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Original Research Article

Postural Stability Analysis with Inertial Measurement Units in Alzheimer's Disease

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Key Words

Alzheimer's disease · Postural stability · Inclined surface · Inertial measurement unit · Triaxial accelerometer and gyroscope

Abstract

Background: The cause of frequent falls in patients with Alzheimer's disease (AD) is still not well understood. Nevertheless, balance control and sensory organization are known to be critical for moving safely and adapting to the environment. **Methods:** We evaluated postural stability in 20 AD patients (11 fallers and 9 nonfallers) and 16 healthy controls with an inertial measurement unit (triaxial accelerometers and gyroscopes) attached to the center of mass (COM) in different balance conditions (Romberg on flat surface and frontward/backward-inclined surface, with or without visual suppression) in a motor lab. **Results:** In AD patients, the group of fallers showed a different kinetic pattern of postural stability characterized by higher vulnerability to visual suppression, higher total/maximal displacement and a medio-lateral/anteroposterior range of sway, and a consequent need for more corrections of COM pitch and roll angles. **Conclusion:** Further studies are needed to consolidate the normative values of the discriminatory kinetic variables with the potential of inclusion in a multifactorial analysis of the risk of falls. Nevertheless, these results highlight signs of impairment of central postural control in AD, which may require early therapeutic intervention.

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Introduction

Alzheimer's disease (AD) is the major cause of dementia in the geriatric population in the United States and Western Europe [1]. It is a neurodegenerative cortical disorder associated with posture and gait disturbances and a high risk of falls [2]. In AD patients, falls are more frequent and have more serious traumatic consequences, including hip fracture, than in nondemented elderly people [3, 4].

The underlying mechanisms contributing to falls in AD patients are not clearly understood [5]. Physiological deficits, such as impairment of sensorimotor function, reduced vision [6], peripheral sensory loss and muscle weakness [7] and slowed reaction time [8], either individually or globally [9], detected by a Physiological Profile Assessment test [10], may explain the higher risk of falls in AD. Also, the great variability in gait patterns [11] and increased postural sway [12] may account for this higher risk of falls in AD.

Most postural kinetics studies in AD are based on postural analysis of the center of pressure on force plates. In contrast, inertial measurement units (IMU), with integrated accelerometers and gyroscopes, are small, fully portable devices that are independent of the inclination in space and have proved to be equivalent to force platforms in the measurement of the center of mass (COM) and stability analysis [11–13]. Also, IMU have the advantage of measuring postural stability in several stability and environment scenarios, including inclined surfaces.

Herein, we aim to (1) analyze postural kinetics with IMU in AD patients and healthy controls in different postural stress conditions, such as Romberg, visual suppression, and inclination and (2) try to identify discriminative kinetic parameters in AD patients that may be predictors of falls.

Methods

Subject Selection and Clinical Assessment

The study population was recruited from our hospital outpatient neurology department. Patients with probable AD, according to Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) and National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria [13], were consecutively recruited for the study. The control group included age-matched caregivers of patients that had no history of falls or of neurological or psychiatric disease. Patients or controls were also excluded if there was a history of orthopedic, musculoskeletal or vestibular disorder or alcohol abuse. Demographic data and medical history were collected in both groups. A brief neuropsychological examination was performed using the Portuguese version of the Montreal Cognitive Assessment test (MoCA) with scores normalized to the Portuguese population [14], no more than 1 month prior to the kinetic assessment. Levels of education were categorized by years of schooling: 0 (analphabetic), 1 (1–4 years), 2 (5–9 years), 3 (10–12 years), and 4 (>12 years). The severity of dementia was graded according to the Clinical Dementia Rating (CDR) [15]. AD patients were recorded as fallers (ADF) if they had at least one fall in the previous 6 months. Written consent was obtained from all subjects or their legal guardians, and the study protocol was approved by the local ethics committee.

Kinetic Postural Acquisition and Assessment

Biometric data [weight, height, body mass index, and anthropometric measurements, i.e. shank (ankle-knee) and thigh (knee-iliac crest)] were collected on the day of kinetic postural assessment. Five kinetic sensing modules, harboring an 8051 microprocessor embedded in

CC2530 Texas Instruments SoC (System on Chip) and an IMU MPU6000 (triaxial accelerometer and gyroscope) [16, 17] and operating with a sample rate frequency of 113 Hz on an SD card, were attached by Velcro bands to five body segments: trunk (COM; at 55% of a person's height above the ground) [18], both legs (middle of ankle-knee distance), and both thighs (middle of knee-iliac crest distance). The video capture (sample rate of 60 fps) and the data logging on the five kinetic sensors were synchronized by bidirectional radio signal transmission by an USB coordinator node (connected to a PC with custom-made Matlab software). Outputs from the accelerometers were filtered with a second order Butterworth low-pass filter with a cutoff frequency of 0.5 Hz [19], and the outputs from the gyroscopes filtered with a cutoff frequency of 5 Hz [20].

Final pitch and roll angles were obtained by a complementary filter of accelerometer and gyroscope pitch and roll (β -coefficient of 0.98) [21].

$$\begin{aligned} \text{Pitch}(\theta) &= \beta \cdot (\text{pitch}(\theta)_{\text{gyro}}) + (1 - \beta) \cdot \text{pitch}(\theta)_{\text{accel}} \\ \text{Roll}(\phi) &= \beta \cdot (\text{roll}(\phi)_{\text{gyro}}) + (1 - \beta) \cdot \text{roll}(\phi)_{\text{accel}} \end{aligned}$$

The kinetic sensor orientation in space was calculated by Euler angle spatial representation for pitch (θ) and roll (ϕ) [22, 23]. After definitions of angles, displacement (d) of the COM (H_{COM} ; i.e. 55% of a subject's height) was calculated with the formula:

$$dy = \sin(\text{pitch}(\theta)) \cdot H_{COM}; dx = \sin(\text{roll}(\phi)) \cdot H_{COM}.$$

One of a normal human's mechanisms of maintaining balance is to vary COM by bending knees and trunk. Therefore, the height of COM was constantly adjusted, using the information derived from the length (L) of the shank and thigh (i.e. L_{shank} and L_{thigh} , respectively) and from the angles of the IMU located on the shank and thigh (i.e. θ_{shank} and θ_{thigh} , respectively) by the formula:

$$\begin{aligned} T_1 &= \cos \theta_{shank} \cdot L_{shank} \\ T_2 &= \cos \theta_{thigh} \cdot L_{thigh} \\ H_{COM} &= H_{COM}^{\text{measured}} - (L_{shank} - T_1) - (L_{thigh} - T_2). \end{aligned}$$

From the kinetic measurements derived from the COM displacement, we focused on some that emerged from a systematic review as predictors of falls among elderly people [24]: total displacement (cm) on the transverse plane

$$\sqrt{(x_{i+1} - x_i)^2 + (y_{i+1} - y_i)^2};$$

maximal displacement (cm) with respect to the origin on the transverse plane

$$\text{maximum of } \sqrt{x_i^2 + y_i^2};$$

maximal linear velocity (cm/s) [20]; positioning (cm) on x- and y-axis (mean and range); roll angle (degrees; maximal, minimum, and mean), and pitch angle (degrees; maximal, minimum, and mean).

Test Conditions

Subjects were instructed to perform six different standing Romberg conditions: Romberg test with eyes open/closed on a flat firm surface and Romberg test on a backward/frontward-inclined surface with eyes open/closed. Subjects performed the Romberg test barefoot, with the medial aspects of the feet touching each other. During the tasks, the subjects stood quietly, with their arms hanging at their sides and their head in a normal forward-looking eye position with the eyes directed to an object 2 m away. All tasks were explained, and subjects had the opportunity to practice before the definitive trial. Each task was performed during 30 s, and

Table 1. Demographic, clinical, and anthropometric data of controls and AD patients (ADNF and ADF)

	Controls (n = 16)	AD patients		Intergroup comparison	p
		ADNF (n = 9)	ADF (n = 11)		
Females/males, n	6/10	7/2	7/4	$\chi^2 = 4.02$	0.095
Age, years	72.31±7.08	73.56±8.72	77.64±4.80	$\chi^2_{KW}(2) = 3.77$	0.152
Level of education ¹	1 (0, 4)	1 (0, 2)	1 (0, 2)	$\chi^2_{KW}(2) = 4.383$	0.110
Height, m	1.60±0.11	1.52±0.06	1.53±0.08	$\chi^2_{KW}(2) = 5.208$	0.074
Weight, kg	71.68±9.07	68.90±9.82	65.01±7.84	$\chi^2_{KW}(2) = 4.084$	0.130
Body mass index	27.92±3.44	29.88±5.15	27.80±2.84	$\chi^2_{KW}(2) = 0.572$	0.751
COM, cm	88.27±6.04	83.99±3.33	84.15±4.29	$\chi^2_{KW}(2) = 5.208$	0.074
Duration of disease, years	–	3.33±1.94	2.82±1.47	U = 38.0; z = -0.906	0.407
CDR ¹	–	1 (0.5, 2)	2 (0.5, 2)	U = 43.5; z = -0.490	0.726
MoCA	24.75±3.59	12.22±6.63	10.09±4.42	$\chi^2_{KW}(2) = 24.023$	<0.001
				C vs. ADNF	<0.001
				C vs. ADF	<0.001
				ADF vs. ADNF	0.643

Unless otherwise indicated values represent mean ± SD. C = Controls.

¹ Values in parentheses represent minimum and maximum.

during that time the kinetic data were recorded [25, 26]. The trial was invalidated and started again if subjects moved any part of their body, spoke, opened their eyes for visual aid or did a corrective step.

We set up a fixed 15° inclined platform to standardly compare the adjustments of posture under inclination between the 3 groups. In our laboratory, on experiments of steps of 5° of inclination, healthy subjects started to have a significant change on kinetic measurements after 15° of inclination, being approximately the 20° proposed by other studies [27]. The subject were in the Romberg position, with heels below toes for the task with the backward-inclined platform, and on the same inclined platform, with toes below heels for the Romberg task with the forward-inclined platform. They rested between test conditions to reduce the effect of muscular fatigue, especially with platform tasks [28].

Statistical Analysis

Gender comparisons were analyzed by the χ^2 Fisher exact test. Due to the absence of normality and variance equality amongst groups regarding continuous variables (anthropometrics, MoCA, years of disease, and kinetics parameters) and ordinal variables (education and CDR), the comparison between the groups was carried out by a nonparametric test, the Kruskal-Wallis test (comparison between 3 groups), with a pairwise post hoc analysis with Dunn's test and the magnitude of change in intraindividual tasks by the Wilcoxon matched pair test. Correlation analyses of age, anthropometrics, CDR and years of disease, with kinetic data, were performed with the Spearman test. All statistical analyses were conducted with statistical analysis software (SPSS 20.0) using a 95% level of significance.

Results

Demographic, Clinical, and Anthropometric Data

This study included 20 AD patients [9 classified as nonfallers (ADNF) and 11 as ADF] and 16 controls. There were no statistically significant differences between the groups, regarding age or anthropometric parameters (table 1). In spite of a higher frequency of females in the

Table 2. Inertial measurement unikinetic analysis in different conditions

Conditions	Kinetic variables												
	path, cm		velocity, cm/s		x-axis position		y-axis position		roll angle, degrees		pitch angle, degrees		
	total displacement	maximal displacement	max	mean	range	mean	range	max	min	mean	max	min	mean
<i>Romberg on flat surface</i>													
Eyes open													
Controls	18.67±3.13	2.76±0.98	0.95±0.51	0.84±0.87	2.14±0.69	-0.20±1.2	2.96±1.15	0.73±0.48	-0.65±0.50	0.09±0.46	0.83±0.87	-1.09±0.77	-0.11±0.72
ADNF	20.77±5.96	2.5±0.99	0.81±0.37	1.00±0.79	2.20±0.93	0.02±1.04	2.90±1.22	1.07±0.62	-0.46±0.52	0.30±0.46	1.00±0.79	-0.97±0.74	0.02±0.73
ADF	23.85±5.85	2.82±1.80	1.29±0.70	1.11±0.76	3.10±1.70	0.28±0.90	2.65±0.96	1.29±1.35	-0.84±0.57	0.22±0.82	1.11±0.76	-0.69±0.63	0.20±0.60
Eyes closed													
Controls	21.73±4.95*	2.44±0.82	0.72±0.17	0.91±0.54	2.31±0.96	0.02±0.80	2.79±0.80	0.70±0.60	-0.80±0.60	-0.04±0.59	0.91±0.54	-0.89±0.59	0.02±0.53
ADNF	22.79±7.04	2.37±1.06	0.95±0.55	0.95±0.67	2.53±1.34	0.09±1.02	2.55±1.02	0.62±0.41	-1.11±0.74	-0.20±0.44	0.95±0.67	-0.80±0.78	0.05±0.69
ADF	32.21±11.56*	4.26±2.18*	2.17±1.30	2.01±1.43	4.26±2.61	0.97±1.44	4.04±1.84*	1.67±1.20	-1.25±1.16	0.13±0.70	2.01±1.43	-0.73±0.72	0.65±0.96
<i>Romberg on backward-inclined surface</i>													
Eyes open													
Controls	21.58±6.35	2.74±1.34	1.17±0.64	0.66±0.83	2.34±1.02	-0.38±1.44	2.65±1.42	0.81±0.50	-0.73±0.76	0.003±0.56	0.66±0.83	-1.04±0.95	-0.25±0.90
ADNF	25.05±11.12	2.77±1.31	1.63±1.48	1.17±0.84	2.99±2.09	0.36±0.87	2.67±1.12	0.99±1.09	-1.08±0.82	-0.05±0.63	1.17±0.84	-0.68±0.37	0.26±0.61
ADF	26.22±8.07	2.86±1.46	1.83±1.43	1.03±0.88	3.13±0.88	0.32±0.73	2.31±1.14	1.47±0.98	-0.67±0.56	0.36±0.72	1.03±0.88	-0.53±0.43	0.22±0.50
Eyes closed													
Controls	24.88±8.46	2.73±1.27	1.46±0.77	1.17±0.85	2.45±0.96	0.30±1.23	3.01±1.14	0.75±0.64	-0.84±0.57	-0.026±0.55	1.17±0.85*	-0.79±0.82	0.19±0.82
ADNF	23.81±14.80	2.51±1.30	1.74±1.23	1.11±0.59	2.64±1.58	-0.08±0.59	3.45±1.99	1.14±0.76	-0.66±0.44	0.22±0.37	1.11±0.59	-1.23±0.91	-0.05±0.41
ADF	33.90±12.85*	3.47±1.95	2.29±1.19	1.09±0.77	3.70±1.79	-0.00±0.94	3.19±1.44*	1.56±1.74	-0.94±0.74	0.23±1.04	1.09±0.77	-1.06±0.58	-0.01±0.64
<i>Romberg on forward-inclined surface</i>													
Eyes open													
Controls	20.65±6.15	3.35±2.25	1.55±1.06	1.42±1.58	2.17±1.11	0.39±1.39	3.59±2.60	0.62±0.55	-0.80±0.59	-0.10±0.46	1.42±1.58	-0.92±1.22	0.27±0.91
ADNF	23.85±7.93	2.78±1.95	1.40±1.34	1.26±1.60	2.55±0.92	0.46±1.83	3.21±2.00	0.76±0.47	-0.99±0.59	-0.06±0.41	1.27±1.60	-0.95±0.59	0.34±1.28
ADF	26.03±8.20	3.34±1.47	1.16±0.59	1.61±1.04	2.82±1.31	0.77±1.44	3.33±1.09	0.93±1.11	-1.00±0.65	-0.09±0.64	1.60±1.04	-0.67±0.62	0.53±0.98
Eyes closed													
Controls	24.03±7.86	2.50±1.38	1.40±0.93	0.82±0.69*	2.24±0.89	-0.08±1.14	2.28±1.58	0.97±0.59	-0.48±0.42	0.24±0.37*	0.82±0.69	-0.98±0.94	-0.05±0.76
ADNF	28.89±10.64	2.95±0.97	1.66±1.08	1.05±0.95	2.94±1.12	-0.48±0.91	3.61±1.46	1.06±0.65	-0.94±0.60	-0.04±0.53	1.05±0.94	-1.42±0.57	-0.31±0.61
ADF	32.80±13.18	3.23±1.16	1.80±1.59	0.78±0.70	3.32±1.53	-0.66±1.19*	3.49±1.29	1.02±0.59	-1.26±0.98	-0.18±0.71	0.78±0.70	-1.60±0.83*	-0.45±0.78*

Data are presented as mean ± standard deviation of kinetic variables in different conditions of the Romberg test for controls, ADNF and ADF. Shaded boxes show values where there was statistical significance on Kruskal-Wallis test and post hoc analysis between the 3 groups. * Statistical significance with Wilcoxon matched pair test between eyes open and eyes closed in each condition.

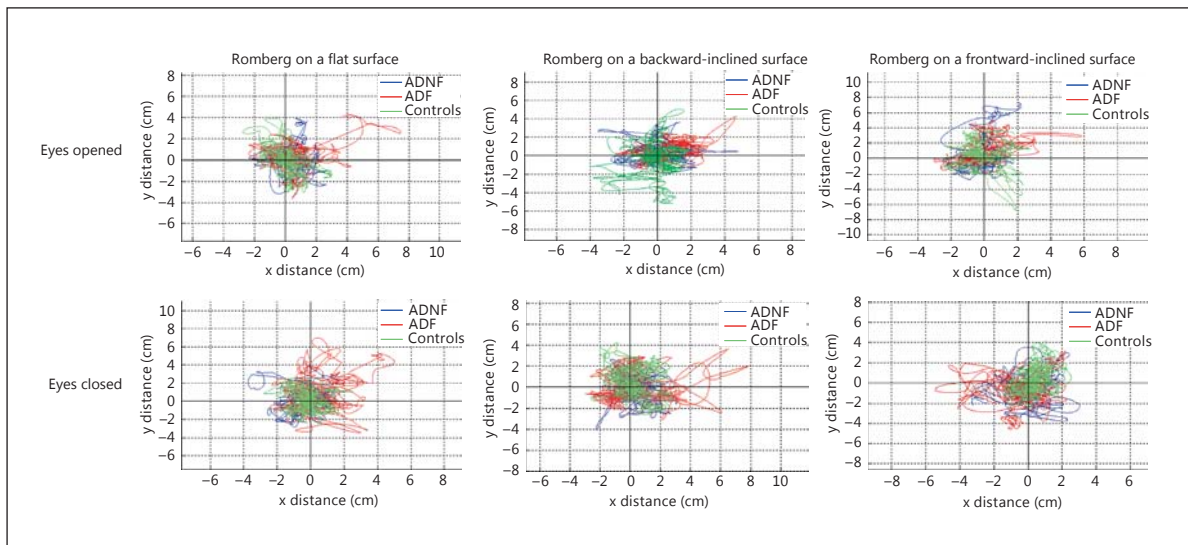


Fig. 1. Displacement plot on the x-axis (mediolateral) and the y-axis (anteroposterior) of the IMU, attached to the COM (at 55% of height), for all subjects (controls, ADF, and ADNF).

AD patients, no statistical difference was detected regarding gender between the controls and ADF and ADNF patients. Moreover, the gender has not been associated with postural sway deficits [27]. The majority of AD patients and controls had an education level of less than 4 years. As expected, AD patients had lower scores on MoCA compared to controls, but there were no differences between ADNF and ADF in the total MoCA score or its subitems. ADF patients did not differ from ADNF patients regarding years of progression or severity of AD. No correlations were found between age, CDR, or years of disease with any of the kinetic variables.

Kinetic Postural Analysis

Romberg Position with Eyes Open/Eyes Closed on Flat Surface

In the Romberg position with eyes open, the kinetic posture measurements were not statistically different between the 3 groups. With eyes closed, the groups differed in the following kinetic posture measurements: total displacement [$\chi^2_{KW}(2) = 6.608$; $p = 0.037$; controls vs. ADF $p = 0.01$; controls vs. ADNF $p = 0.447$; ADF vs. ADNF $p = 0.127$], maximal displacement [$\chi^2_{KW}(2) = 9.241$; $p = 0.01$; controls vs. ADF $p = 0.013$; controls vs. ADNF $p = 0.948$; ADF vs. ADNF $p = 0.005$], and range on x-axis [$\chi^2_{KW}(2) = 9.036$; $p = 0.01$; controls vs. ADF $p = 0.003$; controls vs. ADNF $p = 0.645$; ADF vs. ADNF $p = 0.034$] (table 2). The Wilcoxon matched pair test was used to compare between conditions with eyes open versus eyes closed, revealing that on visual suppression, controls had a statistically significant increase in total displacement ($Z = -2.689$; $p = 0.005$) and the ADF group had a statistically significant increase in total displacement ($Z = -2.490$; $p = 0.01$), maximal distance ($Z = -1.956$; $p = 0.054$), and range on y-axis ($Z = -2.134$; $p = 0.032$) (fig. 1).

Romberg Position with Eyes Open/Eyes Closed on Inclined Platform

On the backward platform, no differences were found between the groups. On the forward platform, with eyes closed, the AD patients, in particular the ADF patients, had a lower minimal roll angle [$\chi^2_{KW}(2) = 10.442$; $p = 0.005$; controls vs. ADF $p = 0.002$; controls vs. ADNF $p = 0.468$; ADF vs. ADNF $p = 0.044$] (table 2).

The Wilcoxon matched pair test was used to compare between conditions with eyes open and eyes closed. On the backward-inclined surface, under visual suppression, the controls had an increase in maximal pitch angle ($Z = -2.223$; $p = 0.025$) towards anterior (positive values) inclination, and the ADF patients had an increase in total displacement ($Z = -2.599$; $p = 0.006$) and the range on the y-axis ($Z = -2.395$; $p = 0.014$).

On the forward-inclined surface, under visual suppression, controls shifted to a lower mean x-axis position ($Z = -2.120$; $p = 0.034$) and had an increase in the mean roll angle ($Z = -2.223$; $p = 0.025$). The ADF group had a significant change in the minimal pitch angle ($Z = -2.667$; $p = 0.005$) towards posterior inclination, almost reaching significance on a more posterior (negative) mean y-axis position ($Z = -1.956$; $p = 0.054$) and on a mean pitch angle ($Z = -1.956$; $p = 0.054$) (fig. 1).

Discussion

The cause of frequent falls in patients with AD is still not well understood. Balance control and sensory organization are known to be critical for moving safely and adapting to the environment. Herein, we have explored the underlying mechanisms for this tendency to fall and we have shown that ADF patients display a different kinetic profile.

Balance is a complex process of coordination of multiple body systems, including the vestibular, auditory, visual, motor and higher level premotor systems, that generate appropriate synergic postural muscle movements of the head, eye, trunk, and limbs to maintain posture [29]; this is achieved by sustaining, achieving, or restoring the body COM relative to the base of support or, more generally, within the limits of stability with a minimal sway [30]. An individual's limits of stability, commonly referred to as functional stability limits, refer to the maximum distance in which one can voluntarily displace one's center of gravity and lean one's body in a given direction without losing one's balance [31].

Visual suppression makes the human body more dependent on vestibular and proprioceptive systems, consequently increasing sway [9], which was confirmed in our study both in healthy and AD subjects. However, the visual suppression effect was stronger in ADF patients. After closing their eyes, the ADF group swayed more (total displacement) and beyond safety limits (maximal displacement). Contrary to controls that presented on visual suppression a normal correction acquiring a more central position (lower mean x- and y-axis positions and range of sway), the ADF group had an increase in the range of mediolateral/anteroposterior sway. Our results agree with previous literature which has shown that the mediolateral sway is associated with a higher risk of falls in elderly people [24], and the anteroposterior sway is a discriminative parameter of AD versus controls [9] and also of fallers versus nonfallers in cognitively able older people [32]. This increased sway also demanded more pitch and roll variations, and ankle and trunk strategies of correction of stability [33] in the ADF group.

We also aimed to evaluate the susceptibility to inclination, as AD patients can walk long distances and thus are subjected to constant environmental postural stress, such as surface inclination, which may account for their falls [34]. Postural control on a tilting support surface is mainly achieved with the help of visual, vestibular, and proprioceptive afferents [27]. On a 20° static inclined surface, the inclination was described to significantly increase postural imbalance in healthy subjects, especially when visual support was interrupted [27]. Contrary to what we had primarily expected, on the inclined surface, there was an attenuation of the differences between groups that were more evident on the flat surface. A learning trial repetition bias [35], an instruction anticipation factor, and a higher demand of attention and focus could have accounted for a better postural sway performance on the inclined surfaces in comparison to the less stressful flat surface condition. However, the controlled lab conditions

are exactly the opposite of the daily living conditions where patients are more relaxed, unfocused, and without the anticipation effect of fear of falling [36] or preparation for episodes of disequilibrium. This clearly highlights the importance of cognition, especially attention, on postural balance [12], and the need for complementing lab analysis with kinetic studies on everyday motion behavior [37].

In a recent study, older adults with presumptive preclinical AD, with higher levels of brain fibrillar amyloid plaques measured by Pittsburgh compound B retention on brain PET imaging, had a short latency time to their first fall [38]. This raises the hypothesis that neuropathological changes that negatively affect postural control and increase the risk of falls may happen subclinically in AD patients [32, 39, 40]. In fact, in our study, ADF and ADNF patients, although having different kinetic performances, were clinically very similar, not differing in age, anthropometric data, neuropsychological assessment, or severity of the disease. Therefore, kinetic postural analysis, in our study measured with IMU, may be a useful tool to preclinically identify AD patients with a higher risk of falls.

Although we need more studies to consolidate normative values of discriminatory kinetic variables acquired by IMU, with the potential of inclusion in a multifactorial analysis of the risk of falls, our results highlight signs of impairment of central postural control in AD, which may require early therapeutic intervention.

Disclosure Statement

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