

Cover Page



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Low cognitive status is associated with a lower ability  
to maintain standing balance in elderly outpatients

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## **Abstract**

**Background:** Evidence is emerging that cognitive performance is involved in maintaining balance and thereby involved in falls in the elderly. The aim of this study was to investigate the association of cognitive status with measures of standing balance in elderly outpatients.

**Methods:** In a cross-sectional study, 197 community-dwelling elderly (mean age (SD) 81.9 (7.1) years) referred to a geriatric outpatient clinic were included and subsequently dichotomized into a group with low and normal cognitive status based on cut-off values of the Mini-Mental State Examination, Montreal Cognitive Assessment and Visual Association Test. The ability to maintain standing balance as well as the Center of Pressure (CoP) movement were assessed during 10 s of side-by-side, semi-tandem and tandem stance with eyes open and eyes closed. Logistic and linear regression were used to examine the association between cognitive status and measures of standing balance adjusted for age, gender and highest completed education.

**Results:** Low cognitive status in elderly outpatients was associated with a lower ability to maintain 10 s of balance in side-by-side stance with eyes closed (Odds Ratio (OR) (95% CI): 3.57 (1.60;7.97)) and in semi-tandem stance with eyes open and eyes closed (OR (95% CI): 3.93 (1.71;9.00) and OR (95% CI): 2.32 (1.11;4.82), respectively). Cognitive status was not associated with CoP movement.

**Conclusion:** Low cognitive status associates with a lower ability to maintain standing balance in more demanding standing conditions in elderly outpatients. This may have implications for routine geriatric screening strategies and interpretation of results of either standing balance or cognitive tests.

## Introduction

Impaired standing balance is one of the major complaints reported by elderly to physicians and is strongly related with falls<sup>1,2</sup>. Standing balance is required for most daily living activities. Impaired standing balance may easily result in serious medical, physical, emotional, and social consequences, including loss of independence and social isolation<sup>1,3</sup>. Understanding underlying determinants of impaired standing balance enables early detection and the development of tailored intervention.

Standing balance depends on the functioning of multiple organ systems, like the sensory (vestibular, proprioceptive and visual), musculoskeletal, nervous and cardiovascular system<sup>4-6</sup>. Moreover, it becomes more and more evident that standing balance relies on high-order cognitive performance controlled by the cerebral cortex instead of being a fully automatic process<sup>7-9</sup>. The involvement of the cerebral cortex on standing balance may be mediated by corticospinal loops and communication with the cerebellum and basal ganglia<sup>10</sup>. Involvement may grow with advanced age as neuroimaging studies showed that elderly exhibit more elaborate brain activation compared to young controls during the performance of fine motor tasks<sup>11-14</sup>. Deterioration of the multiple organ systems with advanced age and diseases for which must be compensated may result in increased involvement of the cerebral cortex<sup>15</sup>. Changes in the white matter of the cortex, like leukoaraiosis and periventricular white matter change, are frequently found in dementia. Those changes may result in less ability to compensate and therefore could result in impaired balance and mobility decline<sup>16-18</sup>.

Previous cross-sectional studies investigated the association between cognitive status with standing balance in relatively homogeneous and pre-specified study populations of middle-aged to older adults. These studies showed that a lower cognitive status is associated with a lower ability to maintain standing balance<sup>19-22</sup> and with increased Center of Pressure (CoP) movement<sup>15,23,24</sup>. CoP movement is a measure for the steadiness of the body while maintaining balance and is assessed using a force plate, which measures the ground reaction forces. In general, an increased CoP movement is assumed to reflect impaired standing balance. However, the association of cognitive status with standing balance remains to be established in a clinically relevant population.

In this study, we assessed the association of cognitive status with the ability to maintain standing balance and Center of Pressure movement in a population of community-dwelling elderly referred to a geriatric outpatient clinic, with its typical variety of comorbidities, use of medication and mobility impairments. Elderly outpatients with low cognitive status were expected to exhibit worse standing balance, as reflected by less ability to maintain standing balance and increased CoP movement, compared with patients with normal cognitive status.

## Methods

### Study setting

The study population consisted of community-dwelling elderly (n=207) referred to a geriatric outpatient clinic in a middle-sized teaching hospital (Bronovo Hospital, The Hague, The Netherlands) between March 2011 and January 2012 for a comprehensive geriatric assessment (CGA)<sup>25</sup>. CGA was performed by trained nurses and medical staff during a 2-hour visit. All measurements were performed in the same conditions, in a quiet room and in a fixed order; first cognitive status tests, second standing balance tests. Therefore, the trained nurses and medical staff were aware of the cognitive status of the patient. Measurements took place between 9 am and 4 pm during the day. The study was reviewed and approved by the institutional review board of the Leiden University Medical Center (Leiden, the Netherlands). Because this research is based on regular patient care, the need for individual informed consent was waived. Ten patients (4.8%) were excluded from the analyses due to missing data, leaving 197 patients.

### Elderly outpatient characteristics

Extensive characterization of the population for validity purposes was performed as described below. Patients were asked to complete questionnaires on marital status, living arrangements, highest completed education, current smoking and alcohol use. Body mass index (BMI) was assessed by measuring weight and height. Information on diseases and use of medication was extracted from medical records. Multimorbidity was defined as the presence of two or more diseases, including chronic obstructive pulmonary disease, heart failure, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson's disease, (osteo)arthritis, transient ischemic attack and stroke. Depressive symptoms were assessed by the Hospital Anxiety and Depression Scale (HADS)<sup>26</sup>; a depression subscore higher than 8 out of 21 points indicated depressive symptoms. Physical functioning was assessed by handgrip strength, preferred gait speed during a steady state 10-meter walk and the Short Physical Performance Battery (SPPB)<sup>27</sup>. Furthermore, patients were asked to complete questionnaires on maximal daily physical activity, experienced falls during the previous 12 months and use of walking aids.

### Cognitive status

Global cognitive status was assessed by Mini-Mental State Examination (MMSE)<sup>28</sup> and Montreal Cognitive Assessment (MoCA)<sup>29</sup>, assessing executive function, arithmetic, memory and orientation in time and space. MMSE and MoCA scores both range from 0 to 30 points. One point was added to the total MoCA score if the highest completed education was at low or middle level (comparable with <12 years of education). Version A of the Visual Association Test<sup>30</sup>, in which a maximum number of six objects can be recalled, was used to assess recollecting memory. VAT scores range from 0 to 6 points. For all cognitive

tests, lower scores indicate lower cognitive status. The tests scores of the three cognitive tests were combined to form two groups of patients, i.e. a group with low and a group with normal cognitive status. Low cognitive status was defined as scoring below clinically used cut-off values (MMSE <24 points, MoCA <23 points and VAT <3 points<sup>30-32</sup>) in minimal two out of three cognitive tests. If only two cognitive tests were available (n=40), low cognitive status was defined as scoring below clinically used cut-off values in minimal one cognitive test. The group including all other cases, i.e. scoring equal to or above the clinically used cut-off points, was defined as the normal cognitive status group. Patients with only one (n=1) or no cognitive tests (n=1) were excluded.

### **Standing balance**

#### *Ability to maintain standing balance*

The ability to maintain balance was measured in six standing conditions, i.e. three different standing positions characterized by a progressive narrowing of the base support both with the eyes open and eyes closed. Patients wore non-slip socks and were asked to maintain standing balance for 10 s without moving their feet, first with their feet as closely together as possible (side-by-side stance), second with the medial side of the heel of one foot touching the big toe of the other foot (semi-tandem stance) and third with both feet in line while the heel of one foot touched the toes of the other foot (tandem stance). A maximum of three trials for each condition was allowed in case standing balance was lost prematurely. When the patients were not able to maintain standing balance in a specific position within the three trials allowed, the consecutive more demanding condition was not performed. All standing conditions were performed in a fixed order, starting with the measurements with eyes open, as part of the SPPB, and subsequently with eyes closed. Six of the 197 patients (3.0%) did not attempt the standing positions with eyes closed due to lack of time or lack of motivation, leaving 191 patients for analyses of standing balance positions with eyes closed.

#### *Center of Pressure movement*

All standing conditions were performed on a triangular 6 degrees of freedom force plate (Forcelink BV, Culemborg, The Netherlands) to measure CoP movement during 10 s. Only successful trials (i.e. completion of 10 s of maintaining standing balance) were considered for further analysis. Due to technical problems (n=18) and unknown reasons (n=29), CoP movement was available for n=136 patients.

As age-related differences have been shown to be most pronounced in medio-lateral (ML) direction<sup>33</sup> and impaired ability to control balance in this direction is well associated with falls<sup>34</sup>, only CoP movement in ML direction was included in the analysis. Time series of CoP movement in ML direction were used to calculate five CoP parameters, i.e. the mean amplitude, the amplitude variability, the range, the mean velocity and the velocity variability. CoP parameters were transformed into z-scores, resulting in standardized CoP

parameters with a mean of 0 and standard deviation of 1. Averaging those z-scores resulted in a composite score of the CoP movement in ML direction<sup>33</sup>.

### **Statistical analysis**

Continuous variables with Gaussian distribution are presented as mean and standard deviation (SD), otherwise as median and interquartile range (IQR) or number and percentage. Independent T-tests, Chi Square tests and Mann-Whitney tests were used to assess whether characteristics of both groups were significantly different. Logistic regression analysis was used to assess the association of cognitive status with the ability to maintain standing balance with adjustments for age, gender and highest completed education. The association of cognitive status with CoP movement was assessed using linear regression analysis with the same adjustments. Furthermore, a subgroup analysis was performed in all patients with available data of the HADS depression score (n=121), in which we additionally adjusted for depressive symptoms. The statistical package SPSS for Windows version 20.0 (SPSS Inc, Chicago, USA) was used for analyzing the data. P-values below 0.05 were considered statistically significant. Graphs were made with GraphPad Prism 5 (GraphPad Software, Inc., La Jolla, USA).

## **Results**

The characteristics of the elderly outpatients are presented in Table 1 together with the characteristics stratified for low and normal cognitive status. Mean age (SD) of the patients was 81.9 (7.1) years. Measures of physical functioning, i.e. handgrip strength, gait speed and SPPB score, were lower in the low compared to the normal cognitive status group. The number of self-reported fall incidents in the previous 12 months was higher in the low cognitive status group.

Figure 1 shows the percentage of elderly outpatients able to maintain balance in different standing conditions stratified for low and normal cognitive status. Ability to maintain balance decreased in both groups with increasing difficulty of standing condition. Less than 2% of the patients were able to maintain tandem stance with eyes closed.

The CoP movement in ML direction is shown in Supplementary Table 1. The CoP parameters, used to calculate the CoP composite scores, were higher in more difficult standing conditions.

### **Cognitive status and standing balance**

#### *Ability to maintain standing balance*

The association between cognitive status and the ability to maintain standing balance is given in Figure 2. Patients in the low cognitive status group were less likely to be able to maintain standing balance in the semi-tandem stance with eyes open (Odds Ratio (OR)

(95% CI: 3.93 (1.71;9.00)) and in the side-by-side and semi-tandem stance with eyes closed (OR (95% CI): 3.57 (1.60;7.97) and OR (95% CI): 2.32 (1.11;4.82)) compared with patients in the normal cognitive status group. The odds ratio was higher for side-by-side stance with eyes closed compared with semi-tandem stance with eyes closed. Additional adjustment for depressive symptoms did not change the results (data not shown).

Table 1 Elderly outpatient characteristics.

	All (N=197)	Cognitive status		p
		Low (N=56)	Normal (N=139)	
<b>Socio-demographics</b>				
Age, years	81.9 (7.1)	83.0 (7.5)	81.5 (6.9)	0.19
Men, n (%)	78 (39.6)	19 (33.9)	58 (41.7)	0.31
Widowed, n (%)	80 (41.5)	23 (41.8)	56 (41.2)	0.94
Independent living, n (%)	154 (79.4)	40 (72.7)	113 (82.5)	0.13
Highest completed education, n (%)				0.44
Low	48 (24.7)	17 (31.5)	31 (22.5)	
Middle	62 (32.0)	18 (33.3)	42 (30.4)	
High	55 (28.4)	12 (22.2)	43 (31.2)	
University	29 (14.9)	7 (13.0)	22 (15.9)	
Current smoking, n (%) <sup>a</sup>	22 (16.2)	4 (10.5)	18 (18.8)	0.25
Excessive alcohol use, n (%) <sup>*</sup>	8 (4.1)	1 (1.9)	7 (5.1)	0.32
<b>Health characteristics</b>				
BMI, kg/m <sup>2b</sup>	25.8 (4.5)	25.8 (4.0)	25.7 (4.7)	0.90
Multimorbidity, n (%) <sup>†b</sup>	95 (50.3)	22 (40.0)	72 (54.5)	0.07
Median number of medication (IQR) <sup>b</sup>	5 (3-7)	5 (3 - 7)	5 (3 - 7)	0.45
HADSd > 8 points, n (%) <sup>‡c</sup>	28 (23.1)	9 (25.7)	19 (22.6)	0.72
<b>Physical functioning</b>				
Handgrip strength, kg	26.1 (8.2)	24.1 (8.4)	27.0 (8.0)	0.028
Gait speed, m/s <sup>§b</sup>	0.87 (0.29)	0.73 (0.32)	0.93 (0.26)	<0.001
Median SPPB, points (IQR)	7 (5-10)	6 (4 - 8)	8 (6 - 10)	<0.001
Indoor daily physical activity, n (%)	31 (16.0)	6 (10.7)	25 (18.1)	0.20
Fall incident previous 12 months	127 (64.5)	45 (80.4)	80 (57.6)	0.003
Use of walking aid	108 (55.1)	36 (64.3)	71 (51.4)	0.10
<b>Cognitive status</b>				
Median MMSE, points (IQR)	27 (24 - 29)	22 (19 - 24)	28 (27 - 29)	<0.001
Median MoCA, points (IQR) <sup>d</sup>	24 (20 - 26)	18 (15 - 20)	25 (23 - 27)	<0.001
Median VAT, points (IQR)	5 (3 - 6)	2 (1 - 4)	6 (5 - 6)	<0.001

All parameters are presented as mean with standard deviation unless indicated otherwise. Abbreviations: BMI, body mass index; HADSd, depression subscore of the Hospital Anxiety and Depression Scale; IQR, interquartile range; SPPB, Short Physical Performance Battery; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; VAT, Visual Association Test. <sup>\*</sup>Defined as >14 units per week for females or >21 units per week for males. <sup>†</sup>Present in case of two or more diseases, including chronic obstructive pulmonary disease, heart failure, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson's disease, (osteo)arthritis, transient ischemic attack and stroke. <sup>‡</sup>Present with a depression subscore >8 on the Hospital Anxiety and Depression Scale. <sup>§</sup>Preferred gait speed during a steady state 10-meter walk. Data available in <sup>a</sup>n=136, <sup>b</sup>n=190, <sup>c</sup>n=121 and <sup>d</sup>n=158.



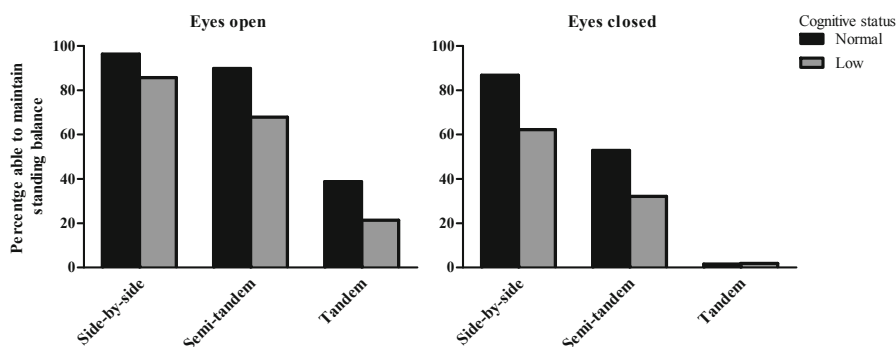


Figure 1 Percentage of elderly outpatients able to maintain balance in different standing conditions, i.e. side-by-side, semi-tandem and tandem stance with eyes open and eyes closed. Results are stratified for low and normal cognitive status.

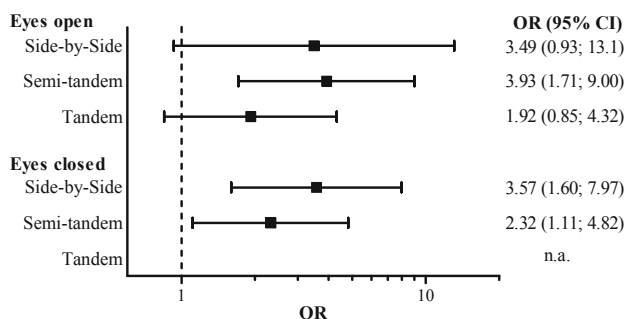


Figure 2 Forest plot of the association between cognitive status and the ability to maintain balance in different standing conditions, i.e. side-by-side, semi-tandem and tandem stance with eyes open and eyes closed. The low and normal cognitive status groups are represented by 0 and 1, respectively. The ability to maintain standing balance is defined as 0 not being able to maintain standing balance and 1 being able to maintain standing balance. Results are presented in odds ratios and 95% confidence intervals adjusted for age, gender and highest completed education. Abbreviations: OR, odds ratio; CI, confidence interval; n.a., not applicable, number of elderly outpatients able to maintain balance in the standing condition is <5.

Table 2 Association between cognitive status and Center of Pressure movement in medio-lateral direction in different standing conditions.

	Side-by-side <sup>†</sup>			Semi-tandem <sup>‡</sup>			Tandem <sup>§</sup>		
	$\beta$	SE	p	$\beta$	SE	p	$\beta$	SE	p
<b>Cognitive status<sup>*</sup></b>									
Eyes open	-0.02	0.18	0.91	0.17	0.21	0.43	0.29	0.35	0.41
Eyes closed	0.35	0.19	0.07	0.29	0.29	0.32		n.a.	

<sup>\*</sup>Cognitive status with 0 representing the group of elderly outpatients with low cognitive status and 1 the group with normal cognitive status based on clinically used cut-off values. Dependent variable: Center of Pressure composite score in medio-lateral direction. Results are adjusted for age, gender and highest completed education. Abbreviations:  $\beta$ , estimate; SE, standard error; p, p-value; n.a., not applicable, number of elderly outpatients able to maintain balance in the standing condition is <5. Data available in <sup>†</sup>n=135 and n=116, <sup>‡</sup>n=119 and n=72, <sup>§</sup>n=56 and n=2 for eyes open and closed, respectively.

### *Center of Pressure movement*

Table 2 shows the results of the association of cognitive status with CoP movement in ML direction. The association was not statistically significant for each standing position, both with eyes open and eyes closed. The association between cognitive status and CoP movement in ML direction during tandem stance with eyes closed was not applicable due to a low number of patients who could perform this standing condition.

## **Discussion**

The aim of this study was to establish the association of cognitive status with standing balance in a clinically relevant population of elderly outpatients. We found that low cognitive status was associated with a lower ability to maintain standing balance. Cognitive status was not associated with CoP movement in ML direction.

Our findings are in concordance with previous studies showing a cross-sectional association between low cognitive status and a lower ability to maintain standing balance in middle-aged to older adults in which the study population is further specified on e.g. cognitive or mobility impairments and the presence of comorbidities<sup>19-22</sup>. In this study, we showed that this relation is also present in community-dwelling elderly visiting the geriatric outpatient clinic with common comorbidities and mobility impairments. In this population, deterioration of the different organ systems involved in standing balance, i.e. the sensory, musculoskeletal, nervous and cardiovascular system, is very likely. The presence of the association between cognitive status and the ability to maintain standing balance supports the important role of the brain in controlling standing balance instead of being a fully automatic process<sup>7-9</sup>. Furthermore, it emphasizes the clinical relevance of measuring standing balance in patients with low cognitive status. Especially because of the large impact of impaired standing balance on most of daily living activities and the strong relation of impaired standing balance with falls<sup>1,2</sup>. The latter is also supported by this study showing a higher reported fall incidence over the previous 12 months in the low compared to the normal cognitive status group. No differences in maximal daily physical activity were found between groups. Although, in this case it is difficult to distinguish cause and effect, as less daily activity could be caused by impaired standing balance, but less daily activity could also cause impaired standing balance.

The association between cognitive status and the ability to maintain standing balance was found in 3 of the 6 standing conditions, namely side-by-side stance with eyes closed and semi-tandem stance with eyes open and eyes closed. This could be explained by the increasing difficulty of the standing conditions, i.e. reducing the base of support and eliminating visual information. More difficult standing conditions put higher demands on balance control. Aforementioned standing conditions will therefore be more difficult for patients with a low cognitive status compared with patients with a normal cognitive status.

No association between cognitive status and the ability to maintain balance in tandem stance with eyes closed could be found, as only four patients were able to maintain balance during this condition.

No association was found between cognitive status and CoP movement. The inconsistency in the association of cognitive status with the ability to maintain standing balance and CoP movement emphasizes that both outcome parameters of standing balance assess different properties. The ability to maintain standing balance is a measure of standing balance referring to whether someone is able to stay upright or not, whereas CoP movement is a more indirect measure of standing balance referring to the steadiness of the body while standing on a force plate<sup>35</sup>. A possible explanation for the absence of an association of cognitive status with CoP movement, is that data on CoP movement is only available from patients who were able to maintain 10 s of standing balance, which may have led to an underestimation of the association between cognitive status and CoP movement. Another possible explanation is the heterogeneity of the study population, especially the presence of more than two diseases in more than 50% of the patients and the deterioration of multiple systems involved in standing balance<sup>4</sup>. As each underlying system could have a different effect on CoP movement, this may interfere with the association between cognition and CoP movement on population level<sup>36</sup>. Further research into the assessment of CoP movement is still needed to get insight into the causal underlying mechanisms of impaired standing balance, which are yet unknown.

One of the strengths of this study is the study population consisting of community-dwelling elderly referred to a geriatric outpatient clinic. Because no exclusion criteria were used, the study population represents an average population encountered in common geriatric practice. This makes the results of this study highly relevant in clinical practice. Measuring standing balance in patients with low cognitive status and, the other way around, measuring cognitive status in patients with impaired standing balance will have an added value in clinical care. Furthermore, the combined assessment of the ability to maintain standing balance, as part of the SPPB, and CoP movement enables to get insight into the clinical utility of both measures. A limitation of the study is that CoP movement was measured during a relatively short time interval of 10 s and data of only one successful trial was available, while previous studies recommend to measure CoP movement more than once and during a longer time period<sup>35,37</sup>. However, in clinical practice and in a population of elderly outpatients it is likely that this it is not feasible due to time limit and fatigue. The cross-sectional design of the present analysis prevents to study causality.

In conclusion, low cognitive status is associated with a lower ability to maintain balance for 10 s in more demanding standing conditions in elderly outpatients. This indicates the clinical relevance of measuring standing balance in patients encompassing those with low cognitive status in routine geriatric screening. Regarding interpretation, in patients with

impaired standing balance the possibility of low cognitive status must be considered and, the other way around, in case of poor performance on cognitive tests the possibility of impaired standing balance must be considered. We could not establish an additional value of assessment of CoP movement in routine geriatric assessment as we found low cognitive status not to be associated with CoP movement. A next step would be to focus on clustering of phenotypes and defining risk populations, which will be of clinical added value and will allow to investigating causality. This obviously requires large study sample sizes.

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## Supplementary material

Supplementary Table 1 Center of Pressure (CoP) movement, represented by CoP parameters, within elderly outpatients able to maintain different standing positions with eyes open and eyes closed in medio-lateral direction.

	Side-by-side*	Semi-tandem†	Tandem‡
<b>Eyes open</b>			
Mean amplitude, cm	0.60 (0.02)	0.72 (0.03)	0.72 (0.03)
Range, cm	3.51 (0.13)	4.25 (0.18)	3.92 (0.17)
Mean velocity, cm/s	4.09 (0.10)	4.78 (0.13)	5.41 (0.21)
Amplitude variability, cm	0.75 (0.03)	0.91 (0.04)	0.88 (0.04)
Velocity variability, cm/s	5.70 (0.14)	6.76 (0.23)	7.55 (0.28)
<b>Eyes closed</b>			
Mean amplitude, cm	0.85 (0.03)	1.03 (0.04)	
Range, cm	4.86 (0.18)	5.64 (0.23)	
Mean velocity, cm/s	5.67 (0.15)	6.76 (0.26)	n.a.
Amplitude variability, cm	1.06 (0.04)	1.27 (0.05)	
Velocity variability, cm/s	7.88 (0.20)	9.33 (0.37)	

Data are given in mean with standard error. Abbreviations: n.a., not applicable, number of elderly outpatients able to maintain balance in the standing condition is <5. Data available in \*n=136 and n=119 and †n=120 and n=75 for eyes open and closed, respectively and ‡n=56 for eyes open.

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