IMPACT OF COGNITION ON THE OCCURRENCE OF FALLS IN PATIENTS WITH PARKINSON'S DISEASE

IMPACTO DA COGNIÇÃO NA OCORRÊNCIA DE QUEDAS EM PACIENTES COM A DOENÇA DE PARKINSON

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ABSTRACT

Introduction: Falls are common in Parkinson's disease (PD), happening to up to 68% of these individuals. Patients with PD present motor and gait impairment that increase the fall risks by three times. This study aimed to compare cognitive impairment and the occurrence of falls in PD patients.
Methods: Retrospective and cross-sectional study through data collection in electronic medical records searching for the occurrence of falls (dichotomous and coded responses: 1=yes and 2=no) in the period of up to three months of cognitive assessment. For data analysis, descriptive statistics, and inferential analyses (Mann-Whitney U Test) were performed to compare the cognitive tests' scores between the two groups (who answered Yes/fallers and non-fallers). A significance level of p<0.05 was adopted.
Results: There was no difference between the subgroups (fallers=23; non-fallers=60) regarding age (p=0.28), schooling (0.51) and years of disease progression (0.99). No difference was observed between the subgroups for most cognitive variables, except Trail Making Test (B and delta). There was a tendency to differ in Addenbrooke's cognitive examination III (ACE-III) (total and attention and memory domains), with lower performance for the fallers subgroup. Worse functionality and more frequent cognitive issues were observed in those with reported falls.
Conclusion: It was observed that cognitive measures, especially attentional and memory measures, interfere with episodes of falls in patients with PD. It is necessary to increase the sample and balance between the subgroups for further evidence of these results.

Keywords: Parkinson's disease; Accidental Falls; Cognition.

RESUMO

Introdução: As quedas são comuns na doença de Parkinson (DP), ocorrendo em até 68% desses indivíduos. Pacientes com DP apresentam comprometimento motor e da marcha que aumentam em três vezes o risco de quedas. Este estudo teve como objetivo comparar o comprometimento cognitivo e a ocorrência de quedas em pacientes com DP.
Métodos: Estudo retrospectivo e de corte transversal, por meio de coleta de dados em prontuário eletrônico sobre ocorrência de quedas (respostas dicotômicas e codificadas: 1=sim e 2=não) no período de até três meses da avaliação cognitiva. Para análise dos dados, foram realizadas estatísticas descritivas e inferenciais (Mann-Whitney U Test) para comparar os escores dos testes cognitivos entre os dois grupos (que responderam Sim/caem e Não/não caem). Foi considerado nível de significância de p<0,05.
Resultados: Não houve diferença entre os subgrupos (caidores=23; não caidores=60) quanto à idade (p=0,28), escolaridade (0,51) e anos de evolução da doença (0,99). Nenhuma diferença foi observada entre os subgrupos para a maioria das variáveis cognitivas, exceto Teste de Trilhas (B e delta). Houve uma tendência de diferença Exame cognitivo de Addenbrooke III (ACE-III) (domínios total e atenção e memória), com desempenho inferior para o subgrupo de caidores. Pior funcionalidade e problemas cognitivos mais frequentes foram observados naqueles com quedas relatadas.
Conclusão: Observou-se que medidas cognitivas, principalmente atencionais e de memória, interferem nos episódios de quedas em pacientes com DP. É necessário aumentar a amostra e o equilíbrio entre os subgrupos para maior comprovação destes resultados.

Palavras-chave: Doença de Parkinson, Acidentes por Quedas; Cognição.

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INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disease which presents cognitive impairment as a prevalent and debilitating non-motor symptom. Non-motor symptoms, such as autonomic nervous system changes, sleep disorders, depression, and cognitive and neuropsychiatric disorders, may precede motor symptoms or appear throughout the disease, impacting the [1,2] .

Cognitive decline is common in PD. Impairment in executive function and mental processing speed are the most prevalent, but attention, memory, language and visuospatial capacity may also be affected.

Executive dysfunction is related to the inability to anticipate, plan, initiate and monitor behavior directed to objectives, which in the face of new information should be adjusted and reformulated[3]. Patients with PD struggle to form concepts and establish rules during the execution of tasks. They are more inflexible; besides, they present reduced performance in concomitant activities and sustained attention. The dysexecutive syndrome is also characterized by difficulties to maintain the sequence of activities necessary to achieve a goal and deficit of mnemonic judgment of regency, that is, the temporal order of events, as well as poor performance in tasks subject to interference [4,5] . In addition to the impairment in domains related to alternating attention (mental flexibility), planning and selective attention, some studies report that the presence of affected visuospatial function, another impaired cognitive function in this population, may represent an early predictor for the development of dementia [6–8] .

Studies have associated some demographic and clinical aspects, such as age of later onset of symptoms, longer time of disease progression, early presence of hallucinations with dopaminergic treatment and rigid-akinetic motor manifestations, with the development of dementia in PD (D-PD) [9–12] . Cognitive decline, especially executive function, is associated with gait impairment and falls risk[13]. It was observed in the study by Sousa and Macedo that motor parameters were significantly related to cognitive abilities, especially with regard to divided attention, evidencing that balance skills and functional mobility are significantly correlated with attentional change between two tasks[14].

Other studies also report that low schooling, motor symptom characteristics (such as motor phenotype of postural instability and gait/fall difficulty), hyposmia and REM behavioral sleep disorder are clinical and demographic predictors for cognitive decline in PD[15,16] .

Falls are also common among people with PD, with an occurrence rate of up to 68%[17]. Individuals with PD present motor and gait impairment that increase the fall risks by three times, unlike individuals without PD[18].

The etiology of falls in people with PD is multidimensional. Falls are associated with primary characteristics (age, disease severity, gait and balance impairment, cognitive impairment) and secondary characteristics that occur in response to falls (anxiety, reduced self-efficacy, weakness and loss of mobility)[19]. To date, the strongest predictor of a future fall is a previous fall, and the clinical evaluation of fall risk is usually triggered when falls are established and not before their occurrence[20].

Studies that correlated performance in the Montreal Cognitive Assessment (MoCA) with motor tests found a significant association with mobility assessed through the Purdue Pegboard Test and the Timed Up and Go Test (TUG). Although no correlation was found between the dominant tremor subtype and cognitive impairment, the postural instability/gait difficulty (SGA) subtype showed an association with inferior performance in cognitive tests [15,21–23] . Another study found interaction between cognitive tests that assess mental flexibility TMT-B and TMT-delta, attention (digit amplitude, direct order), working memory (digit Span-forward and backward) and functional mobility (cognitive TUG) in individuals with PD[24].

Impaired executive function may predict recurrent falls in Parkinson's disease and is associated with postural change, balance, and gait.

Another clinical aspect identified as a potential factor for falls is cholinergic impairment. Studies suggest that cholinergic dysfunction, along with failure of dopaminergic systems and other neurotransmitters, contributes to the generation of a specific set of clinical manifestations. A "cholinergic phenotype" can be identified in people with cognitive decline, falls and REM sleep impairment[25,26].

Some clinical aspects may be associated with a higher falls risk, and identification and management of them in these patients is valuable. It is necessary to analyze orthostatic hypotension and the use of any medications that may increase the fall risk (benzodiazepines, anticonvulsants and those with anticholinergic action), since they may increase sedation/drowsiness[27,28] .

The evaluation and identification of cognitive aspects associated with fall risks can help the care of these individuals, in order to prevent or at least delay the onset of falls.

The aim of this study was to evaluate the correlation between cognitive impairment and the occurrence of falls in patients with Parkinson's disease. And, specifically, to verify which cognitive domains are most related to the occurrence of falls in PD.

METHODS

Study design

Retrospective and cross-sectional study.

Participants

We selected patients who participated in the study (CAAE:57521316.8.0000.0022), diagnosed with

Parkinson's disease, according to the criteria of the Brain Bank of the Parkinson's Disease Society of the United Kingdom[29]. Exclusion criteria were clinical complications that impact on the functionality and mobility of these individuals, as well as mood disorders, anxiety and/or medication use that may impact balance and higher occurrence of falls, such as benzodiazepines.

Data collection procedures

Data were retroactively collected in electronic medical records on reports of falls, through dichotomous responses /yes/ or /no/ and absolute frequency. The data related to cognition were also obtained by searching the medical records, using the third version of the global cognition evaluation battery - ACE-III[30] neuropsychological tests (Digit Span-forward and backward, Corsi Block Tapping Task, Trail Making Test-parts A, B and delta), Control Mental and Fluency Verbal (phonological and semantic).

Procedures for data analysis

Descriptive statistics, with mean, standard deviation, median and interquartile interval. Inferential analyses (Mann-Whitney U Test and Fisher's Exact Test) for comparison between fallers and non-faller groups in relation to demographic variables (sex, age and schooling), clinical (years of disease progression, functionality, depression, anxiety, cognitive complains), motor data and cognitive profile (normal, MCI-PD and D-PD). Significance level was p<0.05.

RESULTS

There was no difference between the groups regarding demographic and clinical variables, but the subgroup of fallers presented mean age and time of disease progression greater than the subgroup of non-fallers. As for the motor data, it was observed that the subgroup of fallers obtained a lower mean velocity, as well as the balance (evaluated through the MiniBest Test). Regarding the mood and anxiety questionnaires, there was also no statistically significant difference between groups. Regarding functional skills measures (functional activities questionnaire-Pfeffer) and cognitive complains (IQCODE) it was possible to observe a statistically significant difference between the two subgroups, with a higher score, that means worse results, in individuals with reports of falls (Table 1).

When analyzing the subgroups (fallers and non-fallers) by cognitive profile/cognitive impairment (without cognitive impairment, MCI-PD and dementia), patients with dementia (n=12) presented higher occurrence of falls when compared to those without cognitive impairment (n=54) and MCI-PD (n=57), however without statistically significant difference between them. The imbalance between the subgroups, however, may have interfered with this result, since there was a higher proportion of individuals with MCI-PD and no reports of falls, as can be observed in Table 2.

Table 1. Demographic and clinical data of the sample.

N=83	Non-Fallers (n=60)	Fallers (n=23)	P-value
Age (years)	63.20 (8.91)	65.57 (9.02)	0.283[1]
Sex (male)	86.67%	56.52%	0.006[2]
Education (years)	10.62 (3.86)	11.26 (4.70)	0.516[1]
Disease duration (years)	5.83 (4.60)	6.91 (3.85)	0.099[1]
BDI	6.70 (4.35)	7.83 (5.34)	0.397[1]
BAI	2.53 (1.90)	3.00 (2.39)	0.539[1]
FAQ (Pfeffer)	2.13 (1.92)	4.48 (2.23)	0.047[1]*
IQCODE	3.47 (0.56)	5.67 (0.60)	0.024[1]*
Minibest Test	22.29 (5.31)	18.44 (8.45)	0.112
TUG Test	0: 16.67 % 1: 57.14 % 2: 26.19 %	0: 16.67 % 1: 55.56 % 2: 27.78 %	0.927
10-meter test	108 (25.87)	86.15 (40.62)	0.054
H&Y	2.40 (0.88)	2.53 (1.19)	0.642

BDI= Beck Depression Inventory; BAI= Beck Anxiety Inventory; Pfeffer (QAF)= Functional Activities Questionnaire; IQCODE= Informant Questionnaire on Cognitive Decline in the Elderly; H&Y= Hoehn and Yahr scale.
[1]Mann-Whitney U Test
[2]Fisher's Exact Test
* P<0.05

Table 2. Cognitive profile and occurrence of falls.

N=83	Non-Fallers (n=60)	Fallers (n=23)	P-value
No cognitive impairment (n=17)	11 (64.71%)	6 (35.29%)	
MCI (n=54)	43 (79.63%)	11 (20.37%)	0.056
Dementia (n=12)	6 (50%)	6 (50%)	

Fisher's Exact Test
MCI=Mild Cognitive Impairment

Regarding motor aspects, a lower score was identified in the dementia subgroup, both in the scale that assesses balance/Minibest Test (W=9.313, p=0.009), functional mobility/TUG Test (W=10.832, p=0.004) and severity of motor symptoms/H&Y (W=8.956, p=0.011).

With respect to the neuropsychological tests and brief battery of cognition evaluation (ACE-III), as can be observed in Table 3, there was a statistically significant difference between the subgroups respecting the executive measures, which assess alternating and divided attention TMT-B and TMT-delta. It should be noted that there was a trend of difference in global cognition and domains of attention and memory (ACE-III).

Table 3. Cognitive performance in fallers and non-fallers subgroups.

N=83	Non-Fallers (n=60)	Fallers (n=23)	P-value
ACE-III (total)	87.0 (16.0)	78.0 (34.0)	0.054
Attention/Orientation	17.0 (4.0)	16.0 (3.0)	0.051
Memory	20.0 (6.0)	16.0 (11.0)	0.053
Fluency	10.0 (4.0)	9.0 (4.0)	0.159
Language	26.0 (1.0)	26.0 (3.0)	0.666
Visuospatial	15.0 (3.0)	15.0 (6.0)	0.315
Mental Control (WMS)	6.0 (1.0)	5.0 (2.0)	0.145
TMT-A	52 (19.5)	85 (22.9)	0.059
TMT-B	106.2 (51.3)	144.7 (54.1)	0.049*
TMT-delta	48.2 (46.9)	88.3 (39.6)	0.042*
RCFT (copy)	30.0 (12.0)	27.0 (21.5)	0.086
RCFT (immediate recall)	14.0 (10.0)	12.0 (15.0)	0.492
RCFT (Long-delay recall)	13.0 (9.0)	14.0 (10.5)	0.611
Digit Span (forward)	5.0 (2.0)	5.0 (2.0)	0.078
Digit Span (backward)	4.0 (1.0)	4.0 (1.0)	0.064
Corsi Block (forward)	5.0 (2.0)	4.0 (2.0)	0.095
Corsi Block (backward)	4.0 (1.0)	4.0 (2.0)	0.066
Verbal Fluency (FAS)	25.0 (12.0)	19.0 (11.0)	0.081
Verbal Fluency (Animals)	16.0 (6.0)	14.0 (9.0)	0.412

Mann-Whitney U Test
ACE-III= Addenbrooke's Verbal Fluency (Animals) cognitive examination, 3rd version; TMT=Trail Making Test; RCFT=Rey Complex Figure Test; Corsi=Corsi Block Tapping Task; FAS=Phonological verbal fluency.
* P<0.05

DISCUSSION

The present study aimed to observe the interaction between the occurrence of falls and almost falls with cognitive impairments present in individuals with Parkinson's disease. Although there was an imbalance between the group of fallers and non-fallers, it was possible to observe that particularly some cognitive domains, when impaired, were related to a higher occurrence of falls.

There was no statistically significant difference in the age and time of disease progression between the two subgroups, as mentioned in previous studies[31], but patients with cognitive complains were those with the highest reports of falls.

In the present study, individuals with reports of falls showed greater functional impairment when answering the questionnaire of activities that investigates independence to perform functional tasks that require motor and cognitive skills.

The cognitive domains, whose decline was significantly correlated with falls, were executive functions related to alternating and shifting attention, but there was also a tendency of difference in the total score and attention and memory domains' scores of the brief battery (ACE-III). Pelicioni *et al*.[32] also found in a cohort study that executive function and overall cognitive status showed worse scores in individuals with the most falls-prone subtype (PIGD). Montero-Odasso and Speechlee[33], in a review aiming to study the role played by cognition in falls in the elderly, found that impaired performance in the attention and executive function tests were associated with reduced gait speed, postural instability and future falls. Jehu *et al*.[34] also found in a meta-analysis involving elderly population that cognitive impairment (CI: [1.03, 1.78]) was correlated with recurrent falls, pointing out that not only sensory and/or motor aspects are risk factors for falls. In the present study, it was also observed that individuals diagnosed with dementia showed worse scores in the Minibest Test, indicating impaired balance.

A meta-analysis highlighted the fact that double-task is often affected in individuals with PD, considering gait and one more task, whether motor or cognitive a dual task[35]. In this review, when performing such activities, the individuals showed a significant reduction in gait speed, demonstrating the direct impact of the demand on mobility. In the present study, impairment was observed in the performance of simultaneous tasks in individuals with dementia, measured through the performance in the TUG associated with the performance of mental calculations.

Gait impairment present when gait performed with a concomitant task is shown to be an indication of fall risk[36]. A meta-analysis that did not involve individuals with PD showed moderate but significant improvement in double-task performance in response to training[37]. while a systematic review exclusively with individuals with PD found indications that this training in mild and moderate conditions of the disease may be beneficial[38]. A randomized controlled trial with individuals without PD but with mild dementia found improvement in spatial-temporal parameters of gait in response to dual-task training. These data indicate the importance of dual-task training as part of interventions to minimize risks of falls.

Cognitive impairment is the most prevalent non-motor impairment in PD[2]. Weintraub *et al*.[39] in a cohort study, which aimed to evaluate PD development prodromes, brought as results the reduction in dopamine transporters as predictors of attention decline and mental processing speed, functions that impact motor performance and fall risk.

There is, therefore, a spiral of deleterious effects related to motor and cognitive symptoms characteristic of PD that occur throughout the evolution of the pathology. These symptoms impact the level of physical activity, quality of life and independence[40], while sedentary lifestyle and reduced perception of quality of life lead to motor and cognitive impairment, increasing the risk of falls[41].

Thus, the results of this study point to the role of executive attention in the fall risks and performance of simultaneous tasks. These findings, combined with the multifactorial origins of falls in PD, indicate that the approaches to prevent falls in this population should focus not only on motor training, but also on strategy and cognitive intervention.

CONCLUSION

This study indicated that cognitive abilities are related to the occurrence of falls in PD. The results show that aspects of attention, especially executive functions, are more impaired in individuals that report falls. Despite the absence of statistically significant difference, the memory domain and total ace-III score was also lower in the subgroup of fallers. Greater severity of motor, postural and functional symptoms was also observed in the subgroup with dementia.

The risk of fall detection through the aid of cognitive indicators can facilitate the possibility of early intervention. Therapeutic options and guidance to patients and their family, leading to adjustment in lifestyle, specific training, and psychoeducational strategies.

The current study had as strengths: (1) use of standardized neuropsychological instruments for this clinical condition (2) pairing of subgroups regarding age, education, sex, and time (in years) of disease progression. However, some limitations should be raised, such as sample size and imbalance between subgroups (fallers and non-fallers). Thus, studies with sample enlargement are necessary for greater evidence of these results.

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Author's contribution

Nariana Mattos Figueiredo Sousa: Study concept and design, literature search, acquisition of data, interpretation of data, statistical analysis, writing of the manuscript, final approval of the manuscript. Roberta Correa Macedo: Design, acquisition of data and writing of the manuscript. Lorena de Oliveira Vaz: Design, acquisition of data and writing of the manuscript. Sonia Maria Dozzi Brucki: Guidance in the preparation and collection of data, corrections, and guidance of the manuscript.

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