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Postural Sway, Falls, and Cognitive Status: A Cross-Sectional Study among Older Adults

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Abstract.
Background: Cognitive impairment-related changes in postural sway increase fall risk among older adults. Better understanding this association could be helpful for fall prevention.
Objective: To examine the center-of-pressure (COP) velocity association with cognitive status and history of falls, in cognitively healthy individuals (CHI), patients with mild cognitive impairment (MCI), and with mild-to-moderate Alzheimer's disease (MMAD).
Methods: Six hundred and eleven older community-dwellers (77.2 ± 7.9 years; 51.8% men) were separated into CHI, MCI, and MMAD participants. By computing the average absolute maximal velocity (AAMV), the bounding limits of COP velocity dynamics were determined while participants were asked to maintain quiet stance on a force platform with eyes open or with eyes closed. Age, gender, history of falls, body mass index, handgrip strength, Timed Up & Go score were used as covariates.
Results: The multivariate ANCOVA, with AAMV in eyes open and eyes closed conditions as dependent variables, showed that the highest AAMVs that bound the COP velocity dynamics of postural sway were associated with cognitive impairment ($p = 0.048$) (i.e., lowest limits in CHI and MCI as compared with MMAD) and falls ($p = 0.033$) (i.e., highest limits in fallers).
Conclusions: These findings identified the bounding limits of COP velocity as a hallmark feature of cognitive impairment-related changes in postural sway, in particular for MMAD. This point is of special interest for clinical balance assessment and fall prevention in MMAD patients in order to plan long-term targeted fall-prevention programs.

Keywords: Accidental falls, Alzheimer's disease, mild cognitive impairment, postural balance

INTRODUCTION

Falls are common in older population and often lead to fractures and psychological trauma, self-imposed restriction in daily activities, and consequently, loss of independence [1–3]. Older adults with cognitive impairment from mild cognitive impairment (MCI) to dementia, have higher prevalence of falls [4–7]. Recently, some studies have characterized some cognitive impairment-related changes in gait performance, suggesting the existence of a motor phenotype of unsafe gait in MCI and mild dementia [8–11]. For example, an increase in the variability of stride-to-stride time (i.e., worst gait performance and control) has been identified as a specific biomarker of MCI patients [12]. In addition, evidence of balance impairment has been widely reported in MCI or Mild-to-Moderate Alzheimer's disease (MMAD) [13–17]. All these data suggest that the implicit postural control strategies in older adults with cognitive impairment may be a clinical hallmark of early cognitive

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dysfunction and may help to diagnose individuals with increased fall risk [18].

Because poorer balance stability is identified as a powerful predictor of falls in older adults with cognitive disorders [19–25], balance assessment and, in particular, the analysis of center-of-pressure (COP) trajectories recorded using force platforms could be helpful to understand cognitive impairment-related changes in postural sway that expose to greater fall risk [18, 26, 27] (Fig. 1). For example, it has been reported that MMAD individuals had increased postural sways, indicative of reduced postural control [28, 29]. Within this framework of postural control, it has been shown that postural sway is left unchecked until a threshold in COP velocity is reached. Velocity series appear to be bounded between upper and lower limits, evidencing a velocity-based corrective control process instead of position-based control of posture [30]. According to this COP velocity-based hypothesis, an active control of velocity dynamics for *non-faller* older cognitively healthy individuals (CHI), unlike age-matched MCI or MMAD subjects, has been shown recently [18]. By assessing the most sensitive velocity-based variables, namely the average absolute maximal velocity (AAMV in mm/s) in the antero-posterior direction, we found a significant effect of cognitive status, with higher limits of COP velocity for MCI and MMAD than CHI. More details about the relevance and the determination of AAMV variables can be read in [18, 27].

We had the opportunity to examine the effects of cognitive decline on COP velocity in the GAIT (Gait and Alzheimer Interactions Tracking) study, which is a cross-sectional study designed to compare gait characteristics of CHI and patients with MCI and MMAD [18]. The objectives of the present study were 1) to compare the limits of COP velocity in CHI, MCI, and MMAD participants, and 2) to examine the association between COP velocity and the cognitive status and history of falls of subjects. We hypothesized that the limits of COP velocity dynamics, as essential sensory information to stabilize posture [30], should allow a fine clinical discrimination between older adults with and without cognitive impairment, and their related fall risk.

METHODS

Participants

From November 2009 to December 2012, a total of 611 older community-dwellers (mean age ± standard deviation, 77.21 ± 7.89 years; 48.23% female) were recruited in the GAIT cohort, which is an observational cross-sectional study designed to examine gait and balance characteristics of CHI and patients with MCI and MMAD. The baseline characteristics of the participants were summarized in Table 1 using means and standard deviations, or frequencies and percentages, as appropriate. This study was approved by the Local Ethical Committee of Angers (reference: n° 2009-A00533-54) and was conducted in accordance with the Declaration of Helsinki (1986). The sampling and data collection procedures have been described elsewhere [31]. In summary, all participants were referred for a memory complaint by their primary care physician to the memory clinic of Angers University Hospital. Eligibility criteria were age 60 years and over and no acute medical illness in the three past months. For the present analysis, exclusion criteria were severe AD (i.e., Mini-Mental State Examination score (MMSE) $\leq$10), neurological and psychiatric diseases with the exception of cognitive impairment, and the inability to stand on one leg for at least five seconds. Participants in the study were included after having given their written consent for research.

Neuropsychological and physical assessment

Neuropsychological assessment was performed during a face-to-face examination carried out by a neuropsychologist. The following standardized tests were used to probe several aspects of cognitive function: MMSE [32] and Frontal Assessment Battery [33], Alzheimer's Disease Assessment Scale-cognitive subscale [34], the Trail Making Test parts A and B [35], the French version of the Free and Cued Selective Reminding Test [36, 37], and the Instrumental Activities of Daily Living scale [37, 38].

The diagnoses of MCI and AD were made during multidisciplinary meetings involving geriatricians, neurologists, and neuropsychologists of Angers University Memory Clinic, and were based on the above-mentioned neuropsychological tests, physical examination findings, blood tests and magnetic resonance imaging (MRI) of the brain. MCI was diagnosed according to the consensus criteria of Winblad et al. [39]. Participants with all categories of MCI were included in this study, i.e., amnestic and non-amnestic, as well as single and multiple affected domains. The diagnosis of AD followed the Diagnostic and Statistical Manual of Mental Disorders, 4th edition and National Institute of Neurological and Communicative

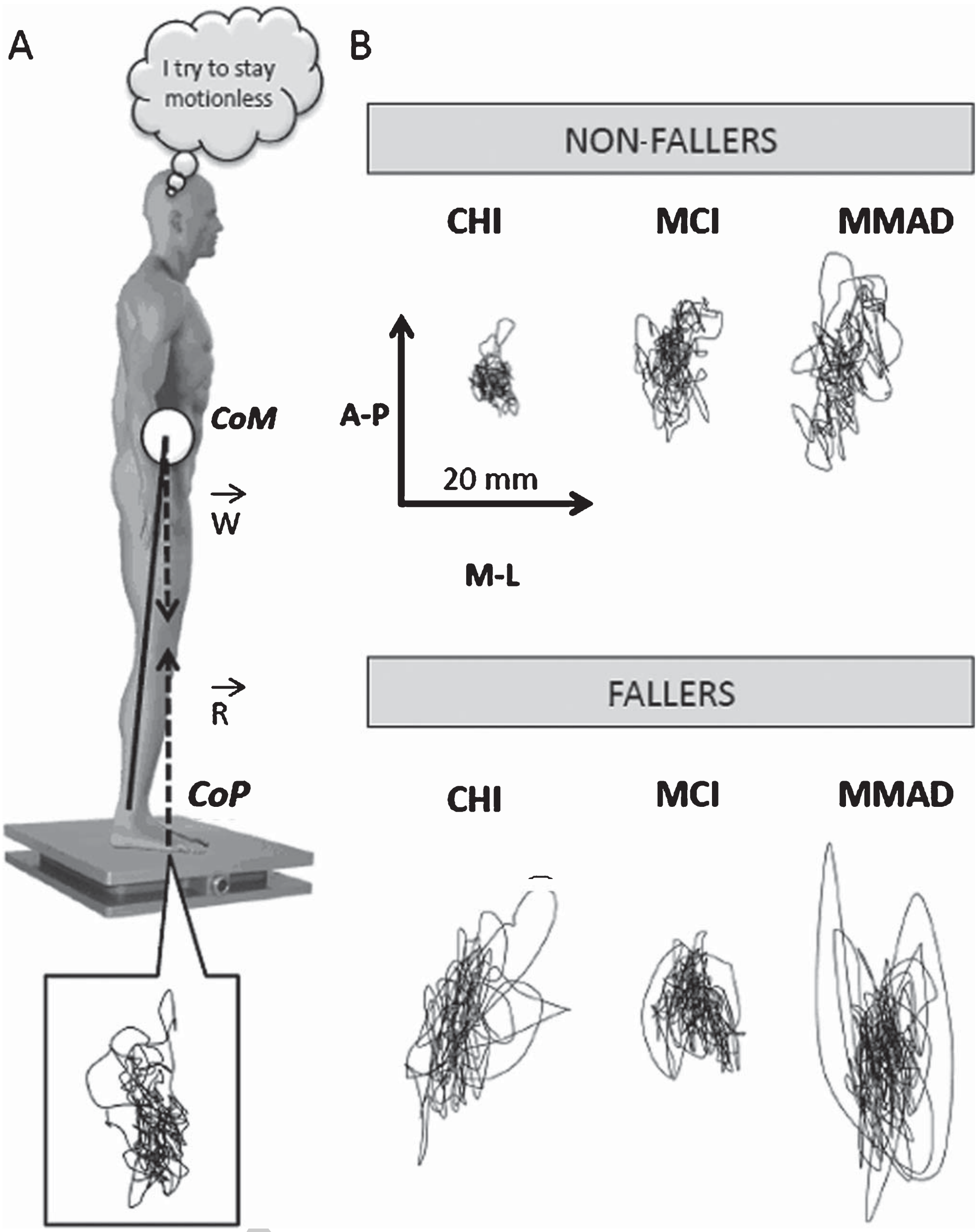

Fig. 1. Representative examples of center-of-pressure (COP) trajectories recorded using a force platform (A), as a function of the cognitive status (CHI, MCI, and MMAD) and fall risk (non-fallers versus fallers) (B). CHI, cognitive healthy individual; MCI, mild cognitive impairment; MMAD, mild-to-moderate dementia; AP, anteroposterior axis; ML, medio-lateral axis.

Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria [40]. A mild stage of MMAD was defined for a MMSE score ≥ 20, and moderate stage for a MMSE score between 19 and 11. Participants who were neither MCI nor AD and who had normal neuropsychological and functional performance were considered as cognitively healthy [9, 18].

Height (cm), weight (kg), and body mass index (BMI) (kg/m2) were assessed for each participant. The use of psychoactive drugs including benzodiazepines, antidepressants, or antipsychotics, and the number of drugs taken per day were also recorded. Education level was evaluated as a categorical variable by the number of years spent in education, as following: 1/no school; 2/secondary school; 3/high school; 4/graduate studies.

Table 1
Baseline characteristics of participants according to their cognitive status ($n = 611$)

	Total	CHI ($n = 228$)	MCI ($n = 140$)	MMAD ($n = 243$)
Age (years), mean ± SD[a (1, 2, 3)]	77.2 ± 7.9	72.5 ± 6.1	74.7 ± 7.3	83 ± 5.8
Female gender, n (%)[a (2, 3)]	290 (47.5)	92 (40.3)	48 (34.3)	150 (61.7)
BMI (kg/m^2), mean ± SD	26.3 ± 4.1	26 ± 3.4	26.4 ± 4.7	30.7 ± 9.9
Education level* (/4), n (%)[a (1, 2, 3)]	1 = 33 (5.4); 2 = 307 (50.2); 3 = 172 (28.1); 4 = 64 (16.2)	1 = 1 (2.3); 2 = 77 (33.8); 3 = 86 (37.7); 4 = 64 (28.1)	1 = 4 (2.8); 2 = 75 (53.6); 3 = 42 (30); 4 = 19 (13.6)	1 = 28 (11.5); 2 = 155 (63.8); 3 = 44 (18.1); 4 = 16 (6.6)
Use of psychoactive drugs (yes), n (%)[a (2, 3)]	82 (13.4)	12 (5.3)	12 (8.6)	58 (23.9)
Medications (total number/day), mean ± SD[a (2, 3)]	4.2 (3.2)	3.1 (2.7)	3.6 (3.1)	5.6 (3.1)
Maximal Handgrip Strength (kg), mean ± SD[a (2, 3)]	26.1 ± 10.3	30.7 ± 9.9	29.5 ± 9.9	19.7 ± 7.6
Timed Up and Go (s), mean ± SD[a (2, 3)]	13.9 ± 6.7	10.8 ± 3.8	11.9 ± 4.3	17.9 ± 7.8
MMSE, mean ± SD[a (1, 2, 3)]	24.1 ± 5.2	28 ± 2.3	26.1 ± 2.4	19.3 ± 4.4
FAB, mean ± SD[a (1, 2, 3)]	14 ± 3.6	16.5 ± 1.7	14.9 ± 2.1	11.1 ± 3.5
Eyes open AAMV AP (mm.s^{-1}), mean ± SD[a (2, 3)]	18.8 ± 9.3	15.9 ± 7.5	17.8 ± 9.3	22.2 ± 9.6
Eyes closed AAMV AP (mm.s^{-1}), mean ± SD[a (2, 3)]	22.7 ± 12.6	19.7 ± 10.3	22.1 ± 14.8	26 ± 12
Falls in previous year, n (%)[a (2, 3)]	230 (37.6)	74 (32.4)	38 (27.1)	118 (48.6)

χ^2 or univariate one-way analyses of variance with HSD-Tukey *post-hoc* test were used to compare CHI, MCI, and MMAD groups. CHI, cognitive healthy individual; MCI, mild cognitive impairment; MMAD, mild-to-moderate dementia; BMI, body mass index; MMSE, Mini-Mental State Examination; FAB, Frontal Assessment Battery; AP, anteroposterior direction; AAMV, absolute average maximal velocity. *Categorical variable in four points: 1/no school; 2/secondary school certificate 3/graduate degree; 4/university degree. [a]Main effect of cognitive status. [1]Significant difference between CHI and MCI groups. [2]Significant difference between CHI and MMAD groups. [3]Significant difference between MCI and MMAD groups.

Basic mobility was assessed with the Timed Up & Go test (TUG) [41]. The maximal isometric voluntary contraction strength of the hand was measured with a hand-held dynamometer; the handgrip measurement was repeated three times on the preferred hand, with a few seconds of recovery between each effort. All readings were recorded in kilograms (kg) with one highest reading chosen for the analysis [42]. Finally, the participants were interviewed using a standardized questionnaire, gathering information on the history of falls over the past year. A fall was defined as an event resulting in a person coming to rest unintentionally on the ground or at other lower level, not as the result of a major intrinsic event or an overwhelming hazard. In case of mild-to-moderate cognitive impairment, information on falls was obtained from a guardian, a nurse, or a person who lived with the participants. All detailed characteristics of the sample are shown in Table 1.

Postural assessment

The standing postural sway on a firm surface was measured using a force platform (101 × 101 cm; BioRescue, Dune®, France), equipped with three pressure gauges. The participants were asked to maintain a barefoot standing position with eyes opened and each foot positioned on a platform plate that maintained the distance between the medial sides of the heel at 8.4 cm with an external rotation angle of 9°. Participants were instructed to look straight ahead, with arms kept by the side of the body, and focused on a visual reference mark placed in front of them at a 100 cm distance. The postural test consisted of two trials of quiet stance: stance with eyes open (EO) and stance with eyes closed (EC). For each trial of 51.2 s duration (sampling frequency of 5 Hz), the system was linked to PosturalRescue® 2.0 software, providing COP series on the antero-posterior (AP) and medio-lateral (ML) directions of sway. None of the collected data relative to the COP parameters were filtered (see Fig. 1). For each visual condition, we deliberately chose to compute only one variable based on COP velocity: the average absolute maximal velocity (AAMV) in AP direction. Indeed, as stated in the introduction, we recently reported that this dependent variable was the most sensitive for characterization of postural control, as a function of visual condition, age, and cognitive impairment [18]. The AAMV was computed from the COP velocity series by extracting the maximum and minimum values of the series within non-overlapping windows (of a length of 2 s). Then the absolute values of these extremes were averaged [18, 27].

Statistics

Participants were separated into three groups based their cognitive status. Firstly, between-group comparisons (i.e., CHI, MCI, and MMAD) were performed using a one way analysis of variance (ANOVA) with Bonferroni corrections, HSD-Tukey *post-hoc*, or Chi-square test, as appropriate.

Secondly, a single multivariate analysis of covariance (MANCOVA) for the two variables of interest (i.e., AAMV direction in EO and EC conditions in the AP direction), with the cognitive status ($\times 3$) (i.e., CHI, MCI, and MMAD) and the fall risk ($\times 2$) (fallers versus non-fallers) as between-participants factors, and age, gender, BMI, education, use of psychoactive drugs, number of drugs taken per day, handgrip strength, and TUG as potential confounding factors (covariates) [21, 43] was performed. The multivariate Wilks' lambda F was used for this analysis. *p*-values <0.05 were considered as statistically significant. Partial eta square (${}_{p}\eta 2$) values are reported as measures of effect size. All statistics were performed using SPSS software (version 20.0; SPSS, Inc., Chicago, IL).

RESULTS

General characteristics

The mean and standard deviations of the baseline characteristics of the three groups (CHI, MCI, and MMAD) are presented in Table 1. Overall, a significant difference between the groups was revealed for all confounding factors: age [$F(2, 608) = 177.52$, $p < 0.0001$], gender [$\chi^2 = 34.2$, $p < 0.0001$], education level [$F(2, 608) = 55.19$, $p < 0.0001$], use of psychoactive drugs [$\chi^2 = 462.5$, $p < 0.0001$], medications (total number per day) [$F(2, 608) = 47.27$, $p < 0.0001$], handgrip strength [$F(2, 608) = 102.63$, $p < 0.0001$], and TUG [$F(2, 608) = 97.52$, $p < 0.0001$]. No main effect of cognitive status was shown for the BMI [$F(2, 608) = 1.654$, $p = 0.192$]. *Post-hoc* analyses systematically showed significant differences between the CHI and MMAD groups, and between the MCI and MMAD groups ($p < 0.05$, Table 1). Taken together, these results revealed that the MMAD patients were significantly older and had a higher prevalence of falls compared to CHI ($p = 0.0003$) and MCI ($p = 0.0001$). They also had a lower handgrip strength compared to CHI ($p < 0.0001$) and MCI ($p < 0.0001$).

Posture, cognitive impairment, and falls

Using the multivariate analysis of covariance, controlling for gender, age, BMI, education level, use of psychoactive drugs, number of drugs taken per day, handgrip strength, and TUG, significant main effects of cognitive status ($p = 0.048$) and fall risk in the past year ($p = 0.033$) were shown (Table 2). *Post hoc* analysis using Bonferroni adjustment revealed that the bounding limits of COP velocity dynamics were significantly lower in CHI and MCI compared with MMAD ($p < 0.001$), but no difference between CHI and MCI was found ($p = 0.102$). In addition, the maximal absolute values of COP velocity in the AP direction were different as a function of fall risk, with higher limits in fallers on average (+0.73 $mm \cdot s^{-1}$, i.e., 3.5%; $p < 0.05$). Note that no cognitive status × fall risk interaction was found ($p = 0.666$). Overall, the increase in AAMVs due to fall risk was statistically identical for each of three listed groups (CHI, MCI, and MMAD).

DISCUSSION

The present cross-sectional study with a prospective collection of data owes its originality to comparison of implicit postural control strategies in older adults with and without cognitive impairment from MCI to MMAD, according to their history of falls (i.e., fallers versus non-fallers). The aim of this study was to test the sensitivity of velocity-based posturographic variables, and to explore the associated postural control strategies in CHI and in MCI-MMAD older patients for discriminating early cognitive dysfunction and potentially diagnosing individuals with fall risk. In line with recent prospective examination of fall risk factors in MCI or Alzheimer's disease [21, 22], our study confirms the importance of velocity information to optimize postural sway [30], and as a variable of specific interest for fall prevention in populations with cognitive impairment [43, 44]. Here, we provide two major findings. First, in support of our hypothesis, the bounding limits of COP velocity dynamics (i.e., the average absolute maximal velocity in the antero-posterior direction) increased with the highest levels of cognitive impairment, as an index of adverse changes in intermittent velocity-based control of posture [27]. Second, the subjects who had fallen showed the highest absolute values of velocity, suggesting that the control of postural sway is implicitly corrected and reversed at high velocity thresholds. Since no cognitive status × fall risk interaction was found, identical effects of falls in past year on the postural performance were observed, whatever the cognitive status. This lack of interaction indicates that fall causes alterations in postural control to the same extent whatever the cognitive status of older adult. This might strengthen the emerging view that the bounding limits of COP velocity dynamics are primarily relevant for capturing the progression of cognitive impairment [18]. But when falls and cognitive

Table 2
Mean values (standard deviations) for center-of-pressure velocity-based variables (average absolute maximal velocity –AAMV- in eyes open and eyes closed conditions in anteroposterior direction) according to cognitive status (i.e., CHI, MCI, and MMAD) and history of falls in the past year (i.e., fallers versus non-fallers) adjusted on baseline characteristics. F and p values are from multivariate analysis of covariance. Significant results are indicated in bold type (i.e., $p < 0.05$). CHI, cognitive healthy individual; MCI, mild cognitive impairment; MMAD, mild-to-moderate dementia

Between-participant variables	F values	*p*-value	eta^2	Eyes open AAMV ($mm \cdot s^{-1}$)	Eyes closed AAMV ($mm \cdot s^{-1}$)
Cognitive status	**2.391**	**0.048**	$_p\eta 2 = 0.009$		
CHI				15.9 (7.5)	19.7 (10.3)
MCI				17.8 (9.3)	22.1 (14.8)
MMAD				22.2 (9.6)	26 (12)
Fall history (yes versus no)	**3.437**	**0.033**	$_p\eta 2 = 0.011$		
Non-fallers				17.9 (8.7)	22.4 (12.6)
Fallers				20.3 (10)	23.3 (12.2)
Cognitive status × fall history	0.595	0.666	$_p\eta 2 = 0.002$		
CHI – Non-fallers				15.5 (6.7)	19.2 (10.3)
Fallers				17.6 (8.8)	20.7 (10.4)
MCI – Non-fallers				17.5 (9.5)	22 (14.5)
Fallers				18.3 (8.9)	22.2 (15.8)
MMAD – Non-fallers				21.8 (8.7)	26.6 (12.3)
Fallers				22.5 (10.6)	25.2 (11.7)
COVARIATES*					
Female gender	**8.817**	**0.000**	$_p\eta 2 = 0.029$		
Age	**5.452**	**0.005**	$_p\eta 2 = 0.018$		
Education level	0.34	0.712	$_p\eta 2 = 0.001$		
Body mass index	**5.47**	**0.004**	$_p\eta 2 = 0.018$		
Use of psychoactive drugs	**0.056**	**0.000**	$_p\eta 2 = 0.001$		
Medications (total number/day)	**1.03**	**0.003**	$_p\eta 2 = 0.008$		
Maximal handgrip strength	0.941	0.391	$_p\eta 2 = 0.003$		
Timed Up & Go	1.684	0.186	$_p\eta 2 = 0.006$		

*Overall to be a female, advanced in age, with increased body mass index, taking a greater number of medications per day tend to enhance the bounding limits of COP velocity dynamics, indicative of reduced postural control.

impairment are analyzed together, the velocity-based variables, despite the good sensitivity for revealing the effects of group or fall risk factors on postural control, may be not sufficient, in particular for MMAD. In fact, there may be real difficulties to take account for multicollinearity among potential confounding variables and the inclusion of multiple parameters in the same model [45]. A data reduction of high-dimensional balance data to a low-dimensional set of essential features may be also helpful to refine the categorization of patients (MCI or MMAD) with or without risk of falls, while scanning a large number of potential confounding variables that may highly constrain the relationship between the cognitive impairment-related changes in postural control and risk of falls. In summary, the original comparison of older adults with different levels of cognitive impairment (CHI, MCI, and MMAD) and the present findings highlighted a promising hallmark of early cognitive dysfunction, even when explored on range of main confounding factors related to postural instability and falls [18, 21, 43].

Like prior studies and the difficulty of accounting for variables associated with force platform data in predicting falls (even in prospective follow-up studies) [46–48], our results support the idea that the dynamic dimension of balance assessment is of primary interest for discriminating elderly populations with and without cognitive impairment and high fall risk [18, 27]. This statement is in line with recent studies showing that changes in postural sway (assessed by path length of COP, a velocity-based variable) are associated with an increased fall risk in MCI [21, 23]. In summary, we argue that the relevant postural variables for identifying early cognitive impairment and the associated fall risk should address more than just the static nature of COP variables but also the analysis of velocity-based postural control strategies as a crucial component of falls prediction (and *de facto* primary prevention programs). In view of the current retrospective recording of falls, further research is required to test and validate this assumption in a prospective independent cohort.

These results may nevertheless have implications for improved clinical utilization of posturography [49], by collecting first and foremost new COP velocity-based variables, namely the AAMV in the AP direction. On that basis, a decline in reweighting of velocity information revealed by high AAMV values both in EO and EC conditions can be an effective index of changes in the sensory integration process, which is essential for maintaining balance in older adults [50]. In neurophysiological studies, velocity information in implicit control strategy during quite stance has been found to be of great importance in CHI, by the modulation of ankle extensor muscle activity [30, 51]. Because of well-documented progressive changes to critical regions of the brain that underlie executive decline and motor dysfunction in MCI and MMAD (e.g., the prefrontal cortex) [52–54], the association between changes in reweighting velocity information, the cognitive status and the fall risk might reflect a deficit in active COP velocity control or correction processes [27, 30]. This assumption is in line with the contribution of the prefrontal cortex to the maintenance of postural balance and the underlying pathophysiology of falls [55, 56].

Some limitations of this study need to be considered. First, it should be noted that the number of persons with MCI identified as fallers in this study was relatively low ($n = 38$), compared with CHI ($n = 74$) and MMAD ($n = 118$), and the size of MCI sample should be increased to reinforce the statistical power. Second, the findings of a powerful postural hallmark of cognitive impairment and associated fall risk reported here are not applicable to patients with severe dementia, although it is likely that these patients will also display an altered intermittent control of velocity (i.e., highest absolute values of the threshold that bound the dynamics of velocity). Finally, the cross-sectional design and the recruitment performed in a single memory clinic may be limitations to exploring the association between the implicit postural control strategies, the cognitive status or the fall risk compared to a prospective cohort design.

CONCLUSIONS

This study identified the bounding limits of COP velocity dynamics through the easy computation of AAMV in EO and EC conditions as a promising postural hallmark of cognitive impairment with a strong association between poorer cognitive ability and poorer balance performance. Moreover identifying people with and without cognitive impairment who are at risk of falls risk via the evaluation of the postural control strategies might be a valuable window of opportunity for fall-prevention interventions. For example, we suggest that the postural control strategies in MMAD might be positively modified by considering a walking exercise program as a safe means for the optimization of this sensory input recalibration process [57, 58]. Precisely, the effects of specific exercise might improve the ability of the central nervous system to predict the muscle activation locomotor pattern needed to perform the movement. This feedforward control process could be recalibrated based on sensory information provided by peripheral commands [59]. With exercise, the central nervous system would become more efficient in predicting the optimal motor response, because of an optimized feedforward control, and possibly in preventing the postural (velocity-based) control alterations and fall risk in the elderly [60, 61]. In any case, further studies focusing upon these specific assumptions are needed to determine whether this potential postural hallmark is also validated and applicable within an independent cohort of cognitively impaired older people for fundamental and clinical purposes of prediction of cognitive decline and associated fall risk.

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