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Functional Connectivity Associated With Gait Velocity During Walking and Walking-While-Talking in Aging: A Resting-State fMRI Study

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Abstract: Gait decline is common among older adults and is a risk factor for adverse outcomes. Poor gait performance in dual-task conditions, such as walking while performing a secondary cognitive interference task, is associated with increased risk of frailty, disability, and death. Yet, the functional neural substrates that support locomotion are not well established. We examined the functional connectivity associated with gait velocity in single- (normal pace walking) and dual-task (walking while talking) conditions using resting-state functional Magnetic Resonance Imaging (fMRI). We acquired 6 minutes of resting-state fMRI data in 30 cognitively healthy older adults. Independent components analyses were performed to separate resting-state fMRI data into group-level statistically independent spatial components that correlated with gait velocity in single- and dual-task conditions. Gait velocity in both task conditions was associated with similar functional connectivity in sensorimotor, visual, vestibular, and left fronto-parietal cortical areas. Compared to gait velocity in the single-task condition, the networks associated with gait velocity in the dual-task condition were associated with greater functional connectivity in supplementary motor and prefrontal regions. Our findings show that there are partially overlapping functional networks associated with single- and dual-task walking conditions. These initial findings encourage the future use of resting-state fMRI as tool in developing a comprehensive understanding of age-related mobility impairments. *Hum Brain Mapp 36:1484–1493, 2015.* © 2014 Wiley Periodicals, Inc.

Key words: fMRI; resting-state; gait; dual-task; aging

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INTRODUCTION

Decline in gait performance is common among older adults, even in the absence of neurological pathology or acute clinical events. Such age-related gait decline has been widely studied and reliably shown to increase the risk for morbidity, hospitalization, and mortality [Newman et al., 2006; Studenski et al., 2011; Verghese et al., 2006]. Age-related gait decline also increases the risk for future cognitive decline and dementia in older adults [Marquis et al., 2002; Verghese et al., 2007b; Waite et al., 2005; Wang et al., 2006]. It is important to note that older adults are

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especially challenged under dual-task gait conditions, which require walking while attending to a secondary cognitive demand [Beurskens and Bock, 2012; Holtzer et al., 2011; Li et al., 2001; Lindenberger et al., 2000]. In fact, walking while talking is conceptualized as a mobility stress test that has been shown to be a reliable predictor of falls, frailty, disability, and mortality in cognitively healthy, community-dwelling older adults [Ayers et al., 2014; Verghese et al., 2002, 2012]. As the population of older adults increases throughout the world, developing a comprehensive understanding of these age-related mobility impairments is an essential public health consideration.

The evidence for cognitive control, notably attention and executive functions, of gait when assessed in single- and dual-task conditions in aging is robust [Holtzer et al., 2006, 2012, 2014c]. However, the underlying functional brain correlates of gait and other mobility outcomes are not well established [Holtzer et al., 2014a]. Investigations of neural activity associated with gait have been particularly challenging because traditional neuroimaging modalities cannot be applied during the act of walking. Recent functional brain imaging studies have used a variety of techniques to circumvent this limitation. Researchers have used radionuclide tracers during locomotion, and subsequently examined distribution patterns in the brain using single photon emission computerized tomography (SPECT) or positron-emission-tomography (PET) [Fukuyama et al., 1997; la Fougere et al., 2010; Malouin et al., 2003]. As these approaches are invasive and expensive to implement, other researchers have used functional near-infrared spectroscopy (fNIRS), a noninvasive, low-cost imaging modality that can map functional brain correlates during dynamic tasks such as gait [Holtzer et al., 2011; Miyai et al., 2001]. Previous studies have also explored the functional neural correlates of gait using mental imagery tasks [Blumen et al., 2014; Jahn et al., 2004; la Fougere et al., 2010; Zwergal et al., 2012]. Imaging is done while participants envision themselves walking, without actual execution. Imagery of movements has been shown to activate similar cortical and subcortical regions as the physical performance of the same movements [Anderson and Lenz, 2011; Jeannerod, 2001]. Investigation of gait through imagery creates new opportunities for the use of functional magnetic resonance imaging (fMRI) in this field.

While the majority of fMRI studies have studied the brain's response to a stimulus or task, resting-state fMRI has emerged as an approach that does not require these conditions. Resting-state fMRI research stems from a seminal study demonstrating that low-frequency (0.01–0.1 Hz) blood-oxygen-level-dependent (BOLD) signals were temporally correlated between regions of the primary sensory motor cortex within and across hemispheres in participants at rest [Biswal et al., 1995]. Large-scale cortical networks corresponding to a variety of core perceptual and cognitive processes have since been widely replicated across a range of analytic approaches at both the group and individual levels in a variety of resting conditions: eyes closed, sleep, and even anesthesia [Damoiseaux et al., 2008; Erhardt et al., 2011; Fox and Raichle, 2007]. Well-established resting-state networks correspond strongly to functional areas identified through the use of task-dependent paradigms, and are widely interpreted as intrinsic neural activity supporting core functional systems [Cole et al., 2010]. There are important limitations and interpretational difficulties of resting-state fMRI because it is an indirect measure vulnerable to several confounding factors including head movements, physiological activity, and acquisition artifacts [Biswal et al., 1996; Friston et al., 1996; Glover et al., 2000]. Nevertheless, resting-state fMRI is a potentially powerful technique to further advance our understanding of the system-wide neural substrates underlying gait.

Our aim for this study was to identify functional neural networks associated with single- and dual-task gait performance in nondemented, community-dwelling older adults using resting-state fMRI. Prior research from our group has demonstrated increased oxygenation levels and BOLD activity in the prefrontal cortex during WWT compared with normal walking in older adults using fNIRS [Holtzer et al., 2011] and fMRI with imagined gait [Blumen et al., in press], respectively. Based on these findings, we expect greater involvement in prefrontal regions in the dual-task condition; however, we used a whole-brain multivariate approach to explore this issue, as we were interested in brain function at a systems level.

METHODS

Study Population

Quantitative gait and MRI data from a convenience sample of 30 cognitively healthy older adults [M (SD) age in years = 72.50 (5.22); % female = 55.17] were used for this study from the Central Control of Mobility in Aging (CCMA) study [Holtzer et al., 2013, 2014c]. The CCMA study recruits older adults (≥65 years) residing in Yonkers, NY and aims to identify cognitive and brain predictors of mobility. General exclusion criteria included severe auditory or visual loss, recent hospitalization that affects mobility, living in a nursing home, serious chronic, or acute illness (e.g., cancer), and presence of dementia or other neurodegenerative disease. Specific MRI exclusion criteria included left-handedness (assessed by Edinburgh Handedness Inventory [Oldfield, 1971]), claustrophobia, and surgically implanted metallic devices (e.g., pacemaker). Written informed consent was approved by the university's institutional review board.

Measures

Quantitative gait assessment

Consistent with the vast literature concerning dual-task methodology, participants completed both the single- and dual-task gait conditions. One trial was completed under each gait condition. To reduce learning effects, participants were not given practice trials or taught strategies. Task order was counterbalanced to avoid practice effects. Quantitative gait data were obtained using a 20-foot instrumented walkway with embedded pressure sensors spanning 14 feet, allowing for 3 feet of initial acceleration and terminal deceleration (GAITRite, CIR systems, Havertown, PA). Monitoring devices were not attached to participants during the test. Each trial was one walkway in length and the software computed gait velocity (cm/s) based on the footfalls recorded. We focused on gait velocity as it is a standard quantitative performance index in gait literature and clinical practice that predicts a variety of adverse outcomes [Studenski et al., 2011; Verghese et al., 2012]. GAITRite assessments have been shown to be reliable and valid in previous research in our center and in other studies [Bilney et al., 2003; Verghese et al., 2002].

Normal pace walking (NW)

In the single-task condition, participants were asked to walk on the instrumented walkway at their normal pace for one trial in a quiet and well-lit room. Start and end points were clearly marked.

Walking while talking (WWT)

In the dual-task condition, participants were asked to walk on the instrumented walkway at their normal pace while reciting alternate letters of the alphabet (skipping the letter in between) for one trial in a quiet and well-lit room. Participants were asked to pay equal attention to their walking and talking [Verghese et al., 2007a].

We have demonstrated reliable dual-task effects using this walking while talking paradigm in many articles using different cohorts of older adults [Brandler et al., 2012; Holtzer et al., 2014c; Li et al., 2014]. Consistent with the cognitive dual-task literature, our findings also revealed increased attention/executive demands in the dual-task compared to the single-task walking condition [Holtzer et al., 2006, 2012, 2014b]. Furthermore, using fNIRS, we provided first evidence that online oxygenation levels in the prefrontal cortex were increased in walking while talking compared with walking in a single-task condition in young and old participants [Holtzer et al., 2011]. Increasing the demands of the cognitive task (reciting letters of the alphabet compared with reciting alternative letters of the alphabet) was more strongly associated with risk of falls in older adults [Verghese et al., 2002] and changing instructions while maintaining the same cognitive and motor tasks in the dual-task paradigm resulted in task prioritization effects [Verghese et al., 2007a]. Strong predictive validity for the walking while talking paradigm was also established in longitudinal cohort studies. Performance on this task has been shown to be a robust predictor of falls, frailty, disability, and mortality in older adults [Ayers et al., 2014; Verghese et al., 2012].

MRI data acquisition

During resting-state MRI acquisition, participants were asked to lie still in the scanner, keep their eyes closed, and not fall asleep for 6 min of recording time [Van Dijk et al., 2010]. MRI scanning was performed with a Philips 3T Achieva Quasar TX multinuclear MRI/MRS system equipped with a Dual Quasar High Performance Gradient System, 32-channel broadband digital RF system, Quadrature T/R Head Coil, RapidView reconstructor, Intera Achieva ScanTools Pro R2.5 Package, NetForum and ExamCards, and SENSE parallel imaging capability. All BOLD (T2*-weighted) images were acquired with echo planar imaging using a whole brain gradient over a 240 mm field of view (FOV) on a 128 × 128 acquisition matrix, 3 mm slice thickness (no gap); $\text{TE} = 30$ ms, $\text{TR} = 2000$ ms, flip angle = 90°, and 42 trans-axial slices per volume. A T1-weighted whole head structural image was also acquired using axial 3D-MP-RAGE parameters over a 240 mm FOV and 1.0 mm isotropic resolution, $\text{TE} = 4.6$ ms, $\text{TR} = 9.9$ ms, $\alpha = 80$, with SENSE factor 2.5. MRI data was obtained a few weeks to months following quantitative gait assessment ($M = 96.53$ days, $\text{SD} = 66.20$ days, range = 14–265 days). Participant health was monitored in the interim through bimonthly telephone interviews.

Image preprocessing

BOLD (T2*-weighted) image preprocessing, using FSL (Version 4.1), FMRIB's Software Library (http://fsl.fmrib.ox.ac.uk/fsl) [Jenkinson et al., 2012; Smith et al., 2004; Woolrich et al., 2009], consisted of nonbrain removal using BET [Smith, 2002], motion correction with MCFLIRT [Jenkinson et al., 2002; Jenkinson and Smith, 2001], slice-timing correction for interleaved acquisitions using Fourier-space time-series phase shifting, highpass temporal filtering using Gaussian-weighted least-squares straight line fitting ($\sigma = 50$ s); spatial smoothing using a Gaussian kernel with full-width half-maximum 8 mm, coregistration to high-resolution T1-weighted images, and normalization to standard space (Montreal Neurological Institute atlas, using resolutions of 4 × 4 × 4 mm) using combined affine and nonlinear registration (FSL FNIRT, with warp resolution = 10 mm).

Statistical Analysis

Independent components analysis and correlation

For each participant, smoothed normalized fMRI images were concatenated across time to form a single 4D image. The 4D images were then analyzed with FSL MELODIC Independent Component Analysis (ICA) software [Beckmann and Smith, 2004]. ICA is a data-driven approach that separates multivariate data into statistically independent spatial components and their associated time series. When applied to resting-state fMRI data, ICA decomposes the BOLD dataset into components representing neural signals of interest, structured noise, and random noise [Beckmann et al., 2005; Cole et al., 2010; Fox and Raichle, 2007; Greicius et al., 2004; Murphy et al., 2013]. This technique does not require a priori modeling, providing flexibility appropriate for our exploratory analysis. We used this technique to identify components that correlated with NW and WWT gait velocity in two separate analyses, and limited each analysis output to 20 components, a dimensionality used in previous resting-state studies [Smith et al., 2009]. Criterion for statistical significance was set as $P < 0.05$.

Manual classification of components

Even after traditional pre-processing steps, several confounding sources of noise may remain in resting-state fMRI data that could compromise interpretation [Bhaganagarapu et al., 2013; Kelly et al., 2010; Power et al., 2012]. ICA accounts for the existence of noise effects by automatically isolating sources of noise within artifactual components. Identification of these components, primarily related to gross participant motion and physiological sources such as cardiac and respiratory cycles, is critical to limit spurious findings in resting-state fMRI analyses [Murphy et al., 2013; Thomas et al., 2002]. We used an operationalized fMRI de-noising procedure to manually classify components as representing artifacts or neural signals of interest via visual inspection. The protocol dictates that components are labeled as artifactual when the thresholded component spatial map shows 90% or more activation or deactivation in peripheral areas or in a random scattered pattern over ¼ or more of the brain without correspondence to functional-anatomical boundaries. Components are labeled as neural signals of interest when the thresholded component spatial map shows 10% or more activation or deactivation in small to large gray matter clusters localized to nonperipheral regions of the brain. Secondary considerations include indications of noise such as high frequency activity, spikes, saw tooth pattern, and sinus coactivation. This procedure has been shown to be reliable and to improve the sensitivity of results from resting-state fMRI data analysis [Kelly et al., 2010].

RESULTS

Characteristics of the 30 participants are presented in Table I. A paired-samples t-test was conducted to evaluate the intraindividual change in gait velocity between NW and WWT conditions (also referred to as dual-task cost in the literature [Holtzer et al., 2014c; Lindenberger et al., 2000; Yogev-Seligmann et al., 2010]). Consistent with the literature, there was a statistically significant decrease in gait velocity from the NW condition ($M = 108.83$ cm/s, SD = 22.52 cm/s) to the WWT condition ($M = 82.69$ cm/s, SD = 25.29 cm/s), $t\ (29) = 7.17$, $P < 0.001$).

TABLE I. Descriptive statistics of demographic information and gait velocity ($N = 30$)

	M (SD)	Range
Age (years)	72.50 (5.22)	65–87
Gender (% female)	55.17	
Education (years)	15.27 (2.99)	12–23
Global health status score	1.37 (1.13)	0–4
RBANS total score	95.2 (13.20)	62–119
Gait velocity NW (cm/s)	108.83 (22.52)	45–146
Gait velocity WWT (cm/s)	82.69 (25.29)	35–144

Note. Global health status score (range 0–10) obtained from dichotomous rating (presence or absence) of diabetes, chronic heart failure, arthritis, hypertension, depression, stroke, Parkinson's disease, chronic obstructive pulmonary disease, angina, and myocardial infarction; RBANS: Repeatable Battery for the Assessment of Neuropsychological Status; NW: normal pace walk; WWT: walking while talking

Resting-State Networks Correlated with NW

Of the 20 components generated from the ICA correlated with NW gait velocity, 16 components were determined to be artifactual following the operationalized fMRI de-noising procedure. The remaining four components were determined to be neural signals of interest (see Fig. 1). All anatomical and functional descriptions were classified with reference to the underlying standard-space images in conjunction with several atlases [Lancaster et al., 1997, 2000]. These components were further identified by comparison to well-established resting-state networks derived from a large meta-analysis [Smith et al., 2009; Ystad et al., 2011]. We describe each of the networks briefly below. Map 1A ("sensorimotor") covers the premotor cortex, primary motor cortex, and supplementary motor area. This network corresponds to activations seen in bimanual motor tasks, and similar patterns have been identified in previous resting-state studies [Beckmann et al., 2005; Smith et al., 2009]. Map 2A ("visual") includes primary, secondary, and associative visual cortices. Strong correspondence between these areas and functionally identified visual domains has been well established in the resting-state literature [Beckmann et al., 2005; Smith et al., 2009]. Map 3A ("vestibular") is primarily composed of the insula, and the primary and secondary auditory cortices. This network appears to be functionally related to both auditory and vestibular paradigms. Similar patterns have been found in resting-state networks in the past [Beckmann et al., 2005; Smith et al., 2009]. Map 4A ("left fronto-parietal") covers the left posterior parietal association areas, left supplementary motor cortex, left frontal eye field, and left prefrontal association cortex. This left

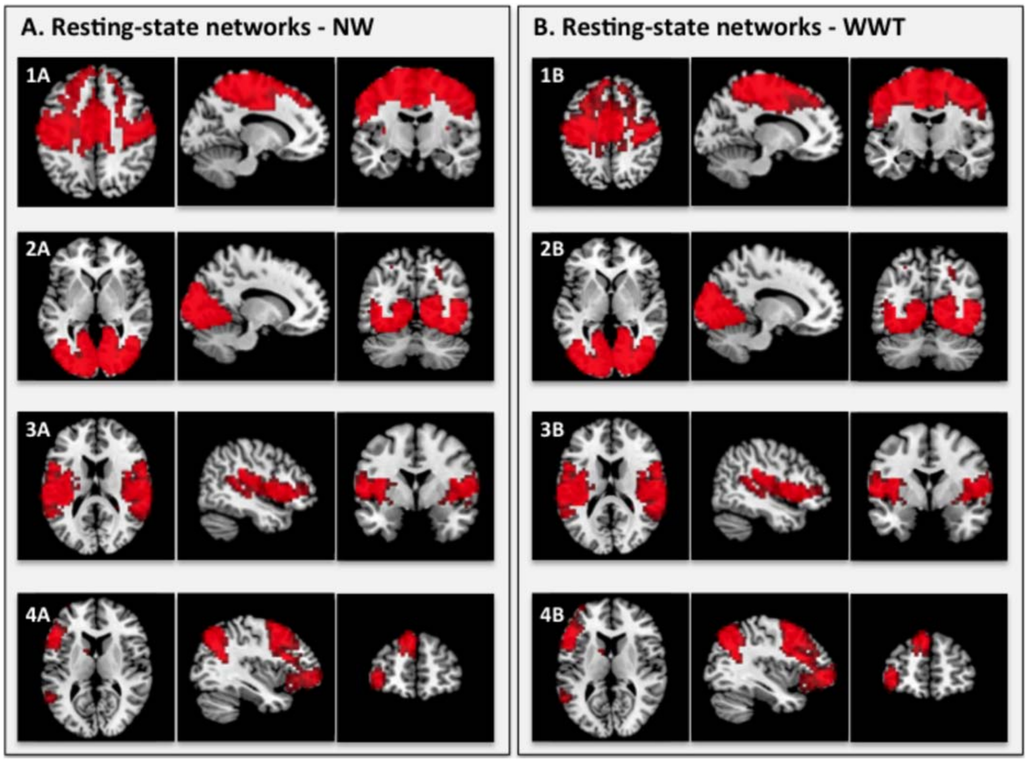

Figure 1.

Resting-state networks associated with NW gait velocity (**A**) and WWT gait velocity (**B**). This figure shows the three most informative axial, sagittal, and coronal slices of each resting-state network superimposed on the Montreal Neurologic Institute (MNI) template supplied by MRIcron software. The left side of the image corresponds to the left side of the brain. All ICA spatial maps were converted to z statistic images via a normalized mixture-model fit, and then thresholded at $z = 2.30$.

lateralized fronto-parietal network also includes regions of the right cerebellum. This is consistent with anatomical and functional connections, as evidenced by recent resting-state studies that have shown cross-lateral connectivity between regions of the cerebellum and the prefrontal and posterior-parietal cortices [Habas et al., 2009; Krienen and Buckner, 2009; O'Reilly et al., 2010]. Fronto-parietal networks were strongly lateralized in the resting-state literature [Smith et al., 2009].

Resting-State Networks Correlated with WWT

Of the 20 components generated from the ICA correlated with WWT gait velocity, 16 components were determined to represent noise, and four components were determined to be neural signals of interest using the operationalized fMRI de-noising procedure. As with NW gait velocity, WWT gait velocity was significantly correlated with functional connectivity in well-established sensorimotor, visual, vestibular, and left-lateralized fronto-parietal resting-state networks (see Fig. 1: Maps 1B, 2B, 3B, and 4B respectively).

NW Compared with WWT

Similar resting-state networks were correlated with NW and WWT gait velocity. The corresponding visual and auditory networks are almost identical. The sensorimotor and left fronto-parietal networks associated with NW and WWT, however, have significant differences (Fig. 2). The sensorimotor and left fronto-parietal networks associated with WWT include greater frontal connectivity in the supplementary motor and prefrontal areas, respectively, compared with the corresponding networks associated with NW.

DISCUSSION

The present study revealed four resting-state networks associated with NW and WWT gait velocity in healthy older adults. Our main findings were as follows: (1) Gait velocity under both walking conditions was associated with similar functional connectivity in sensorimotor, visual, vestibular, and fronto-parietal functional networks at rest in older adults; however, (2) WWT gait velocity was

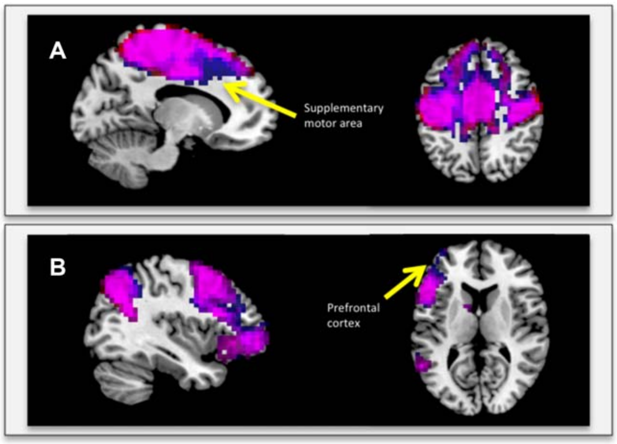

Figure 2.

A: Overlay of the sensorimotor resting-state networks associated with NW (red) and WWT (blue) on the same template. **B**: Overlay of the left fronto-parietal resting-state networks associated with NW (red) and WWT (blue) on the same template. The purple color represents the areas in which the networks overlap. The blue color shows where the WWT networks extend beyond the NW networks.

associated with greater frontal functional connectivity in the sensorimotor and fronto-parietal networks compared with NW.

Shared Neural Correlates of NW and WWT

The resting-state networks associated with NW and WWT gait velocity in our study are consistent with findings from previous neuroimaging studies. As expected, gait in both conditions was associated with functional connectivity in the sensorimotor network. Recent studies using PET, SPECT, fNIRS, and mental imagery to investigate gait identified activations in the premotor cortex, primary motor cortex, and supplementary motor area [Blumen et al., 2014; Fukuyama et al., 1997; Godde and Voelcker-Rehage, 2010; Jahn et al., 2004; Malouin et al., 2003; Miyai et al., 2001; Zwergal et al., 2012]. These areas have been shown to be involved in motor preparation and programming voluntary movement, both critical to locomotion [Fukuyama et al., 1997]. Gait also requires complex motor abilities related to supplementary motor area function. Patients with lesions in premotor and supplementary motor areas have difficulty in tasks such as initiating or terminating gait [Massion, 1992; Viallet et al., 1992].

Gait in both conditions was also associated with functional connectivity in the visual network, which is consistent with results from a range of neuroimaging studies of gait [Fukuyama et al., 1997; Jahn et al., 2004; la Fougere et al., 2010; Zwergal et al., 2012]. Prominent activations in the visual cortex were found across a variety of real and imagined locomotion conditions. Visual function is essential to locomotion because the processing of visual input is necessary for maintaining proper direction and adaptation to obstacles in the environment.

NW and WWT gait performance were associated with functional connectivity in the vestibular resting-state network. Vestibular function is important in locomotion for an appropriate internal representation of the body in space. While vestibular cortical areas have been reliably associated with gait performance, the directionality of the relationship is not well established. Recent evidence suggests activity in vestibular regions during locomotion to be age-dependent. Specifically, while younger subjects exhibited significant deactivations in vestibular cortices during motor imagery, older subjects exhibited a relatively increased activation in the same areas [Zwergal et al., 2012]. Our findings underscore the importance of further investigation into age-related differences in neural correlates of gait performance, especially concerning vestibular functioning.

NW and WWT gait velocity were also associated with functional connectivity in the left-lateralized frontoparietal resting-state network. Studies of real and imagined locomotion consistently demonstrate the involvement of the frontal and frontoparietal regions during these tasks [Blumen et al., 2014; Holtzer et al., 2011; la Fougere et al., 2010; Malouin et al., 2003]. These areas sustain higher-order cognitive processes and attentional processes, which have been shown to be integral to locomotion. Older adults with poorer executive function are at higher risk for falls [Herman et al., 2010; Holtzer et al., 2007]. An intervention study from our group showed that cognitive remediation of attention and executive functions improved gait performance during NW and WWT conditions in older adults [Verghese et al., 2010]. Our findings provide further support for the role of executive functioning and its underlying functional brain substrates in both NW and WWT gait performance.

The known lateralization of fronto-parietal resting-state networks is consistent with recent evidence that the left and right fronto-parietal regions support distinct functions [Smith et al., 2009]. In particular, the left fronto-parietal region has been associated with allocentric spatial processing and object recognition [Guerin and Miller, 2009; Iachini et al., 2009]. The left hemisphere is also associated with the cortical control of speech; however, the lack of verbal activity in the NW condition suggest that this area plays a role in locomotion that cannot be attributed solely to verbal mediation. Consistent with our results, previous studies using fMRI and mental imagery have found a preponderance of activity in the left dorsolateral prefrontal cortex during imagined gait [Jahn et al., 2004; Malouin et al., 2003]. Further investigation is necessary to explore the differential involvement of the left and right fronto-parietal regions in gait.

Importantly, our findings are also in general agreement with prior structural MRI studies of mobility in older adults. Findings across voxel-based morphometry, fluid attenuated inversion recovery sequences, and diffusion tensor imaging studies have emphasized the role of the primary sensorimotor, medial temporal, and prefrontal regions in gait performance [de Laat et al., 2011; Rosano et al., 2007, 2008; Srikanth et al., 2010; Sullivan et al., 2001; Van Impe et al., 2012]. While the origins and functional role of resting-state activity remain unclear, studies suggest that functional correlations derived from resting-state fMRI reflect direct and indirect anatomical connections to a large degree [Greicius et al., 2009; Hagmann et al., 2008; Skudlarski et al., 2008]. Therefore, the converging evidence between our results and structural studies of gait suggests additional cross validation for our findings. Presently, a number of questions remain regarding the relationship between structural and functional connection patterns, and further studies combining structural and resting-state imaging will critical to the interpretation of present and forthcoming results.

Differences in Neural Correlates of NW and WWT

Compared to NW gait velocity, WWT gait velocity was associated with greater functional connectivity in the dorsolateral prefrontal regions of the left fronto-parietal resting-state network. The ability to allocate attention to competing task demands, a distinct component of executive functioning, is sub-served in part by the prefrontal cortex [Stelzel et al., 2009; Szameitat et al., 2002] and is compromised in older adults [Davidson et al., 2006; Holtzer et al., 2004, 2005; Moscovitch and Winocur, 1995; Shimamura et al., 1990; West, 1996]. Numerous studies have demonstrated that performance on measures of executive function, assessed independently of the dual-task paradigm, is related to gait performance in dual-task conditions [Hall et al., 2011; Hausdorff et al., 2008; Holtzer et al., 2006, 2012; Liu-Ambrose et al., 2009; Springer et al., 2006]. Our present findings provide converging evidence in older adults that the prefrontal cortex appears critical in supporting NW and even more so WWT, where cognitive demand is maximized.

Compared with NW gait velocity, WWT gait velocity was associated with greater functional connectivity in the supplementary motor area of the sensorimotor network. The supplementary motor area has been shown to play an important role not only in the planning and coordination of movement but also attention to movement [Johansen-Berg and Matthews, 2002]. Increased supplementary motor area neural resources may reflect the increased attention to postural awareness and movement coordination necessary to ensure successful gait performance under challenging dual-task conditions.

Limitations

Several limitations of this study should be considered. First, while resting-state fMRI is a powerful approach to measure functional brain organization, it is not without its limitations. It is an indirect measure susceptible to several confounding factors that may contribute to between-subject and between-group differences. In addition to head movement and physiological activity, anatomic variability and atrophy are possible confounding sources particularly relevant in older adults. Second, it must be noted that due to the stochastic nature of ICA algorithms, our results may be affected by a degree of run-to-run variability. Although this problem is typical of ICA analyses, it must be noted that results of a single run should be interpreted with caution. We attempted to reduce this type of variability by selecting strict convergence criteria, as described previously. Lastly, the participants in this study were a relatively small sample of non-demented, community-dwelling older adults. The results may not generalize to older adults with significant physical and/or cognitive impairments. Future population-based studies are needed to replicate our findings in larger, more heterogeneous populations. While methodological and interpretational limitations advise caution concerning the present results, the findings represent an exciting initial investigation into the functional neural correlates of gait.

CONCLUSION

Our results show that NW and WWT gait velocities were both associated with well-established sensorimotor, visual, vestibular, and left fronto-parietal resting-state networks in older adults. Compared with gait velocity in the single-task condition, the networks associated with gait velocity in the dual-task condition were associated with greater functional connectivity in supplementary motor and prefrontal regions. The results suggest that WWT may require additional engagement of cognitive and motor neural regions related to attention and movement coordination. To our knowledge, this is the first study to use resting-state fMRI to examine neural correlates of gait performance. These initial findings should encourage the future use of resting-state fMRI as tool to examine functional neural connections underlying age-related mobility impairments. Future avenues of research, including complementary structural and functional imaging techniques, may lead to a better understanding of the multiple neural resources underlying locomotion in older adults and eventually diagnostic or prognostic indicators and more targeted interventions.

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