Title: Parkinson's disease and cognitive-motor dual-task: is motor prioritization possible in the early stages of the disease?

Running head: Parkinson's disease and motor prioritization

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Conflict of Interest Statement

The authors report no conflict of interest.

Abstract

This study aimed to compare the postural phase of gait initiation under single-task (gait initiation) and dual-task (gait initiation plus Stroop test) conditions in healthy subjects and in subjects with Parkinson´s Disease (PD) in the early stages (Hoehn and Yahr scale < 3). The postural phase of gait initiation was assessed through the centre of pressure in single- and dual-task in 10 healthy subjects and 9 with PD. The analysis indicated that in the early stages of PD, an additional cognitive task did not affect the displacement of the gait initiation. No significant effects occurred between the groups and within-subjects ($p > 0.05$). Also, no interaction was found between the groups and the conditions (single- and dual-task). Differences were found in the duration of the mediolateral postural phase ($p = 0.003$), which was higher in PD subjects than in healthy subjects. The findings suggest that subjects in the early stages of PD prioritize gait initiation, since their motor performance was similar to that of healthy subjects.

1. INTRODUCTION

The dual-task condition involves the execution of two tasks simultaneously. One is the main task, and the other is the secondary task (Kelly, Eusterbrock, & Shumway-Cook, 2012b; Nocera, Roemmich, Elrod, Altmann, & Hass, 2013; Sethi & Raja, 2012). The performance of two tasks simultaneously leads to a competition for limited resources that results in the deterioration of the performance of one or both tasks (Kelly, Eusterbrock, & Shumway-Cook, 2012a; Wu & Hallett, 2009).

Biomechanical studies of postural stability have demonstrated that in the dual-task condition, subjects with Parkinson's disease (PD) exhibit impaired postural control. In addition, some authors have suggested that the dual-task condition restricts their anticipatory postural adjustments (APAs), in order to focus on the cognitive task without losing balance (Nocera et al., 2013; Yogev-Seligmann et al., 2010).

Postural phase of gait initiation (GI) is associated to the interval between the first vertical impulse, due to the APAs, until the maximum centre of pressure (CoP) displacement backward and toward the first swing limb. It is characterized by a backward displacement of CoP that results from the APAs causing a forward displacement of the centre of gravity (Caderbya et al., 2013; Yiou, Caderby, & Hussein, 2012). Subjects with PD often have difficulties in generating APAs, particularly in forward propulsion and lateral weight shift when initiating gait (Hall, Brauer, Horak, & Hodges, 2013). Studies involving subjects with PD have shown that the duration of APAs is extended, the backward and lateral displacements of the CoP are reduced and the length and velocity of the first step are shortened (Burleigh-Jacobs, Horak, Nutt, & Obeso, 1997; Crenna et al., 2006; Gantchev, Viallet, & Aurenty, 1996; Hall et al., 2013; Halliday, Winter, Frank, Patla, & Prince, 1998; Rogers et al., 2011), increasing the risk of falls (Kelly et al., 2012a; Schmit et al., 2005).

Difficulties in performing two tasks simultaneously may be associated with executive dysfunction and attention deficits, which are characteristics of PD (Hausdorff et al., 2006). When subjects with PD focus on the motor performance, they can perform normal patterns of movement by activating the uninjured premotor cortex and not using the injured basal ganglia circuit, thereby ensuring the performance of movements. However, in dual-task condition, the use of cortical resources to carry out motor tasks may compromise or influence the performance of one or both tasks (J. D. Holmes, M. E. Jenkins, A. M. Johnson, S. G. Adams, & S. J. Spaulding, 2010; Kelly et al., 2012a; Wu & Hallett, 2009).

Furthermore, several studies have revealed higher instability in upright standing in individuals aged over 65 with and without any pathology that becomes more notorious in the individuals after stage 3 of PD (Tsutiya et al., 2011). However, there is a lack of information about the early stages of PD as well as the influence of the dual-task in GI. Therefore, the aim of this study was to compare the postural phase on GI in single- and dual-task conditions in healthy subjects and in subjects in the early stages of PD (Hoehn and Yahr scale < 3). Therefore, the anteroposterior and mediolateral CoP displacements, the anteroposterior and mediolateral velocities of the CoP displacements and the anteroposterior and mediolateral durations of the postural phase were assessed.

2. METHODS

2.1. Participants

A cross-sectional study was implemented using a non-probabilistic convenience sample (Doherty, 1994) of 9 subjects with PD and 10 healthy subjects, aged between 52 and 80 years old. The size of the sample used is in-line with other studies of this kind, such as the studies of Nocera et al. (2013) with 13 PD individuals; Halliday et al. (1998), with

10 PD individuals; J. Holmes, M. Jenkins, A. Johnson, S. Adams, and S. Spaulding (2010), with 12 PD individuals; Rogers et al. (2011), with 8 PD individuals; Schmit, et al. (Schmit et al., 2005) with 6 PD subjects; and the studies of Hiraoka et al. (2006) with 9 PD individuals, and in (2005) with 11 PD individuals. The subjects diagnosed with PD were patients from the Parkinson's Association in Porto, Portugal, while the healthy controls were community-dwelling volunteers mainly from Porto, Portugal.

Subjects were excluded if they presented one of the following factors: incapable of walking independently (based on the Timed Up and Go test (TUG) score until 10 seconds (Podsiadlo & Richardson, 1991)); unable to speak; and severe cognitive impairment (screened with the Montreal Cognitive Assessment (MoCA) (Hoops et al., 2009)). The option for the MoCA test was based on the study by Chou et al. (Chou et al., 2010) who analyzed 5 statistical tests and recommended it as a standard cognitive screening instrument to be used in clinical trials with PD patients. The reasons for this recommendation are that it can be performed quickly and has the potential to identify subtle executive dysfunctions, while covering the major cognitive domains. Severely disabled PD patients (> 3 Hoehn and Yahr Scale (Hoehn & Yahr, 1967)), patients diagnosed with any other neuromuscular disease, or those who had undergone deep brain stimulation through subthalamic surgery or were under cholinergic medication were also excluded. Healthy subjects that have been diagnosed as adults with any neuromuscular disorder or that cannot be considered sedentary, according to the Centre for Disease Control for the American College of Sports Medicine, were also excluded (Pate et al., 1995).

A trained researcher conducted the data collection based on a structured protocol. The study was approved by the Ethical Review Board of the "Escola Superior de Tecnologia

da Saúde - Instituto Politécnico do Porto", in Portugal. Written informed consent, according to the Helsinki Declaration, was obtained from all participants.

2.2. Instruments

The data collected from all participants included sociodemographic characteristics (age, gender, height, weight and level of education), years of disease, cognitive performance (assessed by the MoCA test), functional mobility (evaluated using the TUG test), number of colours correctly named and errors according to the Stroop test, and values in terms of the Hoehn and Yahr scale (1967).

Hoehn and Yahr scale is commonly used to assess the severity of overall dysfunction in PD subjects. It is a 7-point scale, in which each point represents a different stage of the disease (stages 1 to 5, including 1.5 and 2.5). The scale increases with the severity of dysfunction along with the stage of the disease (Hoehn & Yahr, 1967).

The values of the vertical, anteroposterior and mediolateral components of the ground reaction forces (GRF) were obtained from a force platform, model FP4060-8 from Bertec Corporation (USA), according to a sampling rate of 1000 Hz (Hanke & Rogers, 1992). The platform was connected to a Bertec AM 6300 amplifier (USA) and in turn, this was connected to an analog-digital converter from Biopac Systems, Inc. (USA), and to an analog board of Qualysis Track Manager (Sweden) that can be used for stabilometric analyses. The force platform signals were digitized and stored for subsequent analysis in Acqknowledge (Biopac Systems, Inc., U.S.A).

2.3. Procedures

After an explanation of all the procedures involved, all individuals performed the tasks with shorts and standard shoes (sneakers with laces) that were provided for the study in

order to be similar for all individuals. In the single-task condition, the subjects were asked to remaining in the standing position for 30 seconds, looking at a point at eye level two meters away. After this interval, the subjects were instructed to walk three steps at a self-selected speed. In the dual-task condition, the previous procedures were repeated; however, the subjects were required to perform the Stroop test simultaneously, which consisted of naming the colour used to print the name of a different colour (Romann, Dornelles, Maineri, Rieder, & Olchik, 2012). The order of each condition (single- and dual-task) changed randomly, from individual to individual, in order to avoid a learning effect. There was a one minute rest between each trial, and all necessary repetitions were performed in order to obtain three valid trials to reduce the within-individual variability and increase the statistical power (Mullineaux, Bartlett, & Bennett, 2001). All the experimental data was acquired by the same trained researcher to ensure reproducibility.

The CoP signal was low-pass filtered with a fourth-order Butterworth filter (zero-phase lag) with a cut-off frequency of 8 Hz (Winter, 2009). The postural phase was defined as the interval between the starting of the CoP displacement (T0) until the maximum CoP displacement backward and toward the first swing limb. The T0 was identified as the instant when the CoP signal deviated from the baseline (obtained in standing position) plus 3 standard deviations for a minimum interval of 50 ms (Shiratori & Latash, 2001). The end of the postural phase was defined as the instant associated to the first deflection of the CoP displacement (Tsukahara, Kawanishi, Hasegawa, & Sankai, 2010). The values of the anteroposterior CoP displacement (CoP_{AP}) and mediolateral CoP displacement (CoP_{ML}), anteroposterior duration of the postural phase ($Duration_{AP}$) and mediolateral duration of the postural phase ($Duration_{ML}$) and anteroposterior

velocity of the CoP displacement (Vel_{AP}) and mediolateral velocity of the CoP

displacement (Vel_{ML}) were used for analysis.

2.4. Statistical Analysis

According to the nature of the variables under study, descriptive statistical analyses

were performed using proportions and measures of central tendency and dispersion. All

the variables analysed presented a normal distribution, so MANOVA for repeated

measures was used for multivariance analysis between healthy subjects and PD subjects

in the single- and dual-task conditions, and all variables were assessed simultaneously.

For additional evaluations, the independent samples t test was used to obtain results

regarding the differences for the various conditions between groups, while paired

samples t test was used to analyse the differences between the single- and dual-task

conditions in each group. Two-tailed tests were used in all analyses done and $p < 0.05$

was adopted for statistical significance. All statistical analyses were run using SPSS

Statistics 22.0 (SPSS, Inc., Chicago, IL, USA).

3. RESULTS

The PD sample had 9 subjects (66.7% male), with a mean age of 66 years old (standard

deviation (SD) = 8.2), a mean education of 7.7 years (SD = 5.1) and a mean years of

disease of 10.22 (SD=5.38). Most of these participants were classified as stage 1 and 1.5

of the Hoehn and Yahr scale with a mean of 8.39 (SD=0.86) seconds in the TUG

test. The healthy sample had 10 subjects (50% male), with a mean age of 63.7 years (SD

= 7.6) and a mean education of 8.2 years (SD = 4.5). When both groups were compared,

statistically significant differences were only found in the number of the colours

correctly named on the Stroop test. PD subjects scored less than the healthy subjects, Table 1.

< Insert Table 1 about here >

The analysis of repeated measures MANOVA, indicated that there were no significant multivariate effects between the healthy and PD subjects studied ($F_{(6.11)} = 2.030$, $p > 0.05$, $\eta_p^2 = 0.525$) neither within-subjects independently of their group ($F_{(6, 11)} = 0.973$, $p > 0.05$, $\eta_p^2 = 0.347$). Also, no relation was found between the groups and conditions ($F_{(6, 11)} = 0.982$, $p > 0.05$, $\eta_p^2 = 0.349$). Univariate analysis between the groups indicated that the Duration$_{ML}$ was significantly higher for the PD subjects than for the healthy subjects, $F_{(1, 16)} = 12.494$, $p = 0.003$, $\eta_p^2 = 0.44$). A significant relation was found between the conditions and groups for the Duration$_{ML}$, $F_{(1.16)} = 4.717$, $p = 0.045$, $\eta_p^2 = 0.228$).

Although the CoP$_{AP}$ and Vel$_{ML}$ did not present significant differences between the groups, large between-group effects were found, $\eta_p^2 = 0.07$ and $\eta_p^2 = 0.08$, respectively. Considering the within-group univariate analysis, no differences were detected between the single- and dual-task conditions. Nerveless, within the healthy group, large effect sizes (d) were found for the Duration$_{ML}$, Duration$_{AP}$ and Vel$_{ML}$, and small for the CoP$_{AP}$, CoP$_{ML}$ and Vel$_{AP}$. Within the Parkinson's group, the effect sizes (d) were large for the Duration$_{ML}$, medium for the Duration$_{AP}$ and small for the CoP$_{AP}$ and Vel$_{AP}$, Table 2.

< Insert Table 2 about here >

The significant relations found were explored further. In the dual-task condition, the PD subjects had a significantly higher $Duration_{ML}$ than the healthy subjects, $t(17) = -3.536$, $p = 0.003$). When single- and dual-task conditions were compared, no significant difference was found between the conditions in subjects with PD. However, in healthy subjects, the $Duration_{ML}$ was significantly lower in the dual-task condition than in the single-task condition, $t(9) = -2.496$, $p = 0.034$, Figure 1.

< Insert Figure 1 about here >

4. DISCUSSION

The aim of this study was to compare the postural phase of GI in single- and dual-task conditions in healthy subjects and in PD subjects in the early stages of the disease (Hoehn and Yahr scale < 3). In contrast to what was expected, no significant differences were observed between subjects with PD and healthy subjects regarding the CoP_{AP}, $CoP_{ML,}$ $VelCoP_{AP}$ and $VelCoP_{ML}$. However, the mean CoP_{AP} and CoP_{ML} displacements were lower in the subjects with PD.

Previous studies of APAs associated with GI have shown that the backward CoP displacement might be significantly reduced in PD subjects (Breniere, Do, & Bouisset, 1987; Elble, Moody, & Leffler, 1994; Nocera et al., 2013). This leads to an extension of the first swing phase and to a decrease in the length of the first step and in the walking speed (Yiou et al., 2012). In this study, the mean values of CoP_{ML} also decreased in PD subjects as was observed in the studies by Yiou et al. (2012) and Nocera et al. (2013). Also, the mean values of Vel_{AP} and Vel_{ML} found were less in PD subjects, which is in line with those obtained by Halliday et al. (1998) and Gantchev et al. (1996). Deficits in APAs of PD subjects have been linked to abnormal muscle activation patterns

characterized by an extension of excitatory and reduced inhibitory activity as well as a delay in its onset or even loss of muscular activation and/or deactivation (Crenna et al., 2006; Crenna & Frigo, 1991).

Besides the non-existence of statistically significant differences between the healthy and PD subjects, no variable was significantly influenced by the dual-task condition in the PD group. These findings are surprising considering the frequent and consistent negative effect of dual-task on motor performance in PD subjects (Bloem, Grimbergen, van-Dijk, & Munneke, 2006; J. D. Holmes et al., 2010; Yiou et al., 2012). Some authors have postulated that the nature of this neurodegenerative disease and the cognitive demands of a dual-task condition would limit the performance of one or both tasks (Morris, 2000; Rogers et al., 2011). Thus, before doing this study, it was expected that in GI, the motor performance of the PD subjects would be altered, even in individuals at the initial stage of the disease. Nevertheless, a non-significant difference between the single- and dual-task conditions in GI of PD subjects was also observed in the study by Nocera and co-workers (Nocera et al., 2013).

The non-existence of significant differences between groups obtained in the present study suggests that the PD sample was able to prioritize the motor task in detriment of the cognitive task. This was evidenced by the number of colours correctly named, which was significantly lower in the PD subjects than in the healthy subjects. It is important to note that no differences occurred between the two groups in terms of education and the MoCA test (Kelly et al., 2012b; Souza, Voos, Francato, Chien, & Barbosa, 2013). The MoCA test was applied to both groups to give an indication whether the participants had cognitive deterioration or not and to detect differences of cognitive deterioration between the PD group and the healthy controls before the evaluation, in order to validate the findings and conclusions of the present study.

Moreover, the lack of differences between the healthy and PD subjects may be due to the fact that the underlying anticipatory muscular synergy was preserved and the lower CoP displacement and velocity was probably related to the slowness of execution, i.e. to bradykinetic episodes (Berardelli, Rothwell, Thompson, & Hallett, 2001). In fact, this study found that the CoP_{ML} duration was longer and significantly different for the PD subjects than the healthy subjects. Furthermore, for the healthy subjects the postural phase duration increased in the dual-task condition in relation to the single-task condition. Also these results corroborate other studies suggesting that PD subjects have a lower CoP_{AP}, a higher duration of the postural phase and that the APAs start later during GI in the dual-task condition than in the single-task condition (Carpinella et al., 2007; Nocera et al., 2013; Yiou et al., 2012).

In the same subjects, the CoP_{AP} duration tends to decrease from the single- to dual-task conditions. This decrease has been described as an ineffective strategy for maintaining balance, as it causes decreased backward CoP displacements, resulting in higher risk of falls (J. D. Holmes et al., 2010; Kelly et al., 2012a; Nocera et al., 2013; Schmit et al., 2005). The fact that the PD subjects under study did not show any differences between the single- and dual-task conditions, can also be explained by a greater focus on the motor task, which means that the motor performance is not debilitated despite the worse results in the Stroop test.

In the literature, most studies to characterize the motor deficits in PD subjects have used subjects in advanced stages of the disease and only in the single-task condition. However, most activities of daily living require the simultaneous execution of a cognitive task. Nevertheless, differences between durations were found. In particular, this study indicates that the behaviour of individuals in the early stages of PD may retain the ability to prioritize tasks and choose the motor task in detriment of the

cognitive task. However, it is necessary understand if this prioritization is automatic or it is caused consciously by the individual in order to prevent falls. Therefore, future studies related to the stage of disease in the performance of motor and cognitive tasks independently and simultaneously are essential to clarify this doubt.

Clinical Relevance

This study corroborated that subjects with PD take longer to perform mediolateral displacements, especially in dual-task condition. On the other hand, the mediolateral and anteroposterior displacements found in the subjects with PD were similar to the ones found in the controls. These results indicate that in the early stages of PD, the cognitive performance can be impaired when performing cognitive-motor dual-tasks. Thus, the interventions should not be only focused on the motor performance, which is currently considered the main attention of the interventions, but should also include cognitive training.

Limitations

This study had some limitations. Firstly, the small sample size and the sampling method can limit the results in regard to generalizations, that which leads us to consider it as an exploratory study. Secondly, the potential interference of the experimental environment on the GI of the subjects studied could affect the results obtained. Hence, further studies with larger samples and in different experimental environments are needed.

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TABLE CAPTIONS

Table 1 – Comparison of the sociodemographic and individual variables between the two

groups (significant values (p<0.05) are indicated in bold).

Table 2 - Comparisons between the scores of single- and dual-task conditions for each group.

The results are given as the mean (standard deviation), and the significant values (p<0.05) are in

bold.

FIGURE CAPTIONS

Figure 1 – Mean (bars) and standard deviation (error bars) values for anteroposterior, mediolateral, duration and velocity of CoP displacement in healthy and PD subjects during single- and dual-task conditions.
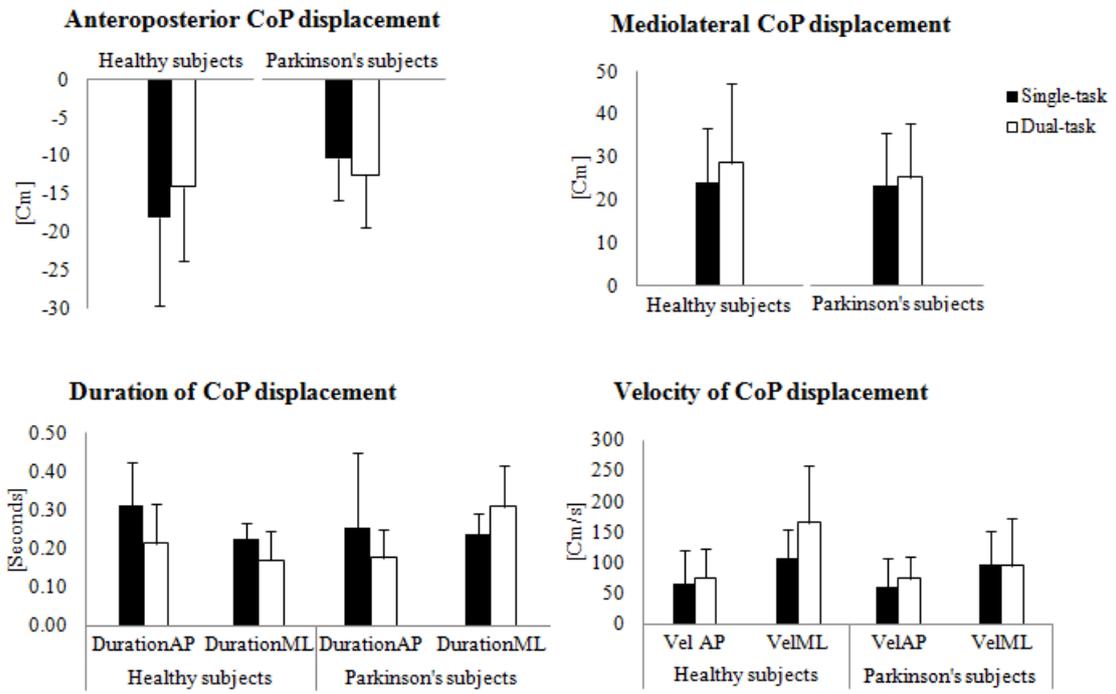
FIGURES

Figure 1

TABLES

Table 1 – Comparison of the sociodemographic and individual variables between the two groups (significant values (p<0.05) are indicated in bold).

	Healthy subjects	Parkinson's subjects	p-value
	M (SD)	M (SD)	
Age (years)	63.70 (2.42)	66.00 (2.74)	0.252*
Male, n (%)	5 (50)	6 (66.7)	0.463**
Education (years)	8.20 (1.43)	7.67 (1.69)	0.696*
Weight (Kg)	72.90 (3.14)	69.33 (4.20)	1.000*
Height (m)	1.64 (0.03)	1.65 (0.03)	0.931*
MoCA	26.50 (1.58)	24.78 (5.57)	0.095*
Stroop test: Nº of named colours	24.30 (5.19)	18.17 (5.21)	**0.035**
Stroop test: Nº of Errors	0.63 (0.49)	1.18 (1.45)	0.968*
Hoehn and Yahr scale			
Stage 1, n (%)		3 (33.3)	-
Stage 1.5, n (%)		3 (33.3)	-
Stage 2, n (%)		1 (11.1)	-
Stage 2.5, n (%)		2 (22.2)	-
Years of PD		10.22 (5.389)	-

Hoehn and Yahr scale: Stage 1 - Unilateral disease; Stage 1.5 - Unilateral and axial disease; Stage 2 - Bilateral disease without impairment of balance; Stage 2.5 - Mild bilateral disease; Stage 3 - Mild to moderate bilateral disease.

* Independent samples t-test and

** chi-square test

M – Mean, SD – Standard deviation

Table 2. Comparisons between the scores of single- and dual-task conditions for each group. The results are given as the mean (standard deviation), and the significant values (p<0.05) are in bold.

	Healthy Subjects (n=10)		Parkinson's subjects (n=9)				Effect Sizes	
	Single-task	Dual-task	Single-task	Dual-task	F	Between Groups η_p^2	Within Healthy Group d	Within Parkinson's Group d
CoP_{AP} [cm]	18.08 (11.54)	14.09 (9.65)	10.67 (5.47)	12.83 (7.04)	1.14	0.07	0.38	0.34
CoP_{ML} [cm]	24.16 (12.57)	28.69 (18.54)	23.65 (12.58)	25.76 (13.04)	0.03	0.00	0.29	0.16
$Duration_{AP}$ [s]	0.31 (0.11)	0.21 (0.10)	0.26 (0.17)	0.18 (0.08)	0.36	0.02	0.95	0.60
$Duration_{ML}$ [s]	0.22 (0.04)	0.17 (0.07)	0.25 (0.05)	0.32 (0.11)	**12.49**	0.44	0.88	0.82
Vel_{AP} [cm/s]	65.67 (53.88)	75.42 (48.81)	61.62 (48.05)	74.60 (35.83)	0.01	0.00	0.20	0.31
Vel_{ML} [cm/s]	107.09 (47.51)	166.16 (92.33)	98.73 (54.79)	96.65 (76.73)	1.43	0.08	0.80	0.03