamnesis, anthropometric measurements, handgrip strength and knee strength, respectively. Also, the data collected were carried out in the morning. Participants were classified in one of four stages of the modified Hoehn and Yahr scale (Goetz et al. 2004), therefore all the participants were assessed in "*on*" medication period and instructed not to do physical exercises 24 hours prior to the tests. Moreover, the handedness for the upper and lower body and the disease onset was defined by volunteer self-report. This study was approved by the Faculty of Health Sciences at the University of Brasília ethics committee, and all volunteers signed the consent form.

Handedness

To assess dexterity, the answers to the questions "Which hand would you use to throw a ball?" and "which foot would you use to kick a ball ?" was used (Van Melick, Meddeler, Hoogeboom, Nijhuis-van der Sanden, & Van Cingel, 2007). The answers were based on the volunteers' current conditions.

Handgrip strength test

To assess upper limbs strength, the Jamar® dynamometer was used with the protocol from the American Society of Hand Therapists (Fess, 1992). Prior to the trials, familiarization was performed with each hand by performing a submaximal squeeze, and the individual can choose with which hand started the test.

Isokinetic dynamometer

To assess lower limbs strength, the Biodex system III Isokinetic Dynamometer (Biodex Medical, Inc., Shirley, NY) was used, with our protocol (Clael et al., 2016). All warm-ups and trials had 60 seconds of rest interval and were performed only on the concentric phase. Participants performed two trials of knee extension for each leg, and the protocol was counterbalanced.

The Warm-up consisted of 1 set of 10 repetitions at 180º/s as follows: subjects were asked to do one maximum contraction and then to do 9 more contractions between 50% and 60% of the maximal effort. The trial consisted of 2 sets of 4 repetitions at 60º/s and 2 more sets of 4 repetitions at 180º/s. The trial with the highest value at each speed was used to determine the Peak Torque (PT).

Statistical analyses

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. An independent *t*-test was used between body sides comparison, and the statistical significance level was set at $p \leq 0.05$. All analyses were performed using the SPSS 24.0 (IBM Corporation, Armonk, NY, USA, 24.0) for iOS.

RESULTS

A total of 26 individuals were right-handed and right-footed, affected from different sides (right or left) in different parts of the body (upper or lower) (Table1).

Table 1. Sample characterization.

Sample (n= 26)	Mean± SD
Age (years)	67.31± 6.09
Height (meters)	1.68± 0.10
Weight (kilograms)	69.92± 12.20
Gender	**Frequency**
Men	18
Women	8
Modified Hoehn & Yard	**Frequency**
Level 1	2
Level 1.5	3
Level 2	11
Level 2.5	6
Level 3	4
Upper limb affected	**Frequency**
Right	16
Left	10
Do not exist	0
Lower limb affected	**Frequency**
Right	15
Left	7
Do not exist	4

SD: standard deviation.

There were no differences between sides in upper limbs affected by the disease (Table 2).

There were no differences between sides in lower limbs affected by the disease (Table 3).

DISCUSSION

Since PD is idiopathic, the way the disease affects the strength in both sides and parts is quite variable because the dopamine reduction in the central nervous system begins to generate incapacity of strength in the dominant or non-dominant side. PD is a neurodegenerative disease characterized by progressive deterioration of the substantia nigra in the midbrain, causing a decrease in dopamine production (Obeso, Rodriguez-Oroz, Rodriguez, Arbizu, & Gimenez-Amaya, 2002). This reduction in dopamine results in a GABA mediated tonic inhibition of the thalamus, reducing the excitation of the thalamus on cortical projection areas. This, in turn, is manifested as an alteration in somatic motor activities commonly observed in patients with PD (Purves, 2005). Also, the results presented no differences between sides of the same part affected for strength. Thus, affirming that patients affected on the right side are weaker than those affected on the left may be a misconception (Frazzitta et al., 2015). In addition, the strength decrease in people with PD is global because after initiating the disease process, all symptoms affect mobility and are progressively incapacitating since the disease is degenerative.

People with PD have bradykinesia and hypokinesia, which are slow movement performance and movement

Table 2. Comparison between Handgrip Strength Test for both sides affected.

	Right side affected n= 16	Left side affected n= 10	p
Handgrip strength test right side	31.56 (± 7.73)	29.20 (± 8.23)	0.467
Handgrip strength test left side	31.19 (± 6.83)	26.50 (± 9.04)	0.146

Presented as mean and standard deviation. Handgrip strength test values are expressed in kilograms.force (kg.f).

Table 3. Comparison between peak torque for both sides affected.

	Right side affected n= 15	Left side affected n= 7	p
PT 60°/s right side	122.74 (± 37.08)	114.94 (± 38.99)	0.665
PT 60°/s left side	123.90 (± 39.76)	104.07 (± 44.75)	0.338
PT 180°/s right side	84.44 (± 25.91)	73.30 (± 23.15)	0.344
PT 180°/s left side	84.53 (± 26.34)	69.01 (± 31.32)	0.287

Presented as mean and standard deviation. PT: peak torque; PT values are expressed in Newton.meter (N.m).

reduction, respectively (Van Hilten, Van Eerd, Wagemans, Middelkoop, & Roos, 1998); because of both symptoms, this population have difficulty performing high-velocity movements. Moreover, over time, the performance of high-velocity movements becomes more difficult due to the advancement of the disease (Bayle et al., 2016) and the ageing process (Clark et al., 2010), hence to use 120º/s as speed may not be appropriate because this speed is not very fast neither very slow speed. Therefore, freezing is a common symptom and highly disabling state that generates fear and anxiety, which increases freezing, consequently rises immobility and generates strength deficits (Frazzitta et al., 2013).

Substantia nigra deterioration in PD starts in one side of the brain, reflecting directly on the somatic motor activities, showing the cross-relation between central command and movement control (Kempster, Gibb, Stern, & Lees, 1989). Scherfler et al. (2012) showed that dopamine transporter is reduced in the left side of the brain compared with the right side, but it is possible a type 2 error because approximately 63.23% of the sample had the right side affected (Field, 2013). Thus, to say that the population with PD is weaker just by having the onset of disease manifested on one side of the body becomes a little strange, and as has been shown by Barrett, Wylie, Harrison and Wooten et al. (2011), handedness is related to disease onset.

The ability to perform maximal strength takes into account some factors, such as the number of muscle fibres, the sending of the central command signal to the target muscle and the reduction of the antagonist's coactivation (William, McArdle, Frank, & Katch, 2016). Although people with PD have a lower percentage of fast-twitch fibres (Rossi et al., 1996), the sending signals for muscle contraction are flawed due to a decrease in dopamine production (Obeso et al., 2002), and antagonist's muscles are coactivated (Glendinning & Enoka, 1994). Also, the diminished strength may be related to diagnosis time (Corcos, Chen, Quinn, McAuley, & Rothwell, 1996), medicaments type (Fabbrini, Brotchie, Grandas, Nomoto, & Goetz, 2007), medicaments interaction (Aquino & Fox, 2015), balanced diet (Tan et al., 2018), sleep (Van Gilst, Van Mierlo, Bloem, & Overeem, 2015) and freezing (Pieruccini-Faria, Jones, & Almeida, 2014).

In healthy young men, there is a strong and positive association between right and left upper body sides (Fink, Weege, Manning, & Trivers, 2014); it appears that there is no asymmetry in this population. In healthy elderlies, most of the population has some asymmetry type between the upper and right sides of the body (McGrath et al., 2021). In healthy or depressed women, the upper right side of the body tends to be stronger (Crews & Harrison, 1994). These studies (Fink et al., 2014; McGrath et al., 2021; Crews & Harrison, 1994), together with our research, show that asymmetry behaves differently in each population.

In individuals with HIV, the dominant lower limb is stronger than the non-dominant one, which generates asymmetry (Oliveira, Wiechmann, Narciso, & Deminice, 2017). In individuals with multiple sclerosis, the lower limb most affected by the disease is weaker, and this causes an asymmetry between the lower limbs in the knee (Workman, Fietsam, & Rudroff, 2020). Healthy elderly people may present asymmetry of the lower limbs (LaRoche, Villa, Bond, & Cook, 2017). In untrained healthy young people, the dominance of the lower limb does not influence the strength of the knee extensors (Maly, Zahalka, Mala, & Cech, 2015), appearing that there is no asymmetry in untrained healthy young people. And a systematic review with meta-analysis showed that the dominant lower limb in healthy adults is stronger, which generates an asymmetry of lower limbs (McGrath et al., 2016). These studies (Oliveira et al., 2017; Workman et al., 2020; LaRoche et al., 2017; Maly et al., 2015; McGrath et al., 2016), together with our study show that asymmetry behaves differently in each population.

A result against our findings performed in individuals with PD found that individuals affected on the right side of the lower limb are weaker (Frazzitta et al., 2015). Asymmetry in individuals with some disease type should be approached with caution, especially in an idiopathic disease, such as PD.

There are limitations associated with the present study. The first limitation is the small sample size which reduces the statistical power and generalizability of our findings. The second limitation is that there are more people with the disease on the right side than the left side, which may have caused a type 2 error because the sample was not paired.

CONCLUSIONS

The results suggest no differences in strength between body sides of the same part affected by the disease. Future studies can fill the gaps that we left open. For practical applications, the affected side or the side of onset of the disease has no association with limb weakness; moreover, people who work with these populations do not need to focus their treatments on the most affected side, working equally on both sides.

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