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ORIGINAL RESEARCH

Deep white matter hyperintensities, microstructural integrity and dual task walking in older people

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Abstract

To examine neural, physiological and cognitive influences on gait speed under single and dual-task conditions. Sixty-two community-dwelling older people (aged 80.0 ± 4.2 years) participated in our study. Gait speed was assessed with a timed 20-meter walk under single and dual-task (reciting alternate letters of the alphabet) conditions. Participants also underwent tests to estimate physiological fall risk based on five measures of sensorimotor function, cognitive function across five domains, brain white matter (WM) hyperintensities and WM microstructural integrity by measuring fractional anisotropy (FA). Univariate linear regression analyses showed that global physiological and cognitive measures were associated with single ($\beta = 0.594$ and β=-0.297, respectively) and dual-task gait speed ($\beta = 0.306$ and β=-0.362, respectively). Deep WMHs were associated with dual-task gait speed only ($\beta = 0.257$). Multivariate mediational analyses showed that global and executive cognition reduced the strength of the association between deep WMHs and dual-task gait speed by 27% ($\beta = 0.188$) and 44% ($\beta = 0.145$) respectively. There was a significant linear association between single-task gait speed and mean FA values of the genu (β=-0.295) and splenium (β=-0.326) of the corpus callosum, and between dual-task gait speed and mean FA values of Superior Cerebellar Peduncle (β=-0.284), splenium of the Corpus Callosum (β=-0.286) and Cingulum (β=-0.351). Greater deep WMH volumes are associated with slower walking speed under dual-task conditions, and this relationship is mediated in part by global cognition and executive abilities specifically. Furthermore, both cerebellum and cingulum are related to dual-task walking due to their role in motor skill performance and attention, respectively.

Keywords Small vessel disease · Leukoaraiosis · Accidental falls · Balance · Gait

Introduction

Falls are an important public health concern in older people. Falling is common from the age of 65 years and has been recognized as an important marker of frailty. From a functional impairment perspective, the determinants of fall risk can be broadly categorized into physiological (e.g., muscle strength, balance) and cognitive (e.g., executive function, processing speed, attention) factors (Delbaere, Close et al. 2010). Gait, as a complex motor-cognitive function, requires input from higher cortical centres, especially from neural networks associated with attention and executive function (Rosano et al. 2012). Gait impairment is common in older people through reduced gait speed and increased step variability, and is associated with an increased risk of falling (Brodie et al. 2017). Many falls occur when older people walk and perform a cognitive task (e.g. talking) simultaneously (Beauchet et al. 2008), which is referred to as Dual

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Task (DT) Walking. It has been suggested that verbal interference tasks impose a higher cognitive demand on the central nervous system, involving more activation of neural circuits and regions (Holtzer et al. 2011; Wu et al. 2013). Attention-demanding dual-task paradigms may therefore be a better reflection of walking in real world settings (Lacour et al. 2008; Wollesen et al. 2016) and may therefore be better at predicting falls in older adults (Verghese et al. 2002). Yet, the neurological mechanisms that explain the association between DT walking and falls are inadequately understood (Montero-Odasso et al. 2012).

Cerebral small-vessel disease is common in old age and affects the integrity of the connectivity of brain systems (Pantoni 2010). White matter (WM) hyperintensity volumes are an important marker of small-vessel disease and increase with age (Pantoni 2010). WM hyperintensity volumes have been associated with accelerated declines in both physical and executive function and increased risk of falling in older adults (Zheng, Lord et al. 2012). However, it is still unknown whether the association between WM hyperintensities and falls is primarily influenced by cognitive or physical pathways (Callisaya et al. 2014). Diffusion Tensor Imaging (DTI) Tractography is a Magnetic Resonance Imaging (MRI) technique that has emerged as a useful tool to measure WM integrity and connectivity based on the strength and direction of water diffusivity in brain tissue.

Previous studies have demonstrated that disruption of WM integrity - especially in the corpus callosum, the cerebellum, cingulum and the corticospinal tract - is closely related to gait and balance disturbance (Bruijn et al. 2014; de Laat et al. 2011; Koo et al. 2012; Van Impe et al. 2012). The corpus callosum interconnects the two hemispheres and is responsible for interhemispheric visual and somatosensory transfer between frontal, occipital and parietal cortices, which has a critical role in attributing a sensorial stimulus and preparing a motor response (D'Esposito et al. 2000; Hausdorff et al. 2005). Loss of microstructural integrity of the corpus callosum could therefore lead to decrease cognitive control on gait performance (Moretti et al. 2005). Another study that specifically looked at community-dwelling older adults found that the reduced FA in the cerebellum (Inferior and Superior cerebellar peduncles) was significantly associated to gait characteristics such as gait speed (Cavallari et al. 2013). The cerebellar peduncles (CP) are part of a neural network connecting the cerebrum and are of importance for coordinating voluntary motor activity, maintaining balance and possibly cognition (Koziol et al. 2014; Wu et al. 2013). It is likely that deteriorated postural control could be associated with cerebellar WM decline. The corticospinal tract mediates fine motor control and movement of contralateral limbs and has been associated with gait impairments and postural control tasks (Bruijn et al. 2014; Caeyenberghs et al. 2010). The impact of impaired neural networks on gait can be observed more clearly when performing motor tasks requiring greater attention (Yogev-Seligmann et al. 2008). Brain changes in regions that are known for memory and executive functioning, such as anterior cingulate gyrus and hippocampus have been associated with increased gait variability and presumably even more so under dual-task conditions (de Laat et al. 2011; Koo et al. 2012; Rosso et al. 2014; Van Impe et al. 2012).

The objective of the present study was to examine influences of the neural integrity of the nervous system (in addition to physiological and cognitive factors) on gait speed under single and dual-task conditions. A verbal interference task was used as a test of divided attention while walking (Verghese et al. 2002). Reduced connectivity between distinct brain regions – due to larger WMH volumes and reduced WM integrity – is likely to affect the efficiency of brain motor and cognitive networks towards the dual-task performance (Wu et al. 2013). Reduced attention and executive functions have also been linked to poor dual-task performance in older adults (Holtzer et al. 2014). Holtzer et al. have suggested underutilization of brain regions responsible for monitoring and coordinating attention resources may account for the relationship between impaired executive function and walking performance (Holtzer et al. 2011). Therefore, the expectation was that both physiological and cognitive factors would explain dual-task walking performance independently, and that the association between WMH volumes and dual-task walking would be mediated primarily by cognitive factors. Furthermore, it is hypothesised that lower integrity of neural pathways that are related to walking (cerebellum, corticospinal tract) are associated with single-task gait impairment and those pathways that are related to both walking and cognition pathways (Cingulum, Cerebellum, Corpus Callosum, Corticospinal tract), are associated with dual-task gait impairment.

Methods

Participants

Sixty-two consecutive attendees were invited to participate in the present study. They were recruited from 313 community-dwelling older people participating in balance and imaging components of the Sydney Memory and Aging Study (MAS, 2008–2009) and were assessed on gait in addition to their standard assessment (Sachdev et al. 2010). The participants who were not assessed on the gait component did not differ in any of the measures ($p > 0.05$). Exclusion criteria were: dementia, Mini-Mental-State-Examination of < 24 (Folstein et al. 1975) (adjusted for age, education, non-English-speaking background), inability to walk independently for 20 m; diagnosis of progressive neurological

condition, psychotic symptoms and developmental disability. The University of New South Wales' Human Study Ethics Committee approved the study and informed written consent was obtained from participants.

Baseline measures

Medical conditions, medication use, and history of falls were assessed in a face-to-face interview in order to gain a complete medical history of each participant. As a measure of comorbidity, each medical condition was given one point from a list of nine system-related conditions (that is, cardiovascular, respiratory, musculoskeletal, endocrine, urogenital, cancer, neurological, mental health, and eye diseases). A cardiovascular risk factor index was assessed and implemented based on the D'Agostino et al. regression model [Available from: http://www.framinghamheartstudy.org/index.html] using the following baseline data: Age, current smoking status (self-reported), diabetic status (self-reported), systolic blood pressure (from MAS medical exam), total cholesterol level (from blood analysis), high-density lipoprotein (HDL) level (from blood analysis), and currently taking antihypertensive medication (self-reported). General disability was assessed across six domains (understanding and communicating, mobility, self-care, interpersonal interactions, household and work activities, and participation in society) using the 12-item World Health Organization Disability Assessment Schedule (WHODAS II; total score range 0–36). Hours of physical activity per week was assessed using the Incidental and Planned Exercise Questionnaire (Delbaere et al. 2010; Zheng; Lord et al. 2012).

Walking assessment Participants were asked to walk 20 m at their usual (self-selected) speed under single (ST) and dual task (DT) conditions in a long corridor. Start and end points for each trial were clearly marked. The cognitive dual task comprised reciting alternate letters of the alphabet. Previous research has shown that walking performance under these DT conditions is related to increased attention demands and to risk of falls (Verghese et al. 2002). Participants were instructed to be as accurate as possible when performing the cognitive task and were reminded to keep walking for the full 20 m. The order of ST and DT gait conditions were presented randomly to avoid systematic bias. The time taken to complete the 20 m walk, in seconds, was used in the analyses.

MRI assessment Magnetic resonance imaging (MRI) acquisitions were performed on a Philips-3 T-Intera-Quasar scanner (Philips Medical Systems, Best, The Netherlands) (Sachdev et al. 2010). Fluid attenuation inversion recovery (FLAIR) sequence scans were acquired with TR = 10,000 ms, TE = 110 ms, TI = 2800 ms, matrix size = 512 × 512, slice thickness = 3.5 mm without gap, and in plane resolution = 0.488 × 0.488 mm. WMH volumes – manifest as hyperintense signals in the white matter on T2-weighted MRI – were delineated from T2-weighted FLAIR scans by using an automated computer algorithm described elsewhere (Wen and Sachdev 2004). WMHs clusters within a band of 10 mm in width surrounding the lateral ventricles were further classified into periventricular WMH or deep WMH when located elsewhere (Fazekas et al. 1987; Zheng; Delbaere et al. 2012). For the analyses, we included total, deep and periventricular WMH volumes (corrected for intracranial volume) (Srikanth et al. 2009).

DTI assessment DTI scans were acquired in the same MRI session as for the FLAIR sequence scans with an 8-channel head coil. Two acquisitions of 32-directional DTI (b = 1000s/mm^3) were obtained using a single shot echo planar imaging (EPI) sequence with TR = 7638 ms, TE = 68 ms, 55 slices with slice thickness = 2.5, gap = 0 mm, acquisition matrix size = 96 × 96. DTI data were pre-processed and analysed with the FSL version 4.1.7 (Smith et al. 2004). Voxelwise statistical analysis of the FA data was carried out using TBSS (Smith et al. 2006). TBSS projected all subjects' FA data onto a mean FA tract skeleton, before applying voxelwise cross-subject statistics. This process was followed by ENIGMA-DTI protocols (http://enigma.ini.usc.edu/protocols/dti-protocols/). We then extracted the mean FA across the full skeleton and subsequently calculated average FA values bilaterally for twenty-one intra-hemispheric and for four inter-hemispheric tracts, yielding a total of 46 regions of interest (ROIs) of which 8 ROIs were investigated further as part of this analysis: Superior cerebellar peduncle, Inferior cerebellar peduncle, Cingulum, Corpus Callosum (genu), Corpus Callosum (body), Corpus Callosum (splenium), and Corticospinal Tract (left and right).

Physiological fall risk assessment The Physiological Profile Assessment (PPA) comprises five validated measures of sensorimotor function (Lord et al. 2003): (i) visual contrast sensitivity (assessed using Melbourne-Edge-Test), (ii) proprioception (measured using lower-limb-matching task), (iii) quadriceps strength (measured isometrically with participants seated), (iv) simple reaction time (measured using light as stimulus and finger press as response), (v) postural sway (path area in square millimetres, measured using a sway meter recording displacements of the pelvis with participants standing on foam-rubber mat with eyes open). Weighted contributions from these measures can discriminate between older fallers and non-fallers with an accuracy of up to 75% (Lord et al. 2003). For the analyses, we used the total PPA score, quadriceps and individual postural sway measures (Taylor et al. 2012).

Cognitive assessment A cognitive assessment was administered by trained psychology graduates to evaluate five cognitive domains (Brodaty et al. 2013; Delbaere 2012): (i) attention and processing speed (measured by WAIS-3 Digit-Symbol test, Trail-Making test part-A), (ii) memory (measured by Logical-Memory-Story-A, Rey-Auditory-Verbal-Learning test, Benton-Visual-Retention Test), (iii) language (measured by Boston-Naming test, animals semantic-fluency test), (iv) visuo-spatial ability (measured by Block-Design test) and (v) executive functioning (measured by Trail-Making test part-B, Controlled-Oral-Word-Association test). Raw scores were converted to Z-scores using baseline mean and standard deviation (SD) values for a cognitively normal reference group drawn from the MAS baseline sample (n = 504). Composite measures for each domain were computed by averaging z scores of each component test. Global cognition scores were calculated by averaging domain scores (Brodaty et al. 2013). For the analyses, we used the total cognitive score, and individual executive function and attention/processing domain scores (Yogev-Seligmann et al. 2008).

Statistical analysis

Data were analysed using SPSS 19.0 for windows (SPSS Inc., Chicago, IL). Associations with $p < 0.05$ were considered statistically significant. Univariate linear regression analyses were used to examine associations between gait time and neural, physiological and cognitive measures. A series of multivariate linear regression analyses were performed to determine how much physiological and cognitive covariates reduced the strength of the association (i.e. mediated) between neural correlates and gait speed. The data in the multiple linear regressions were bootstrapped to overcome possible Type II errors (Kirby and Gerlanc 2013). The standardized beta coefficients were reported in the tables to allow comparisons of coefficients across models. Independent covariates that led to a substantial reduction (> 10%) in the standardized beta between WMHs and gait speed were considered mediators of the relationship (Baron and Kenny 1986). An hypothesis-driven approach was used when looking at the associations between dual task gait speed and FA values. A number of regions of interest were selected based on the literature: corpus callosum (genu, splenium and body), Cerebellar Peduncle (inferior and superior), Corticospinal Tract (left and right) and Cingulum. To correct for multiple comparisons, a Bonferroni correction was applied based on the number of regressions performed (p = 0.05/7 = 0.007). All analyses using MRI data were controlled for age, sex, years of education, Intra-Cranial Volume and Cardiovascular Risk.

Results

Demographic, medical and neuroimaging descriptive data are shown in Table 1.

Table 2 summarizes results of univariate linear regression analyses. Within the physiological domain, the PPA composite score showed the strongest correlation with both ST and DT gait speed. Quadriceps strength was significantly correlated with ST gait speed and postural sway was not associated with gait speed under either condition. Within the cognitive domain, controlling for education, executive function showed the strongest association with both ST and DT gait speed, followed by global cognition. Attention was only associated with DT gait speed. Within the neural domain, deep WMHs were significantly associated with DT gait speed and no associations were found between the WMH measures and ST gait speed.

Greater deep WMH volumes remained significantly associated with slower DT gait speed after controlling for PPA (*standardized* $\beta = 0.265$). Global cognition mediated the relationship between deep WMHs and DT gait speed, reducing the strength of the association by 27% (*standardized* β decreased from 0.257 in univariate analyses to 0.188). Executive function mediated the relationship between deep WMHs and DT gait speed more so, reducing the strength of the association by 44% (*standardized* β decreased to 0.145). In the final multivariate model when PPA, global cognition and deep WMHs were all entered in the model (controlling for education), only global cognition remained significantly associated with DT gait speed (*standardized* β=-0.402).

The results of DTI analysis, i.e. the associations between FA values and gait speed, are shown in Table 3. Single task

Table 1 Characteristics of the study population (n = 62)

	Mean (*SD*) or Number (%)
Age *(years)*	80.0 (4.2)
Female gender *(number)*	29 (46.8%)
English Speaking Background *(number)*	45 (72.6%)
Years of education *(years)*	12.4 (3.6)
Body Mass Index *(kg/**m**^{2})*	26.9 (4.0)
One or more falls in the past year *(number)*	22 (35.5%)
Health-related quality of life (*WHODAS score)*	18.0 (5.3)
Planned exercise *(hours per week)*	2.1 (3.2)
Total activity *(hours per week)*	8.4 (8.0)
Single task gait speed *(meters per second)*	1.12 (0.21)
Dual task gait speed *(meters per second)*	0.86 (0.25)
Grey matter volume *(milliliter)*	5.28 e^5 (0.61 e^5)
White matter volume *(milliliter)*	3.90 e^5 (0.60 e^5)
Intracranial volume *(milliliter)*	15.85 e^5 (1.80 e^5)

Table 2 Univariate associations between gait and physiological, cognitive and neural function

	Mean (SD)	ST gait Standardized β	DT gait Standardized β			
Physiological domain						
PPA score	0.7 (0.9)	**0.594****	**0.306***			
Quadriceps strength	31.3 (11.9)	**-0.296***	-0.079			
Postural sway	186 (88)	0.214	0.138			
Cognitive domain (z-score)						
Global cognition ǂ	-0.5 (1.4)	**-0.297***	**-0.362****			
Attention/processing speed ǂ	-0.2 (1.1)	-0.241	**-0.256***			
Executive function ǂ	-0.2 (1.2)	**-0.334***	**-0.421****			
Neural domain				*Controlling for PPA*	*Controlling for global cognition*	*Controlling for executive function*
Total WMH/ICV	0.49 (0.26)	0.124	0.176			
Deep WMH/ICV	0.88 (0.50)	0.112	0.257*	0.265*	0.188	0.145
Periventricular WMH/ICV	0.39 (0.28)	0.118	0.058			

ST Single Task, *DT* Dual Task, *PPA* Physiological Profile Assessment, *WMH* White Matter Hyperintensities; ICV: Intra-Cranial Volume. ǂ All analyses with cognitive measures were controlled for years of education. Bold values indicate statistical significance, with * $p<0.05$ and ** $p<0.01$

Table 3 Univariate associations between gait speed and Fractional Anisotropy (FA) values of Regions of Interest

	Single task gait dual-task gait					Dual-task gait			
	FA value *Mean (SD)*	Beta	p	Beta	p	Low FA group *(N=12)* *Mean gait time (SD)*	High FA group *(N=50)* *Mean gait time (SD)*	Beta	p
Superior cerebellar peduncle	0.69 (0.03)	-0.237	0.087	-0.284	**0.040**	32.3 (10.9)	24.0 (7.8)	-0.421	**0.001**
Inferior cerebellar peduncle	0.58 (0.03)	-0.077	0.567	-0.155	0.249	27.6 (8.7)	25.1 (9.1)	-0.126	0.348
Cingulum	0.53 (0.06)	-0.209	0.117	-0.351	**0.007**	31.3 (11.6)	24.3 (7.8)	-0.364	**0.007**
Corpus Callosum (genu)	0.63 (0.03)	-0.295	**0.029**	-0.103	0.454	26.8 (9.6)	25.3 (8.9)	-0.109	0.430
Corpus Callosum (body)	0.56 (0.04)	-0.175	0.217	-0.164	0.249	27.3 (9.0)	25.2 (9.1)	-0.119	0.411
Corpus Callosum (splenium)	0.75 (0.03)	-0.326	**0.017**	-0.286	**0.038**	26.3 (9.3)	25.4 (9.0)	-0.101	0.474
Corticospinal Tract (left & right)	0.60 (0.03)	-0.127	0.344	-0.028	0.836	25.3 (9.2)	25.7 (9.1)	-0.001	0.996

All analyses are control for age, sex, year of education, Intra-cranial volume and cardiovascular risk. Bold values indicate statistical significance with $p<0.05$

gait was only associated with the corpus callosum, while dual task gait speed was associated with the Superior Cerebellar Peduncle, Cingulum and splenium of the Corpus Callosum. After correction for multiple comparisons, only the association between dual task gait speed and FA in the cingulum remained significant.

Discussion

While several studies have investigated the association of gait, cognition and microstructural integrity of central nervous system in older adults (Bruijn et al. 2014; de Laat et al. 2011; Rosario et al. 2016), patients with Parkinson's disease (Iseki et al. 2015; Youn et al. 2015) and multiple sclerosis (Hubbard et al. 2016), our study was, to the best of our knowledge, the first which evaluated the association of dual task walking with physiological and cognitive domains together with microstructural integrity in older people. The current study confirms that, while physiological function is imperative for gait under all conditions, cognitive function assumes greater importance when performing a secondary task (Tekin and Cummings 2002). Several studies have shown that two concurrent tasks (measured by walking and a verbal interference task in our study) compete for the same cognitive resources, resulting in reduced performance

(Al-Yahya et al. 2011). The theoretical model of capacity sharing argues that the central capacity of processing of multiple tasks in parallel is limited. When this capacity to perform two tasks simultaneously is further limited by cognitive ageing, one task will be prioritized over the other. This is consistent with the model of task prioritization (Yogev-Seligmann et al. 2008), which suggests that when there is competition for attentional resources the person will prioritize the task which will keep them safe or minimize their risk of falling. This decision-making process influences the dual-task interference in each task and has been associated with increased brain activity. Functional MRI studies have showed that DT performance using a manual task is associated with increased activity in brain areas involved in attention and executive functioning, such as the cingulate gyrus (Nagamatsu et al. 2013; Rosso et al. 2014). Holtzer et al. further demonstrated that oxygenation levels are increased in the prefrontal cortex during DT walking compared with ST walking using functional near-infrared spectroscopy (Holtzer et al. 2011).

Increased WMH volumes may result in a disruption of the deep frontal-subcortical neuronal networks that interconnect various cortical areas (Tekin and Cummings 2002), which is likely to have a direct impact on gait (Srikanth et al. 2010). Our data supported this hypothesis, showing that larger volumes of deep WMHs contribute to slower DT gait speed, mainly through reduced cognitive function. It has been suggested that older people need to recruit more brain regions when undertaking simple motor tasks compared to younger people (Mattay et al. 2002), which is exacerbated when undertaking more complex tasks (Linortner et al. 2012), such as DT gait. Our study suggests that the disturbance of frontal-subcortical circuits (represented by larger volumes of deep WMH) might affect the ability to use this compensatory brain activation successfully and, in consequence reduce gait speed when cognitive resources have to be shared across two concurrent tasks.

The findings revealed a negative linear association between ST gait and corpus callosum – genu and splenium, which corroborates findings of previously conducted studies (de Laat et al. 2011; Koo et al. 2012). The genu of the corpus callosum connects the prefrontal cortex and has a critical role in the cognitive aspect of preparing motor responses (Chao et al. 2009; Park et al. 2008). Therefore, loss of microstructural integrity of commissural fibres that interconnect the bilateral prefrontal cortex could lead to decreased cognitive control on gait performance (Amboni et al. 2013). This clinic-anatomical correlation is consistent with the concept of the importance of integrated frontal executive function for the maintenance of gait and balance (Iaboni and Flint 2013). The splenium of the corpus callosum connects superior parietal and occipital cortices that are required for the integration and interhemispheric transfer of visual and somatosensory inputs (Park et al. 2008). Therefore, WM disruption in the splenium may lead to mobility and gait impairment (Moscufo et al. 2012) and explain the results of this study.

The association between DT gait speed and the Corpus Callosum was less pronounced. DT gait speed was more strongly related to the Cingulum and the Superior Cerebellar Peduncle FA values, especially in participants within the worst quintile of FA values. The Superior Cerebellar Peduncle could be inherently correlated with DT gait considering its projections to the premotor and primary motor cortex as well as its role in mental rehearsal of movement and motor learning (Cavallari et al. 2013; Vercruysse et al. 2015). The Cingulum interconnects the Cingulate Gyrus, dorsal and medial prefrontal cortex and plays an important role in converting short- to long-term memory and cognitive function (Jones et al. 2013; Metzler-Baddeley et al. 2012; Sasson et al. 2013). Previous studies found slowing of gait and gait characteristics are associated with lower FA-values in the Cingulum, some of which correlate with cognitive functions (de Laat et al. 2011; Koo et al. 2012; Rosso et al. 2014; Van Impe et al. 2012). In comparison to single task walking, DT walking requires greater cognitive demand. Therefore, the association found between lower FA-values in the Cingulum and slower DT gait speed is possibly mediated by reduced cognitive functioning. These findings are supported by several studies which have shown the relationship between processing speed, executive function and gait in older adults (Holtzer et al. 2014; Rosano et al. 2012; Rosario et al. 2016), as well as the moderating role of FA in the association between walking speed and WMH (van der Holst et al. 2016). Despite the findings of previous studies that showed the corticospinal tract may be important in control of walking speed in older adults (Bhadelia et al. 2009; Griebe et al. 2011), we did not find a significant correlation between DT gait speed and the FA values of the corticospinal tract.

Study limitations are a small sample size and the exclusion of some participants who were unable to undergo MRI could potentially influence the representativeness of our sample. The numbers of errors made by participants in reciting alternate alphabets was not recorded, and could therefore not be considered in the statistical analyses. Lacunar infarcts, brain atrophy or medication use were not included in the study, which are factors that could potentially affect gait. Furthermore, we focussed solely on fractional anisotropy measures for the present analyses. While FA is highly sensitive to microstructural changes, future studies should also use multiple diffusion tensor measures to better characterize the tissue microstructure. The addition of functional MRI could further clarify the influence of microstructural lesions in the central nervous system on single and dual task gait impairments in older people.

In conclusion, greater deep WMH volumes were associated with slower walking speed under dual-task conditions, and this relationship was mediated in part by executive function. Furthermore, both cerebellum and cingulum are related to dual-task walking due to their role in motor skill performance and attention, respectively. Increased WM hyperintensity volumes and reduced WM integrity are markers of small vessel disease (Basile et al. 2006). Early vascular management and interventions, such as treating high blood pressure, should remain a primary health care priority (Mancia et al. 2009). It has potential to slow down WMH progression (Dufouil et al. 2005) and might therefore also reduce age-related gait impairment. Considering the mediating effect of cognitive function on the association of WMHs and gait, it might be possible to improve daily gait with cognitive training, as proposed by preliminary findings (Verghese et al. 2010). Cognitive training and risk factor management of small vessel disease may be protective against age-related gait abnormality. Moreover, dual-task walking exercises need to be considered as an integral part of fall prevention programs in non-demented older people, as they can trigger the central and peripheral nervous system, and possibly postpone the rate of deterioration in the central and peripheral nervous system.

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Compliance with ethical standards

Conflict of interest Author S. L. The Physiological Profile Assessment is commercially available through Neuroscience Research Australia.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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