

Title: The importance of parkinsonian signs for gait and balance in patients with Alzheimer's disease of mild degree

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Abstract:

Parkinsonian signs are common in patients with Alzheimer's disease (AD) of mild degree and predict functional decline, but their relationship with gait speed and balance is unclear. The aims of this study were to describe characteristics of patients with parkinsonian signs among 98 patients with AD of mild degree (with no comorbid Parkinson's disease), and to examine associations between parkinsonian signs with gait speed and balance. A cross sectional study at a memory clinic was conducted. Presence of each parkinsonian sign (bradykinesia, rigidity and tremor) was derived from the UPDRS, regular gait speed was recorded over 10 meters and balance was assessed using the Mini-Balance Evaluation Systems Test (Mini-BESTest). Bradykinesia was present in 30.6 % of the sample, rigidity in 13.3 % and tremor only in one patient. Patients with bradykinesia were older, had worse cognitive impairment and worse gait and balance performance than those without bradykinesia. More men than women had rigidity. Bradykinesia was significantly associated with mini-BESTest after adjusting for demographic factors ($p < 0.001$, explaining 13.3 % of the variance), but was not significantly associated with gait speed. Rigidity was not associated with either gait speed or balance. We conclude that assessment of bradykinesia should be included in examination of balance control in patients with AD of mild degree.

Keywords:

Gait – balance – Alzheimer disease – bradykinesia - rigidity

1. Introduction

Gait and balance impairments have been described even in mild and preclinical stages of Alzheimer's disease (AD) [1-3]. Among potential contributing factors are parkinsonian signs which occur frequently in patients with AD (without comorbid Parkinson's disease (PD)) [4]. Parkinsonian signs (bradykinesia, rigidity and tremor) are typically milder in patients with AD compared to patients with PD, and tremor is more rare [5]. Still, presence of parkinsonian signs predicts functional and cognitive decline, institutionalization and death in patients with AD[6], and is associated with higher fall risk in patients with advanced AD [7]. However, the relationship between parkinsonian signs and gait and balance is not studied in patients with AD of mild degree. The first aim of the study was to describe what characterize patients with bradykinesia and rigidity among patients with AD of mild degree. The second aim was to examine the associations between bradykinesia and rigidity for gait speed and balance after adjusting for demographic variables.

2. Methods

2.1 Design and participants

This cross-sectional study included 98 patients with AD of mild degree according to research criteria of ICD-10. They were recruited consecutively from the memory clinic at Oslo University Hospital, Ullevål in Norway. To be included the patients should walk independently, be home-dwelling and able to follow instructions in Norwegian. Excluded were patients who had pain when walking, moderate or severe dementia, other dementia disorder, other comorbid neurological diseases (such as PD), or severe hearing and vision impairment. They gave informed written consent, and the study was approved by the Regional Committee for Medical and Health Research Ethics South East in Norway.

2.2 Assessments

Regular gait speed was recorded from a 10 meter walk. Dynamic balance was assessed with the Mini-Balance Evaluation Systems test (Mini-BESTest) [8], scored from 0-28 points, higher score represent better performance. The Unified Parkinson's Disease Rating Scale (UPDRS) part III motor examination was used to assess parkinsonian signs [9]. Rigidity was assessed using 5 items (neck, left and right arms and legs). Bradykinesia was assessed using 8 items (right and left finger taps, hand movements, rapid alternating arm movements and leg agility) from the UPDRS. We used a dichotomized score to evaluate if bradykinesia or rigidity was present or not. Given the wording of the UPDRS where the score of 1 in many items is "mild" or "could be normal for an elderly person" we evaluated bradykinesia and rigidity as present if the patient obtained a score ≥ 2 on one or more of the mentioned items. Tremor was only present in one patient, and no results will therefore be presented on tremor. Items on gait and posture from the UPDRS are excluded from the analyses to avoid overlapping constructs. All motor function tests were carried out by the same physiotherapist. Global cognitive function was assessed using Mini Mental Status Examination (MMSE) [10]. Executive function was assessed using Trail Making Test A [11]. Information on demographics, medication, cognitive functioning was recorded.

2.3 Statistical analysis

Results are presented as means (standard deviations) or as numbers and percentages. Correspondingly we used Student *t*-tests and Chi-square tests or Fisher's exact test to compare groups with and without rigidity and bradykinesia. Multiple linear regression analyses were performed with gait speed and Mini-BESTest as dependent variables. These independent variables were pre-selected based on clinical reasoning and previous studies; age, sex,

MMSE, TMT A, education, comorbidity and use of cholinesterase inhibitors. All tests are two-tailed, and level of significance was set at $p < 0.05$. Data was analyzed using IBM SPSS Statistics version 20 (IBM Corp, Armonk, New York).

3. Results

Patient characteristics are presented in Table 1. Bradykinesia was present in 30.6 % and rigidity in 13.3 % of the patients. Patients with bradykinesia were older, had poorer cognitive function, slower gait and reduced dynamic balance compared to those without bradykinesia (Table 2). Compared to women more men had rigidity.

Neither bradykinesia nor rigidity was **however** significantly associated with gait speed in the multiple linear regression models **where we adjusted for demographic factors**.

Bradykinesia, was significantly associated with Mini-BESTest, and explained 13.3 % of the variance (Table 3).

4. Discussion

In our sample of patients with AD of mild degree, patients with bradykinesia were older, had more severe cognitive impairment and **worse** gait and balance **performances** compared to those who did not have bradykinesia. More men than women had rigidity. Bradykinesia was significantly negatively associated with dynamic balance in the regression model.

We have not been able to find other studies investigating the influence of parkinsonian signs on gait and balance in patients with AD of mild degree. However, in studies of patients with severe AD, mostly living in nursing homes, an association between parkinsonian signs and

gait have been observed [7, 12]. Olazaran and colleagues found that the presence of parkinsonian signs predicted gait disturbance [12]. Camicioli and colleagues observed that patients with parkinsonian signs had reduced regular gait speed and stride length; however they found no relationship between parkinsonian signs and dual task walking or walking fast in the same study [7]. None of these studies studied each parkinsonian sign separately, so we do not have the possibility to compare the relative importance of bradykinesia or rigidity with our findings.

It may also be valuable to compare our results to studies that included elderly without dementia. Rigidity was associated with both self-reported balance impairments and use of walking device in a study of community-dwelling elderly [13], while bradykinesia was not studied separately. In another study of cognitively healthy elderly, severity of bradykinesia, but not rigidity, was associated with gait performance [14]. The lack of association between parkinsonian signs and gait speed in our study is hard to explain as bradykinesia and rigidity is characterized by slowness and stiffness in movements. It could be that walking at regular speed, undisturbed on an even surface is not sufficiently challenging for our relatively healthy group. Still, we observed a relative wide and normally distributed range of gait speed from 0.55 – 1.82 m/s in our sample.

We chose a conservative approach by defining the presence of rigidity or bradykinesia based on a score of at least 2 points on the relevant items of each sign. This may have limited the sensitivity to detect the more subtle associations between parkinsonian signs and gait and balance in our study, especially concerning rigidity which was present in only 13 % of our sample. Another limitation is the cross-sectional design of the study, which does not allow us to draw conclusions about causality. Strengths of the present study include the use of the same

rater for all motor examinations in all patients, and the use of a comprehensive assessment for dynamic balance.

In conclusion, bradykinesia was significantly associated with dynamic balance in our study and should be included in examinations of balance control in patients with AD. Future studies may seek to answer if interventions aimed at improving balance control also improve bradykinesia, or if the improvements are irrespective of presence of parkinsonian signs.

Conflict of interest statement

The authors do not have any financial or personal relationships with other people or organisations that could inappropriately influence (bias) their work.

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