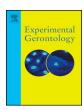
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White matter correlates of gait perturbations resulting from spontaneous and lateralized attention in healthy older adults: A dual-task study



Susana A. Castro-Chavira^a, Torgil R. Vangberg^b, Marta M. Gorecka^a, Olena Vasylenko^a, Knut Waterloo^{a,c}, Claudia Rodríguez-Aranda^{a,*}

- ^a Faculty of Health Sciences, Department of Psychology, University of Tromsø, The Arctic University of Norway, Tromsø, Norway
- ^b Department of Radiology and Nuclear Medicine, University Hospital of North Norway, Tromsø, Norway
- ^c Department of Neurology, University Hospital of North Norway, Tromsø, Norway

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ABSTRACT

To date the neural mechanisms behind gait perturbations caused by dual-task paradigms are still unknown. Therefore, the present study examined white matter correlates of gait perturbations caused by a dichotic listening task where spontaneous (free focus of attention) and lateralized attentional control (voluntary attention directed to right or left-ear) were tested. Fifty-nine right-handed, healthy older adults (59–88 years) were evaluated during single-task walking and three dual-task conditions. Dual-task costs were calculated for mean (DTCM) and coefficients of variation (DTCCoV) in gait speed, step length, stride length and step width. Volume, fractional anisotropy and mean diffusivity were estimated using global probabilistic tractography for the 18 major brain tracts and correlated with the DTCs. Data demonstrated that DTCs on gait speed and step length significantly correlated with white matter integrity and volume in various tracts. Perturbations on gait speed caused by spontaneous attention were related to frontal circuitry integrity including corpus callosum, while perturbations on gait speed and step length produced by voluntary lateralized attention were associated to tracts subserving visuomotor integration and frontal function.

1. Introduction

The involvement of cognitive processes during walking increases in aging and this is a leading cause for why the number of falls rises in older populations as cognitive decline occurs during late adulthood (Amboni et al., 2013). To achieve understanding of how cognition and gait interact with each other in the older adult, the dual-task paradigm has been employed (Yogev-Seligmann et al., 2008). In this paradigm, the subject performs a cognitive task while walking, which creates a divided-attention situation that challenges the execution of both, walking and the cognitive task. The effects exerted by the experimental situation can be calculated as "dual-task costs", which are the difference between single- and dual-task performances. Numerous cognitive tests have been used to challenge gait, however, it has been proven that type of cognitive task matters (Beauchet et al., 2005). For this reason, tasks evaluating concrete cognitive capacities are needed to understand how a specific cognitive process affects specific gait parameters. A convenient task to achieve this understanding is the dichotic listening (DL) test, which assesses two cognitive processes that take place in daily life, namely spontaneous versus voluntary lateralized attentional control in

the auditory modality. In DL, subjects are exposed to a series of simultaneous pairs of syllables that differ for each ear on each trial. During three conditions, the focus of attention is manipulated by asking participants to either report freely the best perceived syllable or to attend stimuli specifically from right or left ear. Thus, DL assesses various facets of attentional control including the subject's spontaneous choice to attend a stimulus versus the ability to voluntarily direct focus of attention to right or left ear. Spontaneous choice of stimuli depends on automatic responses often called "bottom-up" or "stimulus-driven" answers that are triggered by salient stimuli, which in turn rely upon brain structures belonging to "the ventral attention system" integrated by the ventral frontal cortex and the temporal-parietal junction (Fox et al., 2006). The regular processing of spoken language among righthanded individuals relies on directing attention towards stimuli applied to right-ear. This is due to the anatomical decussation of the auditory pathways that facilitate right-ear information to be transferred directly to the left cerebral hemisphere where language material is finally processed (Hugdahl, 2005).

In addition to assess spontaneous attention during DL, participants are asked to voluntarily lateralize their focus of attention to either right-

E-mail address: claudia.rodriguez-aranda@uit.no (C. Rodríguez-Aranda).

^{*} Corresponding author.

ear or left-ear. At the same time, they need to ignore opposite information applied to the contralateral ear. These two situations exert different levels of difficulty and attentional control in right-handed persons. Forcing attention to right-ear increases the number of answers coming from this ear as one voluntarily enhance natural perception of the salient stimuli. In contrast, when forcing attention to left-ear, contradictory demands take place since inhibition to attend right-ear information is required at the same time that focusing on left-ear requires higher levels of executive control (Hugdahl and Westerhausen, 2016). Voluntary control of lateralized attention in DL is believed to rely upon frontal areas and the corpus callosum in order to transfer appropriate information from one cerebral hemisphere to the other (Pollmann et al., 2002).

Given the vast knowledge that at present exist on DL (Tervaniemi and Hugdahl, 2003), this test is ideal to be used in the dual-task paradigm as it will be possible to tease apart how specific aspects of the cognitive task affects gait at a behavioral and neural level. Moreover, it is important to highlight that we are assessing the effects of spontaneous versus voluntary attention on gait, which are two basic cognitive processes occurring not only in a laboratory situation. Thus, the ecological validity created in this specific dual-task environment cannot be underestimated. Based on these considerations, our research group recently demonstrated that performance of DL in an over-ground dualtask setting affects gait parameters asymmetrically in healthy older adults (Gorecka et al., 2018). To our knowledge, this is the first study showing asymmetric changes on healthy individuals due to the use of a lateralized cognitive task. Furthermore, we were able to show how spontaneous vs lateralized focus of attention affect gait. Our findings demonstrated mainly asymmetric effects on right foot and alterations on gait speed under spontaneous attention. Additionally, attending right-ear stimuli did not compromise gait, as it was the case when attending left-ear, where subjects showed increased step width and higher asymmetrical variability on stride length.

In spite of the interesting data obtained, that initial study only addressed behavioral outcomes, which made impossible to obtain insights into the causative neural events behind effects on gait due to DL execution. However, we speculated that deficient frontal lobe circuitry, and thinning of the corpus callosum (CC) could be related phenomena. The reason is that deficient frontal lobe circuitry (Pfefferbaum et al., 2005) and CC thinning (Storsve et al., 2016) are leading structural deteriorations in the aging brain, and these changes are central in attentional difficulties and inefficiency to integrate complex sensorimotor information like the one taking place during execution of DL in dual-tasking.

Moreover, these brain deteriorations have been linked to DL performance and gait separately. In DL, the posterior part of CC is critical for interhemispheric transfer of auditory information (Westerhausen and Hugdahl, 2008), while frontal lobe areas subserve DL performance in healthy subjects (Hugdahl et al., 2009), including older adults (Andersson et al., 2009). As for gait, integration of the necessary stimuli to direct locomotor movements has been related to the CC (Nadkarni et al., 2015). In older adults, various white matter deteriorations in CC, such as increased burden of white matter hyperintensities and lower fractional anisotropy in the genu, have been related to impaired gait (Bhadelia et al., 2009; Ryberg et al., 2007). Since the genu has enriched connections with frontal areas, these findings point to the importance of frontal circuitry on gait and balance.

In order to achieve a better understanding of the neural correlates of the observed findings obtained in 2018, the present investigation aims to evaluate the hypotheses that white matter integrity of the CC and frontal circuitry are linked to perturbations on gait due to performing DL during walking. Specifically, we put forward the hypotheses that a) spontaneous attention is associated with frontal lobe tracts and temporal-parietal tracts, while b) lateralized attention should be related to frontal circuitry and CC. However, since the dual-task paradigm employed involves sensorimotor constraints beyond auditory attention, it is likely that a broader brain network is associated. Therefore, we

evaluated the integrity of major white matter cerebral tracts to set into perspective the relevance of the whole-brain white matter circuitry versus frontal lobe circuitry and CC. Tract volume, fractional anisotropy and mean diffusivity derived from 18 major white matter tracts reconstructed with TRACULA (Yendiki et al., 2011) were calculated and evaluated regarding their associations with the dual-task cost on the gait measures. Because the original study demonstrated asymmetric effects of DL on gait, an important issue in the present study is to further explore the possibility of lateralized associations between gait parameters and tracts. Thus, we proceed on this investigation to evaluate the association between cerebral tracts and bilateral measures of gait (both feet taken together) as well as on the lateralized gait measures by limb (separate analyses by foot).

2. Methods

2.1. Participants

Participants were a subsample of subjects who were included in our study from 2018. Briefly, in that study 78 right-handed, communitydwelling older adults ranging in age between 59 and 88 years old were tested. From this original sample, 59 of them were selected for the present study (M age = 70.85; 30 women). Nineteen participants were not included due to incomplete MRI data or suboptimal image quality. As described in the original study, participants were healthy, not depressed according to BDI-II criteria for older adults (Rodríguez-Aranda, 2003) and with normal cognition following MMSE criteria (Folstein et al., 1975). Moreover participants were free of neurological illness or diseases affecting locomotion. The MR images of all participants were acquired at the University Hospital of North-Norway (UNN) and screened by a neuroradiologist to ensure eligibility of the participants. MRI scans were taken within three months after behavioral testing. The study was approved by the local Research Ethics Committee and all participants provided signed, informed consent prior to participation in the study.

2.2. Dual-task paradigm

Complete description of the methods is reported in Gorecka et al. (2018)). The DL test was used as secondary task during walking. The mean (M) and coefficient of variation (CoV) of gait speed, step length, stride length, and step width measurements were obtained with the Optogait©-system. All gait parameters were recorded during overground walking in single situation or baseline condition (i.e., only walking) and in three dual-task conditions (i.e., walking + DL) as follows: a) in a non-forced condition (NF) where participants were instructed to freely report the best perceived stimuli regardless of ear; b) in a forced-right condition (FR) where participants were asked to report stimuli administered to the right ear and c) in a forced-left condition (FL) where participants were asked to report stimuli administered to the left ear. In the original study both DL results and gait outcomes were analyzed and controlled for hearing status. However, on the present study only behavioral data from gait are employed to correlate with white matter tracts.

Results from single walking provided the baseline (BL) for comparison of the gait measurements during dual-tasking. To evaluate the association between the different white matter (WM) tracts of the brain and the gait parameters, we calculated dual-task cost (DTC) scores on the mean (DTCM) and CoV (DTCCoV) of all spatio-temporal gait parameters, which were used in the correlational analyses instead of the numerous dependent variables that exist across DL conditions. The reason to employ DTC scores instead of raw data was to avoid overfitting (Mwangi et al., 2014). DTCs were calculated by determining the difference between gait parameters in single walking and gait parameters during the three dual-task conditions (e.g., gait scores in BL minus gait scores in non-forced, forced-right and forced-left).

2.3. Statistical analyses for behavioral data

All statistical analyses were performed using the SPSS 25 software. A series of 3 (non-forced, forced-right, forced-left) X 2 (right, left foot) repeated measures ANOVAs were performed for the DTC scores per gait measure. Because DL affected gait measures asymmetrically in the original study, we decided to assess lateralized differences on DTC scores in the present data. Geisser-Greenhouse corrections were chosen when the sphericity assumption was not met. Significant results were followed with the corresponding post hoc tests.

2.4. MRI acquisition

MR images were acquired in a Siemens Skyra 3.0 T MR scanner. Three-dimensional, T1-weighted sagittal images were obtained using a magnetization prepared rapid-gradient echo (MPRAGE) sequence (TE/TR/TI = 2.98/2300/900 ms, flip angle: 9°, slice thickness 1.2 mm, and FOV 252 \times 252 mm). Diffusion weighted images (DWI) were obtained using a single-shot SE-EPI sequence with TE/TR = 80/10700 ms, 70 axial slices, slice thickness 2.25 mm, FOV 252 \times 252 mm and in-plane resolution 2.25 \times 2.25 mm². Diffusion gradients were applied in 15 directions with b = 1000 s/mm², in addition a volume without diffusion weighting was acquired. The diffusion sequence was repeated three times to increase the signal-to-noise ratio.

2.5. MRI analyses

Image preprocessing included image corrections for magnetic field inhomogeneities, head motion, and eddy currents performed using specific tools of the FSL version 5.0.7 (FMRIB Software Library, fsl. fmrib.ox.ac.uk/fsl/fslwiki/) software. DWI images were registered to the corresponding individual anatomical images and the MNI152 (Montreal Neurological Institute) template. The individual, T1weighted anatomical images, processed using the FreeSurfer version 6.0.0 (surfer.nmr.mgh.harvard.edu) to obtain the brain subcortical segmentations, were used as reference for the DWI tract analysis performed with the TRActs Constrained by Underlying Anatomy tool (TRACULA), included in the FreeSurfer software. TRACULA was used to perform the reconstruction of 18 major white-matter pathways from DWI through global probabilistic tractography (Yendiki et al., 2011). Anatomical reconstructions of the tracts per subject, as well as the corresponding statistical measurements of volume, fractional anisotropy (FA), and mean diffusivity (MD), per tract, were obtained.

2.6. Statistical analyses for MRI data

The statistical analyses were conducted for FA, MD and volume with the SPSS 25 software. Partial Pearson's correlation quotients controlling for age and gender were calculated first for bilateral DTC scores (i.e., values for both limbs taken together) and DTI measures by tract. Thereafter, analyses were performed between the lateralized DTCs (i.e., values for right and left limb separated) and WM tracts. For the volume data, Partial Pearson's correlation quotients were controlled for age, gender and estimated intracranial volume (eICV). Z scores were used to perform the correlations. Due to multiple comparisons, the Bonferroni adjustment was applied.

3. Results

3.1. Behavioral and demographic results

Characteristics of the participants are presented in Table 1.

The factorial repeated measures ANOVAs of the DTC scores on the mean (DTCM) gait data showed a main effect of condition on gait speed, step length and stride length (p < 0.001 for all gait parameters), though no significant interactions existed. Pairwise comparisons

Table 1
Demographics.

	Mean (SD)		
Age (years)	70.85 (6.39)		
Women, n (%)	30 (50.8%)		
Education (years)	12.81 (3.78)		
MMSE score	29.02 (1.61)		
BDI II score	4.68 (4.64)		
Grip strength (kg)	35.63 (10.26)		
Estimated total intracranial volume (cm ³)	1575.04 (172.40)		
Total cerebral white matter volume (cm ³)	450.71 (57.03)		
Baseline gait speed (m/s)	1.12 (0.17)		
Lateralization index ^a (%) Non-forced condition	18.29 (25.07)		
Forced-right condition	24.98 (31.46)		
Forced-left condition	10.47 (32.73)		

^a Ratio measure determining degree of hemispheric language dominance. Higher values indicate higher preference to report from right-ear.

demonstrated that during lateralized attention (forced-right and forced-left conditions) DTCM scores were significantly higher as compared to non-forced condition. Concerning step width DTCM, no significant results were observed. Analyses on DTC of coefficients of variations (DTCCoVs) did not show any significant main effect or interaction (see Table 2).

3.2. Correlations between white matter tracts and raw gait scores in baseline

We deemed necessary to conduct an initial exploration of whether any significant correlation existed between the raw scores in gait during baseline and the white matter tracts. Results indicated only one significant association by foot on step width in which CoV of the right-foot correlated with MD of the left angular bundle of the cingulum (p=0.005; r=-0.366) and M of left-foot step width correlated with MD of the right angular bundle of the cingulum (p=0.006; r=0.362). No further significant correlations were found between any of the gait parameters during baseline and indices of WM tracts.

3.3. Correlations between white matter tracts and DTC scores

Significant correlations were found on six of the eighteen tracts: Forceps minor (anterior corpus callosum), forceps major (posterior corpus callosum), right anterior thalamic radiation (ATR), right inferior longitudinal fasciculus (ILF) and both uncinate fasciculi.

3.3.1. Bilateral analyses (i.e., both limbs taken together)

Only four significant correlations were found (marked in bold on Table 4), for gait speed and step length in the conditions where attention is forced to one ear, mostly to left ear. These correlations yielded DTCM gait speed and right ILF (r = 0.389) in the forced-left condition. DTCCoV step length in the forced-left condition correlated with right ATR (r = 0.398) and right ILF (r = -0.350). DTCM step length in the forced-right condition correlated with right ILF (r = 0.378).

3.3.2. Lateralized analyses by foot

Seven additional correlations were found. Five of them yielded DTCM gait speed in the non-forced condition and one for DTCCoV gait speed in the forced-right condition. The other correlation was found for DTCM step width in the non-forced condition (Tables 3 and 4).

3.4. Gait speed and WM tracts

3.4.1. Non-forced condition (Fig. 1A)

DTCM gait speed of right foot correlated with integrity measures of the forceps minor (FA r=-0.398, MD r=0.415; Table 3), right ATR (FA r=-0.361; Table 4) and uncinate fasciculi (right FA r=-0.362, left FA r=-0.350; Table 4).

Table 2
Factorial ANOVA on dual-task gait costs (DTCS) on each gait measure by foot.

		Dual-task conditions			F	<i>p</i> -Value
		NF	FR M (SD)	FL		
		M (SD)		M (SD)		
Dual-task cost on mean (DTCM)					
Gait speed (m/s)	R	0.061 (0.129)	0.130 (0.137)	0.119 (0.119)	12.46	< 0.000 [†]
	L	0.073 (0.093)	0.127 (0.130)	0.117 (0.110)		
Step length (cm)	R	2.027 (9.829)	3.663 (9.707)	3.320 (9.880)	15.13	< 0.001 [†]
	L	2.949 (3.173)	4.368 (3.951)	4.312 (4.013)		
Stride length (cm)	R	6.836 (7.884)	9.717 (9.832)	8.671 (9.775)	14.70	< 0.001°
	L	5.720 (7.245)	9.175 (8.820)	8.849 (8.303)		
Step width (cm)	R	-0.348 (3.570)	-1.097 (3.665)	-1.248 (3.183)	1.02	NS
	L	-0.907 (2.034)	-1.180 (3.654)	-1.022 (3.055)		
Dual-task cost on CoV (D	TCCoV)					
Gait speed (m/s)	R	-0.834 (5.730)	-3.134 (12.910)	-2.724 (13.039)	0.99	NS
	L	-1.564 (5.002)	-4.136 (11.951)	-3.166 (12.131)		
Step length (cm)	R	-0.168 (3.254)	-1.346 (5.714)	-0.709 (4.492)	1.32	NS
	L	-1.017 (3.913)	-1.724 (6.026)	-1.390 (5.810)		
Stride length (cm)	R	-0.166 (9.065)	-1.307 (8.818)	-2.649 (9.772)	1.23	NS
	L	-2.048 (8.389)	-2.105 (7.879)	-2.531 (8.497)		
Step width (cm)	R	4.512 (47.195)	0.741 (42.955)	0.727 (51.956)	0.84	NS
- '	L	-2.895 (53.371)	-7.048 (50.488)	-3.125 (54.512)		

Note. NF, non-forced condition; FR, forced-right condition; FL, forced-left condition; M, mean value; SD, standard deviation; L, left foot; R, right foot; CoV, coefficient of variation

Table 3Correlations between dual-tasks costs (DTC) by foot and areas of corpus callosum.

		Forceps minor		Forceps major	
		FA	MD	Volume	
DTCM Gait speed R Step width R	NF NF	r = -0.398 r = 0.416	r = 0.415		
DTCCoV Gait speed L	FR			r = -0.379	

Note. DTCM, dual-task cost on means; DTCCoV, dual-task cost on CoVs; FA, fractional anisotropy; MD, mean diffusivity; CoV, coefficient of variability; R, right foot; L, left-foot; NF, non-forced condition; FR, forced-right condition.

3.4.2. Forced-left condition (Fig. 1B)

DTCM gait speed of right foot (r = 0.376) and left foot (r = 0.401) correlated with right ILF volume (Table 4).

3.4.3. Forced-right condition (Fig. 1C)

DTCCoV gait speed of left foot correlated negatively with volume of forceps major (r = -0.379) (Table 3).

Only significant correlations shown; p < 0.05, corrected for multiple comparisons.

3.5. Step length associations with WM tracts

3.5.1. Forced-left condition (Fig. 2A)

DTCCoV step length correlated positively with volumes of right ATR (right-foot, r=0.350; left foot, r=0.400; Table 4). Also, DTCCoV step length of the left foot correlated negatively with the volume of right ILF (r=-0.352).

3.5.2. Forced-right condition (Fig. 2B)

DTCM step length of left foot correlated with right ILF (r = 0.352; Table 4).

Table 4
Correlations between dual-task costs (DTC) and integrity measures and volumes in projection and association tracts.

		Anterior thalamic radiation		Inferior longitudinal fasciculus		Uncinate fasciculus	
		Left hemisphere	Right hemisphere	Left hemisphere	Right hemisphere	Left hemisphere	Right hemisphere
DTCM							
Gait speed R	NF		FA r = -0.361			FA r = -0.350	FA r = -0.362
•	FL				r = 0.376		
Gait speed L	FL				r = 0.401		
Step length L	FR				r = 0.352		
DTCCoV							
Step length R	FL		r = 0.350				
Step length L	FL		r = 0.400		r = -0.352		

Note. Correlation coefficients correspond to the volume of the tract, except in the cases indicating otherwise. Bold values denote correlations that also were found in bilateral analyses. DTCM, dual-task cost on means; DTCCoV, dual-task cost on CoVs; R, right foot; L, left-foot; FA, fractional anisotropy; CoV, coefficient of variability; NF, dual-task cost for the non-forced condition; FR, dual-task cost for the forced-left condition. Only significant correlations shown; p < 0.05, corrected for multiple comparisons.

^{*} FR > NF and FL > NF (p < 0.001).

 $^{^{\}circ}$ FR > NF (p = 0.000) and FL > NF (p = 0.002).

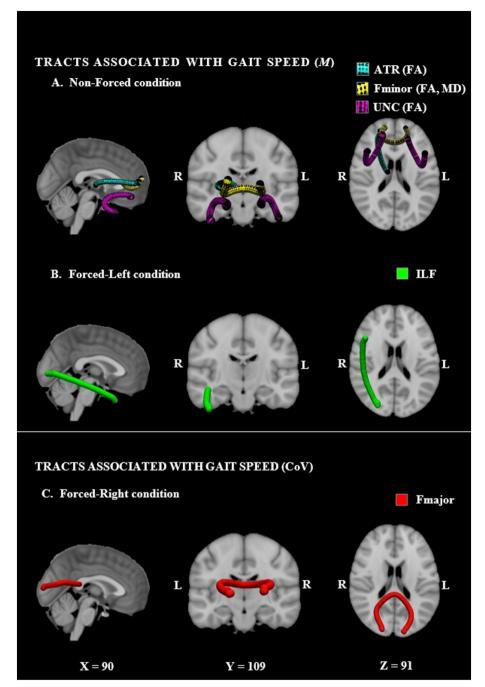


Fig. 1. White-matter tracts associated with dual-task cost scores of gait speed. Hachured tracts represent fractional anisotropy (FA) and mean diffusivity (MD) metrics. Solid-colored tract represent volume. DTC = dual task cost, M = mean; CoV = coefficient of variability; Fminor = forceps minor; Fmajor = forceps major ATR = anterior thalamic radiation; ILF = inferior longitudinal fasciculus; UNC = uncinate fasciculus. Radiological views are shown; R = right hemisphere; L = left hemisphere.

4. Discussion

The present findings demonstrated a significant association between status of WM tracts in healthy older adults and gait perturbations caused by performing DL during walking. Inspection of the associations between gait measures during baseline and WM tracts showed practically no significant associations, the only correlation found was with step width measures, which no longer was observed in dual-tasking. Thus, these results suggest that age-related changes on WM properties are significantly associated with the effects of DL in the dual-task paradigm. Moreover, we hypothesized that WM indices of frontal circuitry and CC would be significantly related to gait perturbations,

which as a whole was corroborated as we found associations with forceps minor, forceps major, ATR and UF. However, our specific expectations were not completely confirmed. We estimated that a) spontaneous attention would be related to frontal and temporal-parietal tracts while b) lateralized attention (forced-right and forced-left attention) would be related to frontal circuitry and CC.

First of all, not all gait perturbations were associated with WM tracts. Only perturbations on gait speed and step length showed significant correlations. The former were negatively related to FA in frontal pathways including CC during the spontaneous attention condition, while both gait speed and step length were positively related to tract volumes in frontal and occipito-temporal tracts in the lateralized

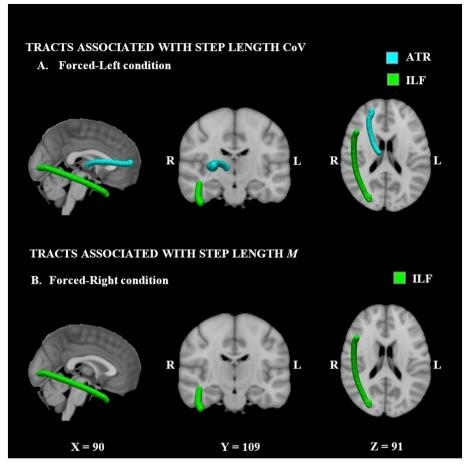


Fig. 2. White-matter tracts associated with dual-task cost scores of step length. DTC = dual-task cost; M = mean; CoV = coefficient of variability; ATR = anterior thalamic radiation; ILF = inferior longitudinal fasciculus. Radiological views are shown; R = right hemisphere; L = left hemisphere.

attention conditions. In order to understand these findings we first need to address the behavioral data. At the behavioral level, comparisons of DTC scores across DL conditions showed that only DTCM of gait speed, step length and stride length were significantly different. These data showed that DTCs increased significantly in the forced-attention conditions when the control of attention was directed to either the right or left ear. Thus, deliberate control of attention to one specific ear while walking seems to affect gait outcomes to a greater extent than if one freely chooses to attend stimuli. However, no interaction existed with data by foot, which could be regarded as contradictory to our findings from 2018. Nevertheless, in Gorecka et al. (2018) no calculations of DTCs were conducted, but rather raw scores were inspected and lateralized effects on gait were found. Through those analyses, perturbations due to DL in dual-tasking were seen as shorter steps and strides, as well as slower speed. In the present data using DTCs, no lateralized effect was observed, suggesting that the cost of the dual-task is equivalent for both feet but the impact of DL during walking is greater when attention is voluntarily directed to one specific ear.

4.1. Correlations between WM tracts and gait speed costs

4.1.1. Spontaneous attention (non-forced condition)

Our hypothesis that spontaneous attention would be related to tracts of the ventral attention system (Fox et al., 2006), i.e., frontal tracts and temporal-parietal pathways, was partially true for DTCMs of gait speed since the majority of the correlations for this gait parameter were found during the non-forced condition and with frontal circuitry. Indeed dual-task costs during spontaneous attention condition were associated negatively with the integrity of the anterior part of CC and

tract volumes belonging to frontal circuitry, including right ATR and both uncinate fasciculi. However, no significant relationship was found between DTCMs on gait speed and temporal-parietal tracts, which suggest that age-related changes on ventral frontal areas are the relevant ones in the association with gait alterations induced by spontaneously attending a stimulus.

All in all, our results are in agreement with studies reporting correlations between forceps minor of CC (Bhadelia et al., 2009), thalamic radiations (Verlinden et al., 2016) and gait speed. Similarly, our data corroborated that slower gait speed was related to lower FA in uncinate fasciculi (Tian et al., 2016; Verlinden et al., 2016). These data support the relevance of frontal lobe functioning and connectivity to gait speed in healthy older adults (Rosano et al., 2012).

The fact that 5 out of the 13 significant correlations involved frontal tracts and gait speed under the non-forced condition is worth noting. The original results from 2018 showed that raw data of gait speed were affected asymmetrically only on this condition. As stated in the introduction, during non-forced condition, right-handed individuals tend to report mostly right-ear information. This phenomenon called the right-ear advantage (Penner et al., 2009) is caused by the decussation of the auditory tracts that send information directly from right-ear to left hemisphere in which language is processed. For this reason, it is proposed that spontaneous attention during non-forced condition is "stimulus-driven" or "bottom-up" based (Hugdahl and Westerhausen, 2016). Notwithstanding, our dual-task paradigm creates a very demanding situation as subjects need to walk and give a free response simultaneously based on their perceptual capacities. Studies of auditory scene analysis have shown that attention can be diverted by self-motion processes related to head movements that naturally occur to locate a

sound (Kondo et al., 2012). In our study, participants were moving the entire body freely, which might divert attention even more than what head movements evoke. Thus, the effort to cope with the uncertainty of which syllable is best perceived and report loudly an answer while maintaining a regular walking pace affects gait speed in a conspicuous manner. Our observations at the laboratory, albeit not quantified, allow us to suggest that fluctuations seen on gait speed during the spontaneous attention condition might be partially caused by the fact that older adults slow down their locomotion irregularly, probably to concentrate on the clearest perceived stimuli that vary from trial to trial. Thus, correct performance in our dual-task situation not only depends on specific bottom-up/top-down mechanisms proper to each DL condition as described by Hugdahl and Westerhausen (2016) but on additional executive cognitive strategies necessary to deal with multitasking situations (Meyer and Kieras, 1997) such as walking and performing DL simultaneously. That white matter integrity of the frontal circuitry significantly correlated with gait speed in this condition can be interpreted as a sign of frontal executive involvement that relies on good integrity of WM pathways to integrate all sensorimotor information occurring in this dual-task context.

4.1.2. Focus of attention to left ear (forced-left condition)

Mean DTC scores from both feet correlated in the forced-left condition with the volumes of the right ILF. These data converge with past findings (Rosario et al., 2016). According to the literature on DL (e.g., Hugdahl et al., 2009) the forced-left condition is the one exerting the highest difficulty level, which is even more demanding for older adults due to the normal decline of executive functions occurring in this population (Andersson et al., 2008). Thus, the difficulty of this condition leads to increased dual-task demands and hence, greater reliance on higher order control. Interestingly, ILF together with the other projection tracts, has been linked to higher-order control of gait (Nadkarni et al., 2013).

4.1.3. Focus of attention to right ear (forced-right condition)

In this condition, DTCs on the variability of gait speed (CoVs) were associated with tract volumes of forceps major, which connects the occipital lobes and runs through the splenium. In line with the involvement of ILF, this tract also subserves visuospatial integration and is proposed to be involved in interlimb coordination during gait (Verlinden et al., 2016). Taken together, these findings confirm our expectations that associations between DTCs on gait should also be related to a white matter network beyond frontal circuitry.

4.2. Correlations between WM tracts and step length costs

The other important finding in the present study concerns associations between DTCs of step length and the lateralized attentional conditions. Most of the correlations were found when gait was affected by reporting left-ear stimuli. Nonetheless, one significant association existed when reporting from right-ear. As already mentioned, reporting from left-ear is highly challenging for older adults (Andersson et al., 2008), which is in agreement with the observed gait perturbations produced by focusing attention to left-ear.

4.2.1. Forced-right condition

The mean of DTCs on step length were associated with right ILF volume. In the literature, global white matter in a wide range of tracts, including the ILF, is reported to correlate with both gait speed and step length in healthy older adults in cross-sectional (Callisaya et al., 2014) and longitudinal studies (Callisaya et al., 2013). The fact that DTCMs on this specific gait measure correlated with right ILF suggests that pathways involved in visuospatial processing might be related to gait perturbations caused by our dual-task paradigm.

4.2.2. Forced-left condition

This time, DTCs of step length variability of both limbs were positively associated with volumes of the ATR and ILF. In the past, the posterior thalamic radiation has been repeatedly linked to step-by-step variability (Tian et al., 2017), while the ATR has been correlated with gait stability (Bruijn et al., 2014). In addition, ILF is associated to increased step length variability in older people over 65 years (Nadkarni et al., 2013). Thus, both tracts seem to be associated with perturbations of step length variability when left-ear stimuli is attended.

4.3. Associations with WM volumes and integrity indices on right hemisphere

Results showed that only DTCMs of gait speed correlated negatively with integrity (FA values) of WM tracts. As it is typical in aging studies, correlations of DTCs and FAs were negative, and positive with MD. This indicates that higher DTCs corresponds to lower integrity of the tracts. Thus, higher perturbation in mean gait speed corresponds to lower integrity in frontal tracts including forceps minor.

As for associations with the volumes, mostly step length results and the variability of gait speed correlated with volume tracts positively, suggesting that larger volumes were associated with larger gait disturbances. The idea that larger volumes represent a deleterious state of tracts in normal aging is not new, as it has been proposed that redundant myelin and bubbles occurring in the myelin sheets of older individuals (Peters and Sethares, 2002) may increase the volume of WM tracts (Fjell et al., 2008). Still, negative correlations with volumes were found for variability of gait speed and step length. Two out of the 4 correlations obtained for CoVs and volumes were negative. Possibly, measures of gait variability are distinctly associated with different features of WM volumes (Fjell et al., 2008) as volumes do not reflect unique properties of the tracts.

Finally, all the correlated, intrahemispheric tracts were in the right hemisphere. Only the uncinate fasciculi correlated bilaterally. One possibility is that right-handed subjects present more extensive connectivity in left hemisphere (Guye et al., 2003) and possibly more resistance to degeneration than left-handers. It remains to be proved whether this lateralization in the correlations may vary in left-handers. Alternatively, association with the right tracts may reflect the importance on gait alterations of the ventral attention network, which has been proven to be lateralized to the right hemisphere in various experimental and neuroimaging studies (Corbetta et al., 2008).

4.4. Right vs left foot correlations

Separate analyses by foot were deemed necessary in order to follow-up our earlier asymmetric findings on gait (Gorecka et al., 2018). Even though no asymmetric results were observed in DTCs, we did found a number of interesting correlations by foot. When DTCs from both feet (i.e., bilateral analyses) were analyzed together, the same associations existed than for analyses by foot. This implies that even though some small asymmetries in DTCs induced significant results to one specific foot, these associations exist in both feet during the directed attention conditions. The interesting data that emerged from the lateralized analyses concerns exclusively gait speed of right foot during non-forced condition. That right foot is the one displaying significant association with WM tracts could be due to right-handers being more prone to better control right foot (Dargentpare et al., 1992). As this remains speculative, the effect observed on right foot speed during spontaneous attention needs to be further investigated.

4.5. Limitations

In spite that TRACULA is a popular and reliable method to estimate white matter tracts as it allows assessment of areas with high uncertainty such as those with low anisotropy or crossing tracts, a

potential disadvantage could be the incapacity to identify anisotropic characteristics that are not uniformly present along a tract (Mamah et al., 2019). Since myelin properties reflected by FA and MD indices in the course of normal aging have proved to be heterogeneous along the tracts (Mårtensson et al., 2018), alternative techniques for more accurate white matter tract segmentation need to be taken into account in order to corroborate the present findings. Following standard procedures, we only looked at average properties of each tract. We can therefore not say whether the observed changes are in a specific region in a given tract or if it is reflecting a global change of the tract. Despite this limitation, the current investigation is a first step towards understanding white matter correlates of gait perturbations in older adults.

5. Conclusions

Our data indicate that perturbations in gait speed generated by spontaneous attention relates to frontal circuitry, including CC, which are pathways related to the ventral attention network that detects salient environmental stimuli. Association to frontal circuitry is probably due to higher degrees of executive control that are needed to adapt mobility to a challenging environment. When lateralized attention is demanded, mostly to left-ear, increased step variability occurs, which correlates with tracts connecting cortical regions like the ILF and those connecting cortical and subcortical areas like ATR. Association to these tracts suggest that tracts subserving visuomotor integration and frontal function are linked to perturbations on gait emerging by voluntary lateralized attentional control. To our knowledge, this is the first study presenting significant associations between WM indices of cerebral tracts and gait perturbations caused by specific attentional mechanisms during a dual-task situation. In this way, we corroborated the relevance of employing DL as a concomitant cognitive task while walking to better apprise the effects of spontaneous attention vs lateralized attention on gait.

Findings from the present investigation are relevant to understand the occurrence and risk of falls in the older adult when walking, listening and talking converge in real-life settings. Although, the present findings need to be replicated, from a clinical perspective the results suggest that it might be best to walk and talk on the side of the older person's dominant ear in order to preserve a safe walk. Finally, future research should employ the present approach to evaluate older adults with reduced cognitive capacities and early dementia.

Declaration of competing interest

The authors of the present investigation have no conflict of interest to disclose. None of the authors in this study has financial or commercial involvements in relationship with the present article. There are no other agreements that could be seen as involving a financial interest in the present work.

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References

- Amboni, M., Barone, P., Hausdorff, J.M., 2013. Cognitive contributions to gait and falls: evidence and implications. Mov. Disord. 28, 1520–1533.
- Andersson, M., Reinvang, I., Wehling, E., Hugdahl, K., Lundervold, A.J., 2008. A dichotic listening study of attention control in older adults. Scand. J. Psychol. 49, 299–304.

- Andersson, M., Ystad, M., Lundervold, A., Lundervold, A.J., 2009. Correlations between measures of executive attention and cortical thickness of left posterior middle frontal gyrus - a dichotic listening study. Behav. Brain Funct. 5, 41.
- Beauchet, O., Dubost, V., Gonthier, R., Kressig, R.W., 2005. Dual-task-related gait changes in transitionally frail older adults: the type of the walking-associated cognitive task matters. Gerontology 51, 48–52.
- Bhadelia, R.A., Price, L.L., Tedesco, K.L., Scott, T., Qiu, W.Q., Patz, S., Folstein, M., Rosenberg, I., Caplan, L.R., Bergethon, P., 2009. Diffusion tensor imaging, white matter lesions, the corpus callosum, and gait in the elderly. Stroke 40, 3816–3820.
- Bruijn, S.M., Van Impe, A., Duysens, J., Swinnen, S.P., 2014. White matter microstructural organization and gait stability in older adults. Front. Aging Neurosci. 6, 104
- Callisaya, M.L., Beare, R., Phan, T.G., Blizzard, L., Thrift, A.G., Chen, J., Srikanth, V.K., 2013. Brain structural change and gait decline: a longitudinal population-based study. J. Am. Geriatr. Soc. 61, 1074–1079.
- Callisaya, M.L., Beare, R., Phan, T.G., Chen, J., Srikanth, V.K., 2014. Global and regional associations of smaller cerebral gray and white matter volumes with gait in older people. PLoS One 9, e84909.
- Corbetta, M., Patel, G., Shulman, G.L., 2008. The reorienting system of the human brain: from environment to theory of mind. Neuron 58, 306–324.
- Dargentpare, C., Deagostini, M., Mesbah, M., Dellatolas, G., 1992. Foot and eye preferences in adults relationship with handedness, sex and age. Cortex 28, 343–351.
- Fjell, A.M., Westlye, L.T., Greve, D.N., Fischl, B., Benner, T., van der Kouwe, A.J.W., Salat, D., Bjornerud, A., Due-Tonnessen, P., Walhovd, K.B., 2008. The relationship between diffusion tensor imaging and volumetry as measures of white matter properties. NeuroImage 42, 1654–1668.
- Folstein, M.F., Folstein, S.F., McHugh, P.R., 1975. Mini mental state: a practical method for grading the cognitive state of patients for the clinician. J. Psychiatr. Res. 12, 189–198.
- Fox, M.D., Corbetta, M., Snyder, A.Z., Vincent, J.L., Raichle, M.E., 2006. Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. Proc. Natl. Acad. Sci. U. S. A. 103, 10046–10051.
- Gorecka, M.M., Vasylenko, O., Espenes, J., Waterloo, K., Rodríguez-Aranda, C., 2018. The impact of age-related hearing loss and lateralized auditory attention on spatiotemporal parameters of gait during dual-tasking among community dwelling elderly adults. Exp. Gerontol. 111, 253–262.
- Guye, M., Parker, G.J.M., Symms, M., Boulby, P., Wheeler-Kingshott, C.A.M., Salek-Haddadi, A., Barker, G.J., Duncan, J.S., 2003. Combined functional MRI and tractography to demonstrate the connectivity of the human primary motor cortex in vivo. NeuroImage 19, 1349–1360.
- Hugdahl, K., 2005. Symmetry and asymmetry in the human brain. European Review 13, 119–133.
- Hugdahl, K., Westerhausen, R., 2016. Speech processing asymmetry revealed by dichotic listening and functional brain imaging. Neuropsychologia 93, 466–481.
- Hugdahl, K., Westerhausen, R., Alho, K., Medvedev, S., Laine, M., Hamalainen, H., 2009. Attention and cognitive control: unfolding the dichotic listening story. Scand. J. Psychol. 50, 11–22.
- Kondo, H.M., Pressnitzer, D., Toshima, I., Kashino, M., 2012. Effects of self-motion on auditory scene analysis. Proc. Natl. Acad. Sci. U. S. A. 109, 6775–6780.
- Mamah, D., Ji, A., Rutlin, J., Shimony, J.S., 2019. White matter integrity in schizophrenia and bipolar disorder: tract- and voxel-based analyses of diffusion data from the Connectom scanner. Neuroimage-Clinical 21.
- Mårtensson, J., Lätt, J., Åhs, F., Fredrikson, M., Söderlund, H., Schiöth, H.B., Kok, J., Kremer, B., van Westen, D., Larsson, E.M., Nilsson, M., 2018. Diffusion tensor imaging and tractography of the white matter in normal aging: the rate-of-change differs between segments within tracts. Magn. Reson. Imaging 45, 113–119.
- Meyer, D.E., Kieras, D.E., 1997. A computational theory of executive cognitive processes and multiple-task performance. 1. Basic mechanisms. Psychol. Rev. 104, 3–65.
- Mwangi, B., Tian, T.S., Soares, J.C., 2014. A review of feature reduction techniques in neuroimaging. Neuroinformatics 12, 229–244.
- Nadkarni, N.K., Studenski, S.A., Perera, S., Rosano, C., Aizenstein, H.J., Brach, J.S., Van Swearingen, J.M., 2013. White matter hyperintensities, exercise, and improvement in gait speed: does type of gait rehabilitation matter? J. Am. Geriatr. Soc. 61, 686–693.
- Nadkarni, N.K., Perera, S., Studenski, S.A., Rosano, C., Aizenstein, H.J., VanSwearingen, J.M., 2015. Callosal hyperintensities and gait speed gain from two types of mobility interventions in older adults. Arch. Phys. Med. Rehabil. 96, 1154–1157.
- Penner, I.K., Schlafli, K., Opwis, K., Hugdahl, K., 2009. The role of working memory in dichotic-listening studies of auditory laterality. J. Clin. Exp. Neuropsychol. 31, 959–966.
- Peters, A., Sethares, C., 2002. Aging and the myelinated fibers in prefrontal cortex and corpus callosum of the monkey. J. Comp. Neurol. 442, 277–291.
- Pfefferbaum, A., Adalsteinsson, E., Sullivan, E.V., 2005. Frontal circuitry degradation marks healthy adult aging: evidence from diffusion tensor imaging. NeuroImage 26, 891–899.
- Pollmann, S., Maertens, M., von Cramon, D.Y., Lepsien, J., Hugdahl, K., 2002. Dichotic listening in patients with splenial and nonsplenial callosal lesions. Neuropsychology 16, 56–64.
- Rodríguez-Aranda, C., 2003. Reduced writing and reading speed and age-related changes in verbal fluency tasks. Clin. Neuropsychol. 17, 203–215.
- Rosano, C., Studenski, S.A., Aizenstein, H.J., Boudreau, R.M., Longstreth, W.T., Newman, A.B., 2012. Slower gait, slower information processing and smaller prefrontal area in older adults. Age Ageing 41, 58–64.
- Rosario, B.L., Rosso, A.L., Aizenstein, H.J., Harris, T., Newman, A.B., Satterfield, S., Studenski, S.A., Yaffe, K., Rosano, C., 2016. Cerebral white matter and slow gait: contribution of hyperintensities and normal-appearing parenchyma. J. Gerontol. A Biol. Sci. Med. Sci. 71, 968–973.

- Ryberg, C., Rostrup, E., Stegmann, M.B., Barkhof, F., Scheltens, P., van Straaten, E.C.W., Fazekas, F., Schmidt, R., Ferro, J.M., Baezner, H., Erkinjuntti, T., Jokinen, H., Wahlund, L.O., O'Brien, J., Basile, A.M., Pantoni, L., Inzitari, D., Waldemar, G., 2007. Clinical significance of corpus callosum atrophy in a mixed elderly population. Neurobiol. Aging 28, 955–963.
- Storsve, A.B., Fjell, A.M., Yendiki, A., Walhovd, K.B., 2016. Longitudinal changes in white matter tract integrity across the adult lifespan and its relation to cortical thinning. PLoS One 11, e0156770.
- Tervaniemi, M., Hugdahl, K., 2003. Lateralization of auditory-cortex functions. Brain Res. Rev. 43, 231–246.
- Tian, Q., Ferrucci, L., Resnick, S.M., Simonsick, E.M., Shardell, M.D., Landman, B.A., Venkatraman, V.K., Gonzalez, C.E., Studenski, S.A., 2016. The effect of age and microstructural white matter integrity on lap time variation and fast-paced walking speed. Brain Imaging and Behavior 10, 697–706.
- Tian, Q., Chastan, N., Bair, W.N., Resnick, S.M., Ferrucci, L., Studenski, S.A., 2017. The

- brain map of gait variability in aging, cognitive impairment and dementia A systematic review. Neurosci. Biobehav. Rev. 74, 149–162.
- Verlinden, V.J.A., de Groot, M., Cremers, L.G.M., van der Geest, J.N., Hofman, A., Niessen, W.J., Van der Lugt, A., Vernooij, M.W., Ikram, M.A., 2016. Tract-specific white matter microstructure and gait in humans. Neurobiol. Aging 43, 164–173.
- Westerhausen, R., Hugdahl, K., 2008. The corpus callosum in dichotic listening studies of hemispheric asymmetry: a review of clinical and experimental evidence. Neurosci. Biobehav. Rev. 32, 1044–1054.
- Yendiki, A., Panneck, P., Srinivasan, P., Stevens, A., Zöllei, L., Augustinack, J., Wang, R., Salat, D., Ehrlich, S., Behrens, T., Jbabdi, S., Gollub, R., Fischl, B., 2011. Automated probabilistic reconstruction of white-matter pathways in health and disease using an atlas of the underlying anatomy. Frontiers in Neuroinformatics 5, 23.
- Yogev-Seligmann, G., Hausdorff, J.M., Giladi, N., 2008. The role of executive function and attention in gait. Mov. Disord. 23, 329–342.