ORIGINAL ARTICLE

Cognitive processes affect the gait of subjects with Parkinson's and Alzheimer's disease in dual tasks

Processos cognitivos afetam a marcha de sujeitos com doença de Parkinson e de Alzheimer em duplas tarefas

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ABSTRACT

Objective: To investigate the relation between gait parameters and cognitive impairments in subjects with Parkinson's disease (PD) and Alzheimer's disease (AD) during the performance of dual tasks. **Methods:** This was a cross-sectional study involving 126 subjects divided into three groups: Parkinson group (n = 43), Alzheimer group (n = 38), and control group (n = 45). The subjects were evaluated using the Timed Up and Go test administered with motor and cognitive distracters. Gait analyses consisted of cadence and speed measurements, with cognitive functions being assessed by the Brief Cognitive Screening Battery and the Clock Drawing Test. Statistical procedures included mixed-design analyses of variance to observe the gait patterns between groups and tasks and the linear regression model to investigate the influence of cognitive functions in this process. A 5% significant level was adopted. **Results:** Regarding the subjects' speed, the data show a significant difference between group *vs* task interaction (p = 0.009), with worse performance of subjects with PD in motor dual task and of subjects with AD in cognitive dual task. With respect to cadence, no statistical differences was seen between group *vs* task interaction (p = 0.105), showing low interference of the clinical conditions on such parameter. The linear regression model showed that up to 45.79%, of the variance in gait can be explained by the interference of cognitive processes. **Conclusion:** Dual task activities affect gait pattern in subjects with PD and AD. Differences between groups reflect peculiarities of each disease and show a direct interference of cognitive processes on complex tasks.

Keywords
Parkinson disease, Alzheimer disease, gait, locomotion, cognitive functions.

RESUMO

Objetivo: Investigar a relação entre parâmetros da marcha e comprometimento cognitivo em sujeitos com doença de Parkinson (DP) e doença de Alzheimer (DA) durante tarefas duplas. **Métodos:** Este estudo consistiu em uma pesquisa transversal envolvendo 126 sujeitos, divididos em três grupos: grupo Parkinson (n = 43), grupo Alzheimer (n = 38) e grupo controle (n = 45). Os sujeitos foram submetidos ao teste *Timed Up and Go*, administrado com distrator motor e cognitivo. Os parâmetros analisados na marcha foram cadência e velocidade, tendo as funções cognitivas avaliadas por meio da Bateria Breve de Rastreio Cognitivo e do Teste do

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Desenho do Relógio. Os procedimentos estatísticos incluíram a análise mista de variâncias para observar os padrões da marcha nos grupos e nas tarefas e o modelo de regressão linear para investigar a influência das funções cognitivas nesse processo. O nível de significância foi estipulado em 5%. **Resultados:** Em relação à velocidade, os dados vislumbram diferença significativa na interação grupo *vs.* tarefa (p = 0,009), com pior rendimento dos sujeitos com DP na dupla tarefa motora e dos com DA na situação de dupla tarefa cognitiva. Sobre a cadência, os resultados não apontaram diferença significativa na interação grupo *vs*. tarefa (p = 0,105), vislumbrando pouca interferência das condições clínicas sobre esse parâmetro. O modelo de regressão linear demonstrou que até 45.79% da variação nos parâmetros da marcha podem ser explicados por processos cognitivos. **Conclusão:** Atividades de dupla tarefa afetam a marcha de sujeitos com DA e DP. A diferença entre grupos reflete peculiaridades de cada doença e demonstra interferência direta de processos cognitivos em atividades complexas.

Palavras-chave
Doença de Parkinson, doença de Alzheimer, marcha, locomoção, funções cognitivas.

INTRODUCTION

Humans are bipeds and either move with unipodal support phases (deambulation), during no contact (running) or remain in orthostatism. This represents an adaptive challenge to the systems that control balance and reinforces the need of transmission of continuous information regarding the position and movement of the body in space[1,2].

Gait is historically considered an automatic and repetitive phenomenon, mainly dominated by reflex basis[3,4]. The neurophysiological mechanisms that control gait involve three mainly domains: 1) the decoding of afferent stimuli by the sensory cortex, 2) the interpretation of this information in the associative cortex and the subsequent transfer of interpretation to corresponding motor areas, and 3) the cortical motor response, with activation of basal nuclei, cerebellum and osteomioarticular system[5,6]. When subjects are required to perform a dual task, however, the activation of the associative cortex (especially in the prefrontal and parieto-temporal-occipital areas) increases, which results in many patients finding it difficult to correctly perform the task due to inefficient synchronization with executive functions[7].

Balance and gait dysfunctions co-exist in healthy older adults[8,9]. This is due to cognitive and mobility decline inherent of aging[10,11]. In fact, recent studies have demonstrated that the influence of superior cortical areas opposes the concept of locomotion as a reflexive automatic task, once the cognitive apparatus interfere constantly on human motricity[8-11].

Regarding neurodegenerative disorders such as Parkinson's disease (PD) and Alzheimer's disease (AD), it is well known that encephalic compromise of a supra- and infratentorial nature culminates in cognitive and functional decline[12]. Previous study already supports the concept that older adults with a moderate impairment of PD and AD experience marked deterioration when required to perform secondary task[13]. Even so, the meta-analysis conducted by Chu *et al.*[14] pointed to the need for more research to ascertain definite conclusions regarding the effect of task type and complexity

In this study we investigated the relation between gait parameters and cognitive impairments in subjects with PD and AD during the performance of dual tasks. It was hypothesized that the changes in cognitive function would result in cadence and speed impairments when compared to healthy control peers – with greater difficulty in the execution of activities that demand dual tasking.

METHODS

This was a cross-sectional study investigating three independent groups: the Parkinson's group (PG), the Alzheimer's group (AG), and the control group (CG). The following inclusion criteria were used for the PG: diagnosis of idiopathic PD[15], aged between 60-80 years old at entry, disease severity of Hoehn-Yahr[16] stages II-IV, and with moderate compromise according to the motor subscale of the Unified Parkinson's Disease Rating Scale[17]. The following inclusion criteria were used for the AG: a diagnosis of probable AD[18], aged between 60-80 years and with moderate impairment according to the Clinical Dementia Rating Scale[19]. The CG consisted of subjects who did not present any neurodegenerative or psychiatric conditions.

Patients were excluded from this study if they could not exhibit independent locomotion, presented with cardiovascular and osteomioarticular comorbidities, already practiced regular physical activity, or had an educational level below four years of study. This research complied with the principles set forth by the Declaration of Helsinki and was conducted with the approval of the institutional ethics committee.

Methodological procedures

All methodological procedures (general setting, participants, variables, data measurement and statistical methods) were supported by the STROBE Statement checklist (Strengthening the Reporting of Observational Studies in Epidemiology)[20].

Figure 1 shows a flow diagram about the selection of subjects. The exclusion rate was higher in the Alzheimer group than in the Parkinson or control groups. The reasons related to that withdraw were: diagnosis of mixed dementia (n = 8), clinical instability (n = 3) and use of tricyclic antidepressants (n = 1).

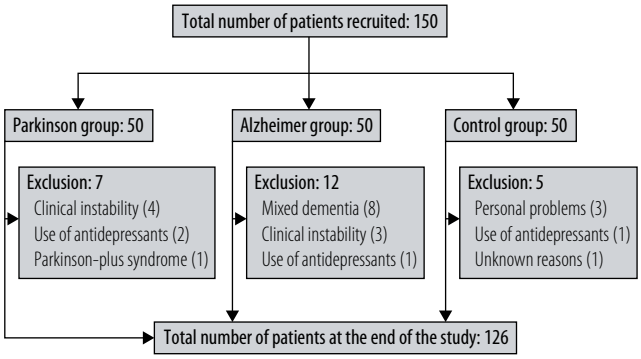

Figure 1. Flow diagram showing sample selection and drop-out rate.

All participants were screened in a private and quiet evaluation room in the Outpatient Clinic of the State University of Campinas. The measures used in this research involved motor and cognitive tests, properly validated in the Portuguese language. The cadence (number of steps per second) and speed (meters per second) analyses were accomplished using observational gait assessments during getting-up, walking, and seating tasks[21,22]. These tasks were judged in situations that required different cognitive and motor capabilities: a normal task, a motor dual task (carrying a glass of water), and a cognitive dual task (counting progressive odd numbers). Functional motor impairments were analyzed using the Pfeffer Index[23], and cognitive impairments were evaluated using the Brief Cognitive Screening Battery[24] and the Clock Drawing Test[25].

Data analysis

The data were first analyzed using descriptive statistics (mean and standard error). Socio-demographic and clinical profiles of the groups were calculated using one-way analysis of variance (ANOVA) with Scheffe's *post hoc* and the chi-square test (χ^2).

To estimate the main effects of dual tasks on gait (i.e., differences between clinical conditions and tasks), we applied mixed-design ANOVA with "task" and "group" as factors. T-tests with Bonferroni corrections for multiple testing were applied to investigate paired comparisons. Covariant factors were used in the cases with baseline differences.

Simple plots, product moment correlation coefficients and linear regression model were used to examine possible relations between gait parameters and executive function (Clock Drawing Test). For all analyses, a significance level of 5% was adopted ($p < 0.05$), under a bicaudal data curve.

RESULTS

This study assessed 126 subjects divided into three groups. The socio-demographic data on the participants are presented in table 1. Chi-square and one-way ANOVA analyses revealed similarities between the groups in terms of sample size (p = 0.734), gender (p = 0.859) and level of education (p = 0.192). Cross-sectional analyses revealed a significant difference in age between the PG and the AG (p = 0.003) and between the AG and the CG (p = 0.001) but not between the PG and the CG (p = 0.845).

Table 1. Characterization of the groups according to social-demographical data

	Parkinson	Alzheimer	Control	p
Sample size (n)	43	38	45	0.734
Gender (male:female)	23:20	18:20	23:22	0.859
Age (years)	68.02 ± 1.44^{a}	$75.23 \pm 1.56^{a,b}$	69.86 ± 1.32^{b}	0.001
Education (years)	4.95 ± 0.35	5.73 ± 0.41	5.88 ± 0.40	0.192

$^{a,b}p < 0.05$. Statistical procedures were assessed by qui-square test and one-way ANOVA with Scheffe's *post hoc*.

Gait pattern during dual tasks

The cadence and speed of the subjects in each group were assessed in three different situations: 1) a walking test with no distractor; 2) a walking test with a motor distractor, and 3) a walking test with a cognitive distractor (Table 2).

Table 2. Speed (m/s) and cadence (steps/second) of the groups, according to the required dual task

	Gait pattern	Normal test	Motor dual task	Cognitive dual task
Parkinson group	Speed	$0.35 \pm 0.02^{a,b}$	$0.28 \pm 0.02^{a,c}$	$0.31 \pm 0.02^{b,c}$
	Cadence	1.05 ± 0.04	1.00 ± 0.03	1.05 ± 0.04
Alzheimer group	Speed	0.20 ± 0.03^{d}	0.16 ± 0.02^{e}	$0.13 \pm 0.01^{d,e}$
	Cadence	0.95 ± 0.05	0.96 ± 0.04	0.95 ± 0.04
Control group	Speed	0.60 ± 0.03	0.59 ± 0.03	0.60 ± 0.03
	Cadence	1.07 ± 0.04	1.10 ± 0.04	1.06 ± 0.05

$^{a,b,c,d,e}p < 0.05$. Statistical procedures were assessed by mixed-design ANOVA and student t test with Bonferroni corrections.

Regarding the cadence, mixed ANOVA pointed no significant effect for group X task interaction (F = 1.93; p = 0.105; power of 57.90%), for group (F = 1.77; p = 0.173; power of 36.6%) or for task (F = 2.27; p = 0.105; power of 45.90%) – showing similar pattern between groups and situations.

Analyzing the effects for dual task performance in speed, mixed-design ANOVA pointed to a main effect for group X task interaction (F = 3.47; p = 0.009; power of 85.70%), indicating a different pattern between groups. Further analyses confirmed the difference for group (F = 47.89; p = 0.001; power of 99.90%) but not for task (F = 0.76; p = 0.465; power of 18.00%).

Analyzing each group separately, paired analyses indicated that subjects with PD presented with the most diffi-

culty under the motor dual task conditions (p = 0.001 when compared with single task and p = 0.043 when compared with cognitive dual task). Important differences were found in all pairwise comparisons in the AD group, such that patients with AD experienced the most difficulty on the cognitive dual task (p = 0.001 when compared to single task and p = 0.012 when compared with motor dual task). The dual task conditions did not affect motion patterns in the control group during the single task, motor or cognitive dual task (p > 0.05 in all pairwise comparisons).

As we identified baseline differences for age, a covariant factor was used to analyze the effect of this variable with regards to the results. Applying mixed-design ANOVA with age as a covariant, we found that it did not affected significantly the subjects performance on the tasks (p = 0.095 for cadence and p = 0.784 for speed).

Functional impairments and cognition

The functional and cognitive scores for the three groups are presented in table 3. The one-way ANOVA revealed significant differences between groups in terms of functional impairment (p = 0.001) and the following cognitive variables: identification/nomination (p = 0.001), incidental memory (p = 0.001), immediate memory (p = 0.001), learning memory (p = 0.001), delayed memory (p = 0.001), recognition (p = 0.001), and the Clock Drawing Test (p = 0.001). Within-group differences were found for all comparisons (p < 0.05) with the exception of identification/nomination (p = 0.976) and recognition (p = 0.266) in the PG and CG.

The regression model shows that up to 45.79% of the variance in gait parameters can be explained by the interference of executive processes. Pearson's correlation test reinforce such information, by showing significant association between the scores of the Clock Drawing Test and cadence (r = 0.302 for single task, r = 0.320 for motor dual task and r = 0.336 for cognitive dual task) and between the Clock Drawing test and speed (r = 0.565 for single task, r = 0.651 for motor dual task and r = 0.677 for cognitive dual task).

DISCUSSION

Every motor action requires orientation and postural balance to ensure the stability of the body in relation to the forces of gravity and acceleration. The current findings provide evidence of different gait patterns and functional impairments in PD and AD during the performance of various dual tasks.

A general consensus holds that neurodegenerative disorders compromise behavioral motor function due to encephalic disturbances. Based on the current findings regarding speed of movement, it seems that patients with PD exhibit less speed during a motor dual task and that patients with AD are slower during a cognitive dual task. These findings are consistent with those reported by Chiba *et al.*[26] and confirm that alterations in gait speed are associated with a greater risk of falling during the dual task conditions studied. In contrast, we observed no differences in cadence between the three groups even when subjects encountered cognitive or motor distractors. It is possible that biomechanical mechanisms coordinate the number of steps taken and the time necessary to perform cadence-related actions, decreasing the risk for falling. Theoretically, this process involves supra- and infratentorial connections and culminates in the stabilization of the body during a particular task.

Regarding PD, it is important to note that the basal nuclei aid in the control of movement and participate in many aspects of sensorimotor integration. The main functions of these neurons include assisting the cortex in the planning of a learned movement, enabling the initiation of the maintenance and soft flow of the sequences of these movements, and keeping the motor repertoire ready for action[27]. Due to the subcortical neurological deficits associated with PD, body imbalance becomes more pronounced.

Yogev-Seligmann *et al.*[28] have confirmed that the associative cortices (particularly the prefrontal cortex) exert a strong influence on gait and that these areas potentiate the risk of falling during dopaminergic hypoactivity. This likely

Table 3. Cognitive scores in the three groups

	Parkinson	Alzheimer	Control	p
Functional impairment	7.4 ± 0.9	19.7 ± 1.2	0.7 ± 0.2	0.001
BCSB				
Identif./nomination	9.86 ± 0.24	6.68 ± 0.53	9.95 ± 0.03	0.001
Incidental memory	5.65 ± 0.25	2.52 ± 0.33	6.73 ± 0.16	0.001
Immediate memory	7.09 ± 0.29	2.42 ± 0.3	8.40 ± 0.20	0.001
Learning memory	7.44 ± 0.32	2.50 ± 0.34	8.95 ± 0.16	0.001
Delayed memory	7.18 ± 0.29	1.86 ± 0.33	8.77 ± 0.33	0.001
Recognition	8.97 ± 0.33	4.31 ± 0.48	9.71 ± 0.09	0.001
Clock Drawing Test	7.18 ± 0.28	3.15 ± 0.36	8.60 ± 0.19	0.001

p < 0.05 in all pairwise comparisons unless identification/nomination and recognition in the Parkinson group *vs* control group. Statistical procedures were assessed by one-way ANOVA and Scheffe's *post hoc*.

occurs due to the fact that alterations within the dopaminergic pathways result in muscle dyssynergy and alter function in the frontal lobe, impairing the performance of complex motor tasks. The current data from the PG demonstrate the strong influence of the disease on motor function relative to the performance of repetitive, simultaneous, and non-automatic movements, inducing alterations in speed.

A major component of AD is the reduction of metabolic function in cells in the associative cortex, affecting executive processes[29,30]. Marshall *et al.*[30] observed that the cingulum and orbitofrontal cortex are vital cortical areas that exhibit diminished activity due to interference in the medial region of the thalamus during the course of neurodegenerative disorders being the disruption of these areas a serious clinical condition due to the subsequent alterations in cognitive functions that result in great difficulty performing in situations that involve decision-making.

Based on the results from the present study, patients with AD exhibit the greatest degree of functional impairment and the most poorly performance during dual task with cognitive distractor. Accordingly, the cognitive measures utilized here substantiate significant deficits. Therefore, it may be inferred that the cognitive dysfunctions reflected in our results corroborate the meta-analysis conducted by Schroeter *et al.*[31], which reported hypoactivation in the prefrontal, transentorhinal, hippocampal, isocortal, and temporal cortices of patients with AD. Still, closer examination of executive functions reveals that poorer accuracy and longer response time are related to risk of falls, making the AD population highly vulnerable to co-morbid processes[32,33].

It is important to mention that the focus of this study was to analyze older adults in routine situations, namely, sitting down, getting up, walk and sitting down again. Despite agreement that analyses of locomotion performance should occur on simple and plain floors, as it does in most laboratories that analyze gait, it is believed that the analyses in our study present an advantage because the tasks used are more representative of the daily routines of individuals.

Limitations

While we believe this study does have merits, the limitations should be pointed out. One limitation is that we used cross-section data that do not allow us to assess causal relations. Longitudinal research aimed at assessing the predictive value of cognitive functions on motion is needed to better understand the mechanisms whereby the central nervous system affects physical function in later years, and to identify possible target areas for interventions.

Another limitation is that the number of patients recruited was relatively small, forcing us to only examine patients with moderate clinical profiles. This may limit the ability to generalize our findings to the whole PD or AD population.

Furthermore the groups were different with regards to age. Even so, we must highlight that, as evidenced by statistical procedures, the age difference did not exert significant interference in the results.

CONCLUSION

The current findings demonstrate that patients with PD and AD exhibit significant functional impairments and utilize different adaptive responses. Whereas patients with PD display a larger variation in speed when required to perform tasks involving additional motor requirements, patients with AD exhibit a larger variation in speed when performing tasks with a cognitive distractor. Despite the fact that both diseases involve debilitating clinical conditions, the maintenance of a constant cadence during the three task situations suggests the use of adaptive biomechanical responses by all groups.

INDIVIDUAL CONTRIBUTIONS

Gustavo Christofoletti and **Guilherme Borges –** Participated in the research design.

Gustavo Christofoletti, **Lilian Assunção Felippe** and **Paulo de Tarso Müller –** Conducted the bibliographic research.

Gustavo Christofoletti and **Fernanda Beinotti –** Participated in the data collection.

Gustavo Christofoletti, **Lilian Assunção Felippe**, **Paulo de Tarso Müller**, **Fernanda Beinotti** and **Guilherme Borges –** Wrote the first draft of the manuscript.

CONFLICTS OF INTEREST

The authors report no declarations of interest.

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