Research Article

Computerized Simple Reaction Time and Balance in Nondemented Parkinson's Patients

Computerized Simple Reaction Time Task and Balance in PD

Aida Arroyo[a], Jorge Andreo[a], José A. Periáñez[b], Marcos Ríos-Lago[c,d], Genny Lubrini[b], Jaime Herreros-Rodríguez[e], Juan García-Caldentey[f] and Juan Pablo Romero[a,d]

[a]Facultad de Ciencias Experimentales, Universidad Francisco de Vitoria, Madrid, Spain

[b]Department of Experimental Psychology, Universidad Complutense de Madrid, Madrid, Spain

[c]Basic Psychology II Department, UNED, Madrid, Spain

[d]Brain Damage Unit, Hospital Beata María Ana, Madrid, Spain

[e]Department of Neurology, Hospital Universitario Infanta Leonor, Madrid, Spain

[f]Department of Neurology, Hospital Quirón Palmaplanas, Palma de Mallorca, Spain

Juan Pablo Romero Muñoz, Facultad de Ciencias Experimentales, Universidad Francisco de Vitoria Carretera Pozuelo a Majadahonda, Km 1.800 Módulo 1, ES−28223 Madrid (Spain), E-Mail p.romero.prof@ufv.es

Abstract

Background

Parkinson's disease (PD) patients are known to suffer from subtle cognitive and balance deficits from the early stages although they usually manifest in advanced stages. Postural instability (PI) has been correlated with slower information processing speed. Simple reaction time (SRT) tasks can be used to measure the speed of information processing. The main objective of this study was to examine the usefulness of SRT as a valid predictor of balance in PD, thus providing a simple and complementary assessment method.

Methods

This cross-sectional study included 52 PD patients without dementia who were evaluated for balance using the pull test (PT) maneuver and Biodex® limits of stability (LOS). In addition, a reaction time task was used to measure processing speed. Correlation and linear regression analyses were performed.

Results

The performance of SRT tasks was correlated with the evaluation of LOS% and PT, suggesting that the SRT may be a predictor of balance performance. Longer reaction time and poorer postural stability were also associated with disease duration but not with age.

Conclusions

Poor performance in a simple reaction task can predict altered PI and can complement staging and evaluation in PD patients.

Keywords: Parkinson's disease; Balance; Information processing speed; Disease staging

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder [1]. This disease is characterized by motor symptoms, such as bradykinesia, tremor, and rigidity [2]. Nonmotor symptoms such as cognitive impairment, anosmia, sleep disorders, or depression are also part of the disease but frequently underdiagnosed [3].

The Hoehn and Yahr (HY) scale [4] is widely used to stage the disease according to the laterality of motor symptoms, stability, and motor disability [5]. The evaluation of postural stability is crucial to progress from mild to moderate (HY II to III) stages of the disease [6].

The most widely used method to assess postural stability is the pull test (PT), included in the UPDRS (Unified Parkinson's Disease Rating Scale) part III, and it evaluates the patient's ability to recover from a forceful and rapid backward pull from the shoulders [7]. This test depends on the evaluator's interpretation of patient performance [8]. The variability in test execution and interpretation has shown that this is a nonreliable method in predicting future falls in PD [9, 10]. Approximately 60% of PD patients fall once a year and 40% recurrently [11]. These falls may be correlated with the inability to achieve compensatory movements to recover the balance when their center of gravity usually oscillates out of their limits of stability (LOS) area, which is reduced in this disease [12].

On the other hand, although severe cognitive impairment can be seen in advanced stages, subtle cognitive symptoms affect up to 20% of PD patients in the early stages [13] and may even precede motor symptom onset [14]. There are cognitive requirements for maintaining balance, and they may be challenged when attention is diverted or reduced [15]. Executive function [16] and processing speed [17] are some of the cognitive functions correlated with postural stability.

Simple reaction time (SRT) is the time taken between the presentation of a reaction stimulus and the moment at which an intentional response to it is produced [18]; in this regard, the SRT task, despite its simplicity, has been considered a reliable measure of information processing speed [19]. Nevertheless, there is controversy about the influence of motor impairment on the execution of computerized SRT task evaluation as the response depends on the fitness to tap a key with a finger. Motor fitness can be evaluated by the computerized finger tapping (FT) task. This task has been demonstrated to be correlated with the repetitive tapping of the index finger against the thumb tip, one of the motor tasks evaluated in UPDRS [20]. FT is one of the most reliable indicators of bradykinesia, correlated with the dopaminergic stimulation status [21].

PD patients used to exhibit slower performance in SRT tasks as compared to healthy controls [22]. Deficit in the dopamine transporter has been correlated significantly with worse SRT task performance [23] as well as more postural impairments [24]. This is in line with Pantall et al. [25] findings, stating that cognitive function and postural control worsen progressively with the progression of the disease.

However, to our knowledge, there are no studies describing correlations between computerized SRT tasks and postural stability. This information will be relevant for the assessment of PD patients since RT measures are accessible simple tasks for the patients, which need simple technical equipment, provide measures relatively stable over time, and provide reliable scores not prone to interpretation. Given this, the main objective of this study was to clarify the ability of computerized SRT task performance to predict the assessment of balance with Biodex LOS and PT evaluation in a cohort of nondemented PD patients. Secondarily correlations with clinical markers of disease evolution such as the HY scale, years of disease evolution, and L-dopa equivalent daily doses (LEDDs) were explored.

The following hypotheses were formulated. First, it was hypothesized that the performance of the PD patient on the SRT task will be correlated with the PT score. Second, the performance of the patient with PD on the SRT task will correlate with the instrumental assessment of balance using LOS. Finally, the performance of the SRT task will be correlated with the markers of the clinical evolution in PD: LEDD, years of disease, and UPDRS III.

Materials and Methods

Participants

For this cross-sectional case study, a total of 54 PD patients were recruited in the movement disorders clinic at the Beata María Ana Hospital from March 2018 to June 2019. Extreme cases (2 standard deviations above the mean) were eliminated. Exclusion criteria were set for patients who were using advanced therapies for PD (apomorphine pump/duodenal dopamine infusion/deep brain stimulation); structural alterations in previous imaging studies; Montreal Cognitive Assessment (MoCA) score <25 [26]; poor response to levodopa or suspicion of atypical parkinsonism; any other neurological disease or severe comorbidity; strength, proprioception, vestibular, and severe visual deficiencies; or history of falls due to postural instability. Inclusion criteria for patients with PD were to be over 18 years of age, idiopathic PD diagnosed according to the London brain bank criteria [27], stage <III in the Hoehn-Yahr scale, not having evident motor fluctuations, and clinical stability (not having changed the antiparkinsonian medication in the last 30 days or antidepressive medication in the last 90 days). All patients were in "ON state" at the time of the evaluation to avoid the influence of motor and nonmotor symptom fluctuations on reaction time [28] and to assure a proper motor execution of the task.

Clinical Evaluation

Evaluation of the participants was carried out in a single session lasting 90 min. Clinical and sociodemographic data were collected. UPDRS III evaluations were video recorded and evaluated by 3 different neurologists (one in real-time [J.P.R.] and the other two by video examination [J.H.R. and J.G.C.]). The scores from the 3 clinicians yielded a kappa value of 0.726. The participants performed the computerized tasks (SRT task and FT task) and stability limits, the same day. The order of the tasks was counterbalanced, and LEDD was calculated for each patient.

Computerized Tasks

Participants were examined with 2 computerized tasks as described below. The tasks were performed using a 15-inch monitor, controlled by using Presentation® software (http://www.neurobs.com). The order of presentation of the task was counterbalanced among the participants. The average RTs in each of the tasks and the percentage of correct answers were measured (Table 1).

Table 1.

The table layout displayed in this section is not how it will appear in the final version. The representation below is solely purposed for providing corrections to the table.

Means (SD) of demographic and clinical data from participants and means (SD) of LOS and RT in milliseconds and percent of correct responses for the RT tasks

	PD
N (male)	52 (37)
Age, years	62.63 (9.18)
Education, years	13.35 (4.12)
Diseased duration, years	5.81 (3.97)
HY	HY I: 14; HY II: 30; HY III: 7
UPDRS III	14.61 (7.32)
PT	PT 0: 30; PT 1: 11; PT 2:10
LEDD	686.72 (432.16)
FT	
RT, ms	215.37 (39.05)
SRT	
RT, ms	360.35 (70.61)
% Correct	96.28 (6.75)

LOS	42.00 (8.70)
LOS-TIME	70.28 (2.03)

PD, Parkinson's disease; HY, Hoehn and Yahr Scale; UPDRS III, Unified Parkinson's Disease Rating Scale III; PT, pull test score in UDPRS III; LEDD, L-dopa equivalent daily dose; FT, finger tapping task; RT, reaction time in milliseconds; SRT, simple reaction time task; % correct, percentage of correct responses; LOS, limits of stability; LOS-TIME, time in seconds to perform the LOS test.

Finger Tapping

The FT task has been used as a measure of motor function [29]. This task is very sensitive to slowing down responses [30]. In studies with PD patients, it has been used as a measure of motor speed [31]. In this task, following the Strauss application norms [30], the participants were instructed to press the spacebar on the keyboard as fast as possible and repeatedly with the index finger. Five 10-s attempts were performed with the dominant hand. Five 10-s trials were performed with the dominant hand. The dependent variable was the average time of the 5 trials, being the score in each trial calculated as the mean of response times recorded between 2 consecutive taps.

Simple Reaction Time

It is inspired by the SRT task of the Computerized Information Processing Testing battery [32]. This task was used as a measure of speed of information processing or the time taken between the presentation of a reaction stimulus, the completion of cognitive processes, and the execution of a motor output [33]. In PD, it has also been previously used as a measure of speed of information processing [34]. Participants were instructed to press the left mouse button as fast as possible when the "+" stimulus appeared in the center of the screen. The order of appearance was constant for all participants, the stimulus remained on the screen for 1 s, there was no presence of distractors, and the size of the stimulus was always 2 × 2 cm. The task consisted of 50 trials lasting 2–3 min.

Limits of Stability Evaluation

Biodex Balance System® "static limits of stability" (LOS) protocol was used. This device provides a high-resolution and adjustable touch-screen LCD display with visual and audio augmented biofeedback [35].

Before the test, the system adjusts feet setting on the platform according to the patient's height. The body movements to shift the gravity center (weight) move the cursor from a central visual target to a blinking target that shuffles in 8 directions. Target placement was preset by the manufacturer at 50% of the expected LOS, based on the height of each volunteer. The participants were instructed to reach each target and back to the center as quick and with less deviation as possible. The test was completed 3 times by each participant. The first 2 attempts were training, and during the third trial, the scores of the dependent variables were obtained. The 2 test-dependent measures were the time in seconds taken by the participant to finish the test (LOS-TIME) and the percentage of the expected LOS reached by the patient (LOS%). Lower LOS% scores and increased LOS-TIME meant poorer stability [36].

Statistical Analysis

Pearson correlations were performed when the 2 variables were quantitative, and Spearman's correlation was performed when the qualitative variables PT and HY scale were involved. Multiple linear regression analysis was performed with the successive steps method with the LOS% variable as the dependent variable. The predictor variables added to the analysis were disease duration in years, age, levodopa dose, UPDRS III, FT task, and SRT task. All analyses were performed using SPSS v 19.0 (IBM Corp., Armonk, NY, USA) with a level of significance $p < 0.05$.

Results

The demographic and clinical characteristics of all the participants are shown in Table 1. The final study sample was 52 patients, and 2 patients were discarded due to their extreme scores on the SRT task.

Correlations between Balance and Reaction Times

As it is shown in Table 2, LOS% was correlated with LOS-TIME and SRT task. There was no correlation between LOS% and FT task, LOS-TIME with FT task and SRT task, and SRT task with FT task.

Table 2.

The table layout displayed in this section is not how it will appear in the final version. The representation below is solely purposed for providing corrections to the table.

Correlations between balance and reaction times

	LOS	LOS-TIME	FT	SRT	PT
m					
r	1	−0.667	−0.098	−0.324	−0.396
p		<0.001*	0.489	0.019*	0.004*
LOS-TIME					
r		1	0.093	0.114	0.398
p			0.510	0.422	0.014*
FT					
r			1	0.141	0.222
p				0.309	0.120
SRT					
r				1	0.620
p					<0.001*
PT					
r					1
p					

LOS, limits of stability; LOS-TIME, time to perform the LOS test; FT, finger tapping task; SRT, simple reaction time task; PT, pull test score in UDPRS III; *r*, Pearson correlation coefficient; *p*, signification.

**p* value significant.

Correlations between Clinical Evolution Variables, Balance, and Reaction Times

Most of the correlations shown in Table 3 were moderate (*r* 0.3–0.7). The SRT task was correlated with UPDRS III and disease duration and weakly correlated with the HY scale. The FT task was moderately correlated only with UPDRS III.

Table 3.

The table layout displayed in this section is not how it will appear in the final version. The representation below is solely purposed for providing corrections to the table.

Correlations between clinical evolution variables, balance, and reaction times

	Age		LEDD		UPDRS III		HY		Disease duration in years	
	r	*p*	*r*	*p*	*r*	*p*	r_s	*p*	*r*	*p*
LOS	−0.162	0.251	−0.358	0.017*	0.071	0.623	−0.348	0.012*	−0.411	0.002*
LOS-T	0.029	0.103	0.231	0.131	−0.023	0.243	0.316	0.024*	0.278	0.046

FT	0.069	0.625	−0.066	0.669	0.360	0.009*	0.088	0.541	0.227	0.105
SRT	0.189	0.179	0.270	0.076	0.364	0.009*	0.298	0.034	0.323	0.019*
PT	r_s 0.223	0.109	r_s 0.343	0.022*	r_s 0.424	0.002*	0.541	<0.001*	r_s 0.244	0.014*

LOS, limits of stability; SRT, simple reaction time task; LOS-T, time to perform the LOS test; FT, finger tapping; UPDRS III, Part III of the Unified Parkinson Disease Rating Scale; PT, pull test score in UDPRS III; LEDD, L-dopa equivalent daily dose; HY, Hoehn and Yahr Scale; r, Pearson correlation coefficient; r_s, Spearman correlation coefficient; p, signification.

*p value significant.

LOS% was correlated negatively with PT, HY scale, and disease duration in years. The only variable correlated with LEDD was LOS%.

LOS-TIME was correlated with the HY scale and weakly with disease duration in years. Age did not correlate with any clinical variable (Table 3).

Linear Regression Analysis

Regression analysis for the variable LOS% indicates that the SRT task can predict the variance with an adjusted R^2 of 0.201 and a significance level of 0.002, and together with the variable disease duration in years, it can predict 26.1% of the variance of LOS% (Table 4). The successive steps method did not include more predictor variables in the model.

Table 4.

The table layout displayed in this section is not how it will appear in the final version. The representation below is solely purposed for providing corrections to the table.

Values of the linear regression for the prediction of LOS% from the SRT task and the duration of the disease in years

Model	Variable	*B*	β	*R*	R^2	Adjusted R^2	*p*
1	SRT	−0.107	−0.448	0.448	0.201	0.181	0.002*
2	SRT	−0.080	−0.334	0.554	0.296	0.261	0.001*
	Disease duration in years	−1.274	−0.329				

Q21

Dependence variable: LOS%.

LOS, limits of stability; SRT, simple reaction time; B, beta; β, typified beta coefficient; *p,* signification.

Discussion

The main objective of this study was to explore the usefulness of reaction times as a simple and complementary assessment method to predict balance in PD patients. In this regard, the evaluation of postural stability is crucial to progress from mild to moderate (HY II to III) stages of the disease [4]. To do so, the relationship between balance measures and RTs from both FT and SRT tasks was explored.

The results revealed that the stability evaluation of LOS% and PT was significantly correlated with the performance of the SRT task in patients with PD. Previous studies indicated that PD patients were slower than healthy controls in the SRT task, even eliminating the motor component, that is, the perceptual and alert component seems to be affected in PD patients [37]. The slowness in perceptual processing may be related to postural stability because PD patients have an altered perception of their verticality, and postural control requires rapid changes in the perception of the environment [38, 39].

None of these correlations in our study were seen with the FT task, suggesting that motor fitness was not modulating cognitive task performance in the present study. As expected, the FT task was only correlated with the total UPDRS III score. Interestingly, the total UPDRS III score was also correlated with SRT task performance that might reflect an association between and more general information processing speed factor and global motor performance. Further studies should explore this point.

Longer disease duration and higher HY staging were correlated with slower performance in the SRT task but also with worst LOS%, LOS-TIME, and PT. LOS% had also a significant negative correlation with the LEDD [40], and this is in line with the known relation of progression of the disease with the worst balance and information processing speed.

The relationship found between the SRT task and all the clinical evolution variables being included indicates that it may be a good marker of disease progression, and this finding is in line with previous reports that suggest that slowness of information processing may be found from initial stages [37]. Interestingly, neither SRT task nor LOS% were correlated with age in PD patients. Although worse balance and the SRT task are expected in older patients, in PD patients, this relationship seems to be influenced mainly by the disease.

Balance is to date a crucial clinical feature used to stage PD patients according to the HY scale and is currently evaluated using the PT. In the present study, PT correlated negatively with LOS% as expected [12]. Nevertheless, objective balance evaluation may be considered in early-stage patients as several studies show balance impairment before alterations in PT become evident [41].

The SRT task, together with the time of disease development, can predict postural stability. This relationship, although moderate, may confirm that slow information processing can be a reliable predictor of balance performance [42].

This study was not without limitations. We did not include PD patients in HY stages >3 because we did not want motor fluctuations or dyskinesias to interfere with balance evaluation or FT task performance. Although this allowed us to have a more homogeneous sample, it may have limited our capacity to explore if the evidenced correlations are still valid in advanced stages of the disease or in absence of dopaminergic stimulation (off state). It should be noted that "processing speed" itself may be influenced by several neural subprocesses that are not differenced in our work such as central pathway conduction and premotor activation. The differentiation of these subprocesses may constitute future research lines.

Although the evidence found has a solid justification, the correlations are just moderated, and this may be due to the limited number of included participants. In concordance with previous results stating that balance posturographic measures may be related to attention performance [42], a more complex battery of reaction time tasks and a complete neuropsychological assessment of frontal lobe-related functions would be desirable to elucidate if there is a particular component of information processing justifying the evidenced slowness in the SRT task observed in the present study.

Conclusions

These results must be interpreted as preliminary requiring further research. However, they raise the clear possibility that the SRT task could be an accessible computer-based instrument that may be as valid as balance evaluation to stage the disease. The computerized reaction time task may have a great impact on the management, classification, and falls prevention in PD patients. Further research is required to validate its impact. The correlation of balance impairments with SRT task performance must lead clinicians to assess balance and information processing speed in parallel from the first stages of the disease.

Acknowledgments

The authors would like to thank Pedro Serrano for his assistance with the balance Biodex assessment and Francisco Sánchez Cuesta for his assistance with data curation.

Statement of Ethics

The project was approved by the institution's bioethics committee (Hospital de Fuenlabrada, Version 1 Code 16/37 in July 2016). All participants were informed of the details of the evaluation and signed their consent to participate in this study, by following the Declaration of Helsinki.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This research was funded by the Ministry of Economy and Competitiveness (Grant DPI2015-68664-C4-3-R [MINECO/FEDER], NeuroMOD therapy development and evaluation of motor and cognitive impact for Parkinson's disease rehabilitation) and Asociación Madrileña de Neurología Research Scholarship 2019.

Author Contributions

Conceptualization: A.A.F. and J.R.; methodology: A.A.F. and J.R.; software: M.R., J.P., and G.L.; formal analysis: A.A.F., J.A., J.R., J.H.R., and J.G.C.; investigation: A.A.F. and J.R.; resources: J.R.; data curation: A.A.F., J.A., J.R., J.H.R., and J.G.C.; writing – original draft preparation: J.A., A.A.F., and J.R.; writing – review and editing: A.A.F., M.R., J.P., G.L., and J.R.; visualization: J.R.; supervision: J.R.; project administration: J.R.; funding acquisition: J.R. All authors have read and agreed to the published version of the manuscript.

Availability of Data and Material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

The corrections made in this section will be reviewed by journal production editor.

[1] Dorsey ER, Constantinescu R, Thompson JP, Biglan KM, Holloway RG, Kieburtz K, et al. Projected number of people with Parkinson disease in the most populous nations, 2005 through 2030. Neurology. 2007 Jan;68(5):384–6. http://dx.doi.org/10.1212/01.wnl.0000247740.47667.03.

[2] DeMaagd G, Philip A. Parkinson's disease and its management: part 4: treatment of motor complications. P T. 2015 Aug;40(8):747–73.

[3] Rana AQ, Ahmed US, Chaudry ZM, Vasan S. Parkinson's disease: a review of non-motor symptoms. Expert Rev Neurother. 2015 May;15(5):549–62.

[4] Bhidayasiri R, Tarsy D. Parkinson's disease: Hoehn and Yahr Scale. In: Bhidayasiri R, Tarsy D, editors. Movement disorders: a video atlas: a video atlas. Totowa, NJ: Humana Press; 2012. p. 4–5. http://dx.doi.org/10.1007/978-1-60327-426-5_2.

[5] Scanlon BK, Katzen HL, Levin BE, Singer C, Papapetropoulos S. A formula for the conversion of UPDRS-III scores to Hoehn and Yahr stage. Parkinsonism Relat Disord. 2008;14(4):379–80. http://dx.doi.org/10.1016/j.parkreldis.2007.09.010.

[6] Kataoka H, Tanaka N, Eng M, Saeki K, Kiriyama T, Eura N, et al. Risk of falling in Parkinson's disease at the Hoehn-Yahr stage III. Eur Neurol. 2011;66(5):298–304. http://dx.doi.org/10.1159/000331635.

[7] Hunt AL, Sethi KD. The pull test: a history. Mov Disord. 2006;21(7):894–9. http://dx.doi.org/10.1002/mds.20925.

[8] Munhoz RP, Li JY, Kurtinecz M, Piboolnurak P, Constantino A, Fahn S, et al. Evaluation of the pull test technique in assessing postural instability in Parkinson's disease. Neurology. 2004 Jan;62(1):125–7. http://dx.doi.org/10.1212/wnl.62.1.125.

[9] Nonnekes J, Goselink R, Weerdesteyn V, Bloem BR. The retropulsion test: a good evaluation of postural instability in Parkinson's disease? J Park Dis. 2015;5(1):43–7.

[10] Munhoz RP, Teive HA. Pull test performance and correlation with falls risk in Parkinson's disease. Arq Neuropsiquiatr. 2014 Aug;72(8):587–91. http://dx.doi.org/10.1590/0004-282x20140082.

[11] Canning CG, Sherrington C, Lord SR, Close JC, Heritier S, Heller GZ, et al. Exercise for falls prevention in Parkinson disease: a randomized controlled trial. Neurology. 2015 Jan;84(3):304–12. http://dx.doi.org/10.1212/WNL.0000000000001155.

[12] Doná F, Aquino CC, Gazzola JM, Borges V, Silva SMCA, Ganança FF, et al. Changes in postural control in patients with Parkinson's disease: a posturographic study. Physiotherapy. 2016 Sep;102(3):272–9.

[13] Lawson RA, Yarnall AJ, Duncan GW, Breen DP, Khoo TK, Williams-Gray CH, et al. Cognitive decline and quality of life in incident Parkinson's disease: the role of attention. Parkinsonism Relat Disord. 2016 Jun;27:47–53.

[14] Rodríguez-Violante M, Zerón-Martínez R, Cervantes-Arriaga A, Corona T. Who can diagnose Parkinson's disease first? Role of pre-motor symptoms. Arch Med Res. 2017 Apr;48(3):221–7.

[15] Chen T, Fan Y, Zhuang X, Feng D, Chen Y, Chan P, et al. Postural sway in patients with early Parkinson's disease performing cognitive tasks while standing. Neurol Res. 2018 Jun;40(6):491–8. http://dx.doi.org/10.1080/01616412.2018.1451017.

[16] Plotnik M, Giladi N, Dagan Y, Hausdorff JM. Postural instability and fall risk in Parkinson's disease: impaired dual tasking, pacing, and bilateral coordination of gait during the "ON" medication state. Exp Brain Res. 2011 May;210(3–4):529–38.

[17] Pal G, O'Keefe J, Robertson-Dick E, Bernard B, Anderson S, Hall D. Global cognitive function and processing speed are associated with gait and balance dysfunction in Parkinson's disease. J Neuroeng Rehabil. 2016 28;13(1):94. http://dx.doi.org/10.1186/s12984-016-0205-y.

[18] Jensen AR. Clocking the mind: mental chronometry and individual differences. Elsevier; 2006.

[19] Woods DL, Wyma JM, Yund EW, Herron TJ, Reed B. Factors influencing the latency of simple reaction time. Front Hum Neurosci. 2015 Mar;9:131. http://dx.doi.org/10.3389/fnhum.2015.00131.

[20] Taylor Tavares AL, Jefferis GS, Koop M, Hill BC, Hastie T, Heit G, et al. Quantitative measurements of alternating finger tapping in Parkinson's disease correlate with UPDRS motor disability and reveal the improvement in fine motor control from medication and deep brain stimulation. Mov Disord. 2005 Oct;20(10):1286–98. http://dx.doi.org/10.1002/mds.20556.

[21] Picillo M, Vincos GB, Kern DS, Fox SH, Lang AE, Fasano A. Learning more from finger tapping in Parkinson's disease: up and down from Dyskinesia to Bradykinesia. Mov Disord Clin Pract. 2015 Oct;3(2):184–7.

[22] Bloxham CA, Dick DJ, Moore M. Reaction times and attention in Parkinson's disease. J Neurol Neurosurg Psychiatry. 1987 Sep;50(9):1178–83. http://dx.doi.org/10.1136/jnnp.50.9.1178.

[23] van Dyck CH, Avery RA, MacAvoy MG, Marek KL, Quinlan DM, Baldwin RM, et al. Striatal dopamine transporters correlate with simple reaction time in elderly subjects. Neurobiol Aging. 2008 Aug;29(8):1237–46. http://dx.doi.org/10.1016/j.neurobiolaging.2007.02.012.

[24] Corrêa PS, Pagnussat AS, Cabeleira MEP, Schifino GP, Rieder CRM, da Silva Junior N, et al. Is the dopaminergic loss associated with gait and postural impairments in subjects with Parkinson's disease at different motor stages? Eur J Neurosci. 2019;50(12):3889–95. http://dx.doi.org/10.1111/ejn.14522.

[25] Pantall A, Suresparan P, Kapa L, Morris R, Yarnall A, Del Din S, et al. Postural dynamics are associated with cognitive decline in Parkinson's disease. Front Neurol. 2018;9:1044. http://dx.doi.org/10.3389/fneur.2018.01044.

[26] Nazem S, Siderowf AD, Duda JE, Have TT, Colcher A, Horn SS, et al. Montreal cognitive assessment performance in patients with Parkinson's disease with "normal" global cognition according to mini-mental state examination score. J Am Geriatr Soc. 2009 Feb;57(2):304–8. http://dx.doi.org/10.1111/j.1532-5415.2008.02096.x.

[27] Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry. 1992 Mar;55(3):181–4.

[28] Witjas T, Kaphan E, Azulay JP, Blin O, Ceccaldi M, Pouget J, et al. Nonmotor fluctuations in Parkinson's disease: frequent and disabling. Neurology. 2002 Aug;59(3):408–13.

[29] Reitan RM, Wolfson D. Relationships between specific and general tests of cerebral functioning. Clin Neuropsychol. 1996 Jan;10(1):37–42. http://dx.doi.org/10.1080/13854049608406661.

[30] Strauss E, Sherman EMS, Spreen O, Spreen O. A compendium of neuropsychological tests: administration, norms, and commentary. 3rd ed Oxford ; New York: Oxford University Press; 2006.

[31] Bronte-Stewart HM, Ding L, Alexander C, Zhou Y, Moore GP. Quantitative digitography (QDG): a sensitive measure of digital motor control in idiopathic Parkinson's disease. Mov Disord. 2000;15(1):36–47.

[32] Reicker LI, Tombaugh TN, Walker L, Freedman MS. Reaction time: an alternative method for assessing the effects of multiple sclerosis on information processing speed. Arch Clin Neuropsychol. 2007 Jun;22(5):655–64. http://dx.doi.org/10.1016/j.acn.2007.04.008.

[33] Costa SL, Genova HM, DeLuca J, Chiaravalloti ND. Information processing speed in multiple sclerosis: past, present, and future. Mult Scler. 2017 May;23(6):772–89. http://dx.doi.org/10.1177/1352458516645869.

[34] Jahanshahi M, Brown RG, Marsden CD. Simple and choice reaction time and the use of advance information for motor preparation in Parkinson's disease. Brain. 1992;115 (Pt 2)(2):539–64. http://dx.doi.org/10.1093/brain/115.2.539.

35. Thompson N, Wilcox D, Jackson K. A clinical guideline for the treatment of patients with Parkinson's Disease using Biodex Technology [Internet]. Biodex; 2016 [cited 2020 May 25]. Available from: https://www.biodex.com/physical-medicine/products/treadmills/gait-trainer-3/clinical-guidelines-0.

[36] Pickerill ML, Harter RA. Validity and reliability of limits-of-stability testing: a comparison of 2 postural stability evaluation devices. J Athl Train. 2011 Dec;46(6):600–6. http://dx.doi.org/10.4085/1062-6050-46.6.600.

[37] Arroyo A, Periáñez JA, Ríos-Lago M, Lubrini G, Andreo J, Benito-León J, et al. Components determining the slowness of information processing in parkinson's disease. Brain Behav. 2021;11(3):e02031. http://dx.doi.org/10.1002/brb3.2031.

[38] Schindlbeck KA, Naumann W, Maier A, Ehlen F, Marzinzik F, Klostermann F. Disturbance of verticality perception and postural dysfunction in Parkinson's disease. Acta Neurol Scand. 2018;137(2):212–7. http://dx.doi.org/10.1111/ane.12859.

[39] Jazaeri SZ, Azad A, Mehdizadeh H, Habibi SA, Mandehgary Najafabadi M, Saberi ZS, et al. The effects of anxiety and external attentional focus on postural control in patients with Parkinson's disease. PLos One. 2018 Feb;13(2):e0192168. http://dx.doi.org/10.1371/journal.pone.0192168.

[40] Mancini M, Rocchi L, Horak FB, Chiari L. Effects of Parkinson's disease and levodopa on functional limits of stability. Clin Biomech. 2008 May;23(4):450–8. http://dx.doi.org/10.1016/j.clinbiomech.2007.11.007.

[41]

Ganesan M, Pal PK, Gupta A, Sathyaprabha TN. Dynamic posturography in evaluation of balance in patients of Parkinson's disease with normal pull test: concept of a diagonal pull test. Parkinsonism Relat Disord. 2010 Nov;16(9):595–9.

[42] Souza CO, Voos MC, Barbosa AF, Chen J, Francato DCV, Milosevic M, et al. Relationship between posturography, clinical balance and executive function in Parkinson's Disease. J Mot Behav. 2018 Apr;51(2):212–21.

Queries and Answers

Q21

Query: Please provide the significance of * in Table 4.

Answer: *p value significant.

General Comment

First atuhor last name should be Arroyo-Ferrer so ir can mathc previous publications of this author. Full name is Aida Arroyo-Ferrer. Author contributions should say A.A.F. where it says A.A. I am sorry for any inconvenience this may cause.