Published in final edited form as:

Neurosci Lett. 2019 November 20; 713: 134526. doi:10.1016/j.neulet.2019.134526.

Spatial task-related brain activity and its association with preferred and fast pace gait speed in older adults

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Abstract

Task-related brain activity is associated with preferred pace gait speed in older adults. Whether similar regional brain activity relates to fast pace gait speed has yet to be determined, but may provide insight into neural substrate important for walking under various conditions. This study measured regional blood-oxygen-level dependent (BOLD) changes using functional magnetic resonance imaging (fMRI) in response to a spatial Simon/Stroop task in community-dwelling older adults (N=20, 63–80y). Preferred pace, fast pace, and dual-task gait speeds (picking up objects at preferred pace; fast walking over obstacles) were measured across a 7-meter course. Time to complete a fast pace 400m walk test was also recorded. Partial correlations were used for all analyses after adjusting for age. Accuracy on incongruent trials of the spatial task was positively correlated with all fast walking conditions (all $p < 0.01$), but not preferred pace walking conditions. BOLD signal change in the left middle frontal gyrus during the spatial task was associated with preferred pace gait speed ($r = 0.51$, $p = 0.02$) and fast walking over obstacles ($r = 0.53$, $p = 0.01$). Interestingly, BOLD signal change in the bilateral precuneus was associated with fast pace gait speed ($r = 0.58$, $p < 0.01$), fast walking over obstacles ($r = 0.48$, $p = 0.03$), and 400m walk time ($r = -0.49$, $p = 0.02$). These results find preferred and fast pace gait speed are associated with different regional task-related brain activity, with activation in the precuneus related with greater performance during fast pace walking.

Keywords

aging; BOLD; functional MRI; gait speed; precuneus; middle frontal gyrus

1. Introduction

The ability to walk, often reported in terms of gait speed, is closely linked to neurocognitive health. The general finding is that older adults with faster gait speed have better cognitive function in terms of accuracy and/or reaction time during tests of executive function, memory, and processing speed [1,2]. This relationship has been interpreted to mean that neural facilities that support cognition are also important for the maintenance of mobility with advancing age. Previous studies have started to examine the neural substrate associated

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with gait speed. For example, resting-state brain activity measured using functional magnetic resonance imaging (fMRI) show multiple regions of the brain to associate with preferred gait speed including visual, sensorimotor, and fronto-parietal cortical areas [3,4]. In addition, using fMRI during cognitive tasks of executive function show activation in the dorsal attention network of the brain to positively correlate with preferred gait speed in older adults [5]. Whether these brain regions also relate to gait speed when performed at a fast pace has yet to be determined, but would provide novel insight into neural substrate that may vary or be shared when walking under various conditions. This is important as fast-pace gait speed decline at an earlier age [6] and at a faster rate [7] than preferred gait speed, so identifying brain regions associated fast-pace gait speed may shed light into cognitive processes involved with early mobility decline.

Assessment of brain activity under motor conditions performed at various speeds show that brain regions differ based on intensity of effort. For instance, slow movement of the foot activates bilateral prefrontal areas while fast movements strongly activate the sensorimotor cerebral cortex [8]. Brain activation patterns measured during imagined walking also show different active brain regions as one transitions from initiating gait to steady-state walking then to walking over obstacles [9]. These findings suggest that multiple brain centers are recruited as functional demand increases while walking. To confirm this observation in the context of task-related brain activity [10], we used fMRI to measure brain activity during performance of a spatial task of executive function to assess the cross-sectional relationship between regional brain activation and gait speed performed under preferred and fast pace walking conditions. We hypothesized that different regional brain activity would correlate with gait speed performed at different speeds.

2. Methods

2.1 Participants

This study is an analysis of unpublished baseline data from a randomized, placebo-controlled investigation on the effect of L-citrulline on vascular function [11]. All participants provided consent to participate in this study (IRB approval #504985). From the 25 subjects in the parent study, five were excluded in the present analysis due to scheduling conflicts (n=2), possible metal in the body (n=2), and significant early-life brain damage (n=1). This left 20 participants (11 women, 9 men) within 63–80y, all of which had complete data used in this study. To be a part of the parent study, participants had to have a body mass index $<30 \text{ kg/m}^2$, no personal history of cardiovascular or pulmonary disease, no history of neurological illness, and not taking medication for high blood pressure or cholesterol. Lastly, participants had to have a fasting blood glucose $<126 \text{ mg/dL}$ (AccuChek Active, Roche Diagnostics) suggesting no diabetes mellitus. These measurements were made at a screening visit that included familiarization with all walking tests. This screening visit was separate from the visit that included the walking tests and MRI scan. This study and its procedures conformed to standards set by the Declaration of Helsinki.

2.2 Gait Speed Assessment

Participants completed four separate walking tasks all across a 7-meter flat course marked by two traffic cones. Two walking tasks were performed at a preferred pace while another two walking tasks were performed at a fast pace. The order was randomized between participants by rearranging the walking tasks completed by the last participant tested such that no consecutive test had the same order. Preferred pace tasks consisted of walking as if “going to check the mailbox”, while the other task was to stop and pick up an object (plastic spoon or fork) placed on the floor at the center of the course. Fast pace tasks consisted of walking “as quickly as possible”, while the other task was to walk over two obstacles placed 2-meters (6cm in height) and 4-meters (30cm in height) from the starting cone. The dual walking tasks of picking up an object and walking over obstacles have been previously reported to produce gait speeds that associate with executive function in older adults [12]. All walking tasks were timed to calculate gait speed in meters per second, and at least four trials were recorded for each task with 15–30s pauses given between trials for a brief recovery. Gait speed was calculated by averaging all trials within each walking condition.

Participants were also asked to “walk as quickly as possible” for 400m in a long, flat hallway. Two cones were placed 20m apart, and participants were asked to complete 10 laps. All participants completed the test without a rest period. Time to walk 400m was recorded along with stride length derived from counting the number of steps taken during the first 20m of the test.

2.3 fMRI Scan

A 3-Tesla MRI scanner (Skyra, Siemens Healthcare Diagnostics, Tarrytown, NY) with a 20 channel head coil was used to collect all images. A T1-weighted sagittal MPRAGE (192 slices) was obtained and used to construct the baseline anatomical brain scans. Functional MRI data (33 axial slices) were acquired using gradient echo-planar imaging with the following imaging parameters: repetition time = 2.0s; total volumes = 245; voxel size = $2 \times 2 \times 3.5$ mm; echo time = 20s; field of view = $192\text{mm} \times 192\text{mm}$; flip angle = 90° . During scanning, participants completed a spatial Simon and Stroop task for 8 min (see Figure 1 for details). The spatial Simon/Stroop task was administered by E-Prime 2.0 software to coincide with fMRI scanning. The task consisted of 120 trials (60 bars, 30 congruent arrows, 30 incongruent arrows) with 2s between presentations. Behavioral data collected during the task consisted of accuracy (percent correct) and reaction time (seconds), which are reported only for incongruent trials as they are the primary stimulus type for inducing Stroop interference and known to tax both attention and executive function.

2.4 Image Processing

Images were processed and analyzed using the fMRI expert analysis tool of the fMRI Software Library (FSL, v5.0.9). Brain extraction was performed using the brain extraction tool (BET) on all anatomical and functional images. All fMRI volumes underwent slice timing correction, motion correction via MCFLIRT to correct for head movements, and spatial smoothing via a full width at half maximum of 5mm; the latter to reduce the effect of noise without compromising activation signal. For each participant, functional images (EPI) were linearly registered onto their individual structural T1 images. All participants

underwent nonlinear registration of their native space into Montreal Neurological Institute (MNI 152) standard space (voxel size= $2 \times 2 \times 2$). Warp resolution with 12 degrees of freedom was applied to correct any misalignment during co-registration. Using a double gamma convolution, first level analysis was conducted for the contrasts of interest, which highlighted activation of inconsistent arrows trials greater than bar (control) trials. Additionally, six motion parameters (3 translational and 3 rotational) were entered into each first level analysis to correct for head movement. FSL higher level analyses were carried out with the group mean and standardized scores (z-scores) of gait speed and age as additional explanatory variables using a fixed effects model (i.e., forcing the random effects variance to zero in FMRIB's Local Analysis of Mixed Effects [13–15]. Z (Gaussianised T/F) statistic images were non-parametrically thresholded using clusters determined by $Z > 2.3$ and a corrected cluster significance threshold of $p = 0.01$ [16].

To limit the scope of our analyses to task-specific brain regions previously shown to be activated during the spatial Simon/Stroop task [17,18], only a-priori regions of interest (ROIs) were analyzed. These included the middle frontal gyrus, superior parietal lobe (SPL), precuneus, and the superior lateral occipital cortex (LOC). Using FSLeyes, masks were created from the Harvard-Oxford Cortical Structural Atlas. The middle frontal gyrus mask (838 voxels) consisted of voxels from the left hemisphere while the precuneus mask (2459 voxels) consisted of voxels from both left and right hemispheres. Both of these ROIs had at least 50% probabilistic location. A higher probabilistic threshold was used to reduce overlap as these ROI are located in close proximity with other brain areas. The superior LOC consisted of voxels from both hemispheres with at least 10% probabilistic location (13631 voxels), while the right SPL mask (1067 voxels) consisted of right hemisphere voxels with at least 20% probabilistic location in this region. Smaller thresholds were applied to these ROI due to their smaller size so that more BOLD activation could be identified. For each of these ROIs, fMRI parameter estimates of signal change were converted to percent signal change using FSL FEATQuery.

2.5 Statistical analysis

Normality was assessed for all variables using Anderson-Darlings tests. Only accuracy was not normally distributed, which was corrected using a Johnson transformation. Pearson correlation was used to assess relationships between gait speed and cognitive variables including accuracy (transformed), reaction time, and regional BOLD percent signal change. Partial correlation was used to assess these relationships after controlling for variance explained by age. Paired t-tests were used to compare gait speeds between walking tasks. There were no sex differences in gait speed or BOLD signal change (data not shown), so all analyses were performed with men and women combined. Significance was set at $p < 0.05$.

3. Results

3.1 Demographic Comparisons

Participant characteristics including gait speed and data collected from the spatial Simon/Stroop incongruent arrow trials are reported in Table 1. Preferred pace gait speed was significantly slower than fast pace gait speed ($p < 0.001$), and dual task conditions (picking up

object, walking over obstacles) slowed gait speed relative to each respective walking pace (both $p < 0.001$). Behavioral performance and BOLD signal change on incongruent arrow trials during the Simon/Stroop task showed a wide range of responses (Table 1).

Interestingly, accuracy on incongruent arrow trials was positively correlated with BOLD signal change in the precuneus ($r = 0.53$, $p = 0.01$), while reaction time during incongruent arrow trials was inversely associated with BOLD signal change in the left middle frontal gyrus ($r = -0.47$, $p = 0.03$).

3.2 Gait Speed and Behavioral Performance

Fast pace gait speed ($r = 0.62$, $p < 0.01$), fast walking over obstacles ($r = 0.63$, $p < 0.01$), and 400m walking time ($r = -0.74$, $p < 0.001$) were significantly correlated with accuracy on incongruent arrow trials during the Simon/Stroop task after adjusting for age, but not reaction time ($p > 0.05$). Preferred pace walking conditions were not correlated with accuracy or reaction time ($p > 0.05$).

3.3. Gait Speed and Brain Activation

Preferred gait speed was associated with BOLD signal change in the left middle frontal gyrus bilaterally ($p = 0.02$), and no association was observed between brain activity and preferred walking while picking up objects (Table 2). After adjusting for age, the association remained between preferred pace gait speed and BOLD signal change in the left middle frontal gyrus bilaterally ($r = 0.51$, $p = 0.02$; Figures 2 and 3).

Unadjusted correlations were found between fast pace walking conditions and multiple brain regions including the left middle frontal gyrus (walking over obstacles: $p = 0.04$), right SPL (fast pace gait speed: $p = 0.03$; walking over obstacles: $p = 0.04$), bilateral precuneus (fast pace gait speed: $p = 0.04$; 400m walk time: $p = 0.04$), and the bilateral superior LOC (fast pace gait speed: $p = 0.03$; walking over obstacles: $p = 0.03$; 400m walk time: $p = 0.04$) (Table 2).

However, after adjusting for age, significant correlations between fast walking conditions and BOLD signal change were only observed in the left middle frontal gyrus bilaterally for walking over obstacles ($r = 0.53$, $p = 0.01$; Figure 2), and in the precuneus bilaterally for fast pace gait speed ($r = 0.58$, $p < 0.01$; Figure 3), walking over obstacles ($r = 0.48$, $p = 0.03$), and 400m walk time ($r = -0.49$, $p = 0.02$) (Figure 2).

4. Discussion

The present study found fast pace walking to associate with greater accuracy on incongruent trials of a spatial task of executive function along with concurrently increased brain activation measured using fMRI in older adults. The association between fast pace gait speed and activation was observed in the precuneus, an area located in the medial aspect of the posterior parietal lobe. The precuneus is characterized as a 'hub' of afferent and efferent connections with both cortical and subcortical networks [19]. While the precuneus is active in multiple behaviors, it plays an important role processing visual information. Indeed, previous studies have reported activation in the precuneus in older adults during successful incongruent trials of the Simon/Stroop paradigm [20,21]. Moreover, the precuneus has been shown to be active under the visual perception of forward bodily movement [22], and part of

a neural network activated during imagined walking with obstacles through a virtual corridor in middle-aged to older adults [9]. Our results corroborate these findings, but we report for the first time that walking at a fast pace has a strong relationship with activity in the precuneus. This was observed under various conditions including fast walking across a short distance, long distance, and short distance over obstacles even after adjusting for chronological age.

The finding that brain activation of the precuneus was positively correlated with accuracy suggests that we examined an area of the brain that was inherently important for performing the spatial Simon/Stroop task. Moreover, the positive relationship between BOLD signal change and accuracy is in agreement with past studies using different cognitive tests of executive function [5,23]. Some researchers have postulated that the relationship between brain activation and behavioral performance is a reflection of adults being pushed past their capacity to perform the task [24], thereby leading to lower BOLD signals in those less successfully engaged. If this is true then it is reasonable to believe that older adults with increased BOLD signals have a greater capacity (or neural reserve) to maintain their engagement during cognitive performance of a novel or challenging task [25]. Using this rationale, it is possible that older adults in the present study exhibiting greater BOLD signal change had higher neural capacity, and thus were able to increase brain activation when challenged with the task of walking “as quickly as possible” as was the case for our fast pace walking conditions. This interpretation is consistent with data demonstrating that fast pace gait speed decreases in a graded fashion with stages of cognitive impairment (i.e., lost neural reserve) [26].

The relationship between preferred pace gait speed and brain activation was observed in the left middle frontal gyrus. Our observation that activity of the middle frontal gyrus was positively correlated with preferred gait speed is consistent with previous studies that find the medial frontal cortex to be active during steady-state walking [27], and that gray matter volume of the middle frontal gyrus is positively associated with preferred pace gait speed [28]. Interestingly, we also observed fast walking over obstacles to associate with brain activation of the middle frontal gyrus. This observation is also in agreement with past work that finds gray matter volume in this region to associate with dual-task gait speed in older adults [29]. Thus, activity of the middle frontal gyrus seems to be important for the motor activity associated with walking at a slower (preferred) walking pace and walking over obstacles at a fast pace.

Limitations of this study include a small sample size of highly functional community-dwelling older adults screened for obesity, cardiovascular, pulmonary, and metabolic disease. Thus, the present results are not generalizable to the average older adult with chronic disease, but rather may reflect physiological links more common in healthy aging. However, it should be noted that we did not screen for cognitive capacity, so our results may not be void of the influence of mild cognitive impairment common in older adults. Another consideration is the cross-sectional design of this study that prevents examining the causal direction of the association reported. Factors such as cardiorespiratory fitness should be examined as a mediating variable in the relationship between brain activation and gait speed

as past research have identified improved spatial task-related brain activation in the medial frontal gyrus and precuneus following regular exercise [30].

In summary, we have demonstrated in healthy older adults that task-related brain activity is associated with preferred and fast pace gait speed. These associations were not due to variance explained by chronological age indicating that the reported relationships were not due to age-related decrements in cognitive function or mobility, but rather reflected an intrinsic interconnectivity between brain function and locomotion. Moreover, we report regional differences in the association between task-related brain activation and gait speed, with the precuneus showing a consistent relationship with fast walking when performed under various conditions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

This work was supported by an American Heart Association Beginning Grant-in-Aid (award number 15BGIA22710012). We would also like to thank Barbara Bowley and Kasey Rieken at the TTU Texas Tech Neuroimaging Institute for their assistance with MRI scanning.

6. References

- [1]. Martin KL, Blizzard L, Wood AG, Srikanth V, Thomson R, Sanders LM, Callisaya ML, Cognitive function, gait, and gait variability in older people: a population-based study, *J. Gerontol. A Biol. Sci. Med. Sci*, 68 (2013) 726–732. [PubMed: 23112113]
- [2]. Mielke MM, Roberts RO, Savica R, Cha R, Drubach DI, Christianson T, Pankratz VS, Geda YE, Machulda MM, Ivnik RJ, Knopman DS, Boeve BF, Rocca WA, Petersen RC, Assessing the temporal relationship between cognition and gait: slow gait predicts cognitive decline in the Mayo Clinic Study of Aging, *J. Gerontol. A Biol. Sci. Med. Sci*, 68 (2013) 929–937. [PubMed: 23250002]
- [3]. Yuan J, Blumen HM, Verghese J, Holtzer R, Functional connectivity associated with gait velocity during walking and walking-while-talking in aging: a resting-state fMRI study, *Hum. Brain Mapp*, 36 (2015) 1484–1493. [PubMed: 25504964]
- [4]. Lo O-Y, Halko MA, Zhou J, Harrison R, Lipsitz LA, Manor B, Gait speed and gait variability are associated with different functional brain networks, *Front. Aging Neurosci*, 9 (2017) 390. [PubMed: 29249961]
- [5]. Jor'dan AJ, Poole VN, Iloputaife I, Milberg W, Manor B, Esterman M, Lipsitz LA, Executive network activation is linked to walking speed in older adults: functional MRI and TCD ultrasound evidence from the MOBILIZE Boston Study, *J. Gerontol. A Biol. Sci. Med. Sci*, 72 (2017) 1669–1675. [PubMed: 28449077]
- [6]. Bohannon RW Comfortable and maximum walking speed of adults aged 20–79 years: reference values and determinants. *Age Ageing* 26, 15–19. 1997.
- [7]. Ko SU, Hausdorff JM, Ferrucci L, Age-associated differences in the gait pattern changes of older adults during fast-speed and fatigue conditions: results from the Baltimore Longitudinal Study of Ageing, *Age Ageing*, 39 (2010) 688–694. [PubMed: 20833863]
- [8]. Sauvage C, Jissendi P, Seignan S, Manto M, Habas C, Brain areas involved in the control of speed during a motor sequence of the foot: Real movement versus mental imagery, *J. Neuroradiol*, 40 (2013) 267–280. [PubMed: 23433722]

- [9]. Malouin F, Richards CL, Jackson PL, Dumas F, Doyon J, Brain activations during motor imagery of locomotor-related tasks: A PET study, *Hum. Brain Mapp*, 19 (2003) 47–62. [PubMed: 12731103]
- [10]. Holtzer R, Epstein N, Mahoney JR, Izzetoglu M, Blumen HM, Neuroimaging of Mobility in Aging: A Targeted Review, *J. Gerontol. A Biol. Sci. Med. Sci*, 69 (2014) 1375–1388. [PubMed: 24739495]
- [11]. Gonzales JU, Raymond A, Ashley J, Kim Y, Does l-citrulline supplementation improve exercise blood flow in older adults?, *Exp. Physiol*, 102 (2017) 1661–1671. [PubMed: 28940638]
- [12]. Coppin AK, Shumway-Cook A, Saczynski JS, Patel KV, Ble A, Ferrucci L, Guralnik JM, Association of executive function and performance of dual-task physical tests among older adults: analyses from the InChianti study, *Age Ageing*, 35 (2006) 619–624. [PubMed: 17047008]
- [13]. Beckmann CF, Jenkinson M, Smith SM, General multilevel linear modeling for group analysis in FMRI, *NeuroImage*, 20 (2003) 1052–1063. [PubMed: 14568475]
- [14]. Woolrich MW, Behrens TE, Beckmann CF, Jenkinson M, Smith SM, Multilevel linear modelling for FMRI group analysis using Bayesian inference, *NeuroImage*, 21 (2004) 1732–1747. [PubMed: 15050594]
- [15]. Woolrich M, Robust group analysis using outlier inference, *NeuroImage*, 41 (2008) 286–301. [PubMed: 18407525]
- [16]. Worsley KJ, Statistical analysis of activation images In Jezzard P, Matthews PM, Smith SM (Eds.), *Functional MRI: An Introduction to Methods* Oxford University Press, 2001.
- [17]. Peterson BS, Kane MJ, Alexander GM, Lacadie C, Skudlarski P, Leung HC, May J, Gore JC, An event-related functional MRI study comparing interference effects in the Simon and Stroop tasks, *Cogn. Brain Res*, 13 (2002) 427–440.
- [18]. Liu X, Banich MT, Jacobson BL, Tanabe JL, Common and distinct neural substrates of attentional control in an integrated Simon and spatial Stroop task as assessed by event-related fMRI, *NeuroImage*, 22 (2004) 1097–1106. [PubMed: 15219581]
- [19]. Cavanna AE, Trimble MR, The precuneus: a review of its functional anatomy and behavioural correlates, *Brain*, 129 (2006) 564–583. [PubMed: 16399806]
- [20]. Sebastian A, Baldernann C, Feige B, Katzev M, Scheller E, Hellwig B, Lieb K, Weiller C, T+ +scher,O., Kl+ppel,S., Differential effects of age on subcomponents of response inhibition, *Neurobiol. Aging*, 34 (2013) 2183–2193. [PubMed: 23591131]
- [21]. Onur ÖA, Piefke M, Lie CH, Thiel CM, Fink GR Modulatory effects of levodopa on cognitive control in young but not in older subjects: a pharmacological fMRI study. *J. Cogn. Neurosci* 23[10], 2797–2810. 2011. [PubMed: 21254797]
- [22]. Jong BM, Shipp S, Skidmore B, Frackowiak RSJ, Zeki S, The cerebral activity related to the visual perception of forward motion in depth, *Brain*, 117 (1994) 1039–1054. [PubMed: 7953587]
- [23]. Baciú M, Boudiaf N, Cousin E, Perrone-Bertolotti M, Pichat C, Fournet N, Chainay H, Lamalle L, Krainik A, Functional MRI evidence for the decline of word retrieval and generation during normal aging, *AGE*, 38 (2016) 3. [PubMed: 26711670]
- [24]. Todd JJ, Marois R, Capacity limit of visual short-term memory in human posterior parietal cortex, *Nature*, 428 (2004) 751–754. [PubMed: 15085133]
- [25]. Mattay V, Fera F, Tessitore A, Hariri AR, Berman KF, Das S, Meyer-Lindenberg A, Goldberg TE, Callicott JH, Weinberger DR, Neurophysiological correlates of age-related changes in working memory capacity, *Neurosci. Lett*, 392 (2006) 32–37. [PubMed: 16213083]
- [26]. Callisaya ML, Launay CP, Srikanth VK, Verghese J, Allali G, Beauchet O, Cognitive status, fast walking speed and walking speed reserve - the Gait and Alzheimer Interactions Tracking (GAIT) study, *GeroScience*, 39 (2017) 231–239. [PubMed: 28374167]
- [27]. la Fougère C, Zwergal A, Rominger A, Förster S, Fesl G, Dieterich M, Brandt T, Strupp M, Bartenstein P, Jahn K, Real versus imagined locomotion: A [18F]-FDG PET-fMRI comparison, *NeuroImage*, 50 (2010) 1589–1598. [PubMed: 20034578]
- [28]. Tripathi S, Verghese J, Blumen HM, Gray matter volume covariance networks associated with dual-task cost during walking-while-talking, *Hum. Brain Mapp*, 40 (2019) 2229–2240. [PubMed: 30664283]

- [29]. Allali G, Montembeault M, Brambati SM, Bherer L, Blumen HM, Launay CP, Liu-Ambrose T, Helbostad JL, Verghese J, Beauchet O, Brain structure covariance associated with gait control in aging, *J. Gerontol. A Biol. Sci. Med. Sci*, 74 (2018) 705–713.
- [30]. Holzschneider K, Wolbers T, Röder B, Hötting K, Cardiovascular fitness modulates brain activation associated with spatial learning, *NeuroImage*, 59 (2012) 3003–3014. [PubMed: 22027496]

Figure 1.

Spatial task followed a Simon/Stroop paradigm. Bars and arrows were presented relative to a fixation point ('+' sign) centered on the screen. For bars, participants were instructed to press one of two fiber optic keys depending on the location of the bars (left or right) relative to the fixation point. All participants were asked to use their right hand. For arrows, participants had to identify congruency or incongruency. Congruent arrows were those that pointed in the same direction as the arrow's location relative to the fixation point, while incongruent arrows were those that pointed in the opposite direction of their location relative to the fixation point.

	Hemi- sphere	Gait Speed	Cluster Size (voxels)	Peak Coordinates			z- score
				X (mm)	Y (mm)	Z (mm)
Left	Preferred Pace	307	-44	24	40	5.12*
	838 voxels
Left	Fast Walking Over Obstacles	355	-50	16	42	4.83*
	838 voxels
Bilateral	Fast Pace	1528	2	-66	42	5.80*
	2459 voxels
Bilateral	Fast Walking Over Obstacles	1545	-2	-62	58	5.93*
	2459 voxels
Bilateral	400m Walk Time	1090	-2	-62	58	4.77*
	2459 voxels						

Figure 2.

Brain maps displaying clusters of voxels that significantly (*, $p < 0.01$) correlated with preferred or fast pace gait speed after adjusting for age. XYZ coordinates reflect the peak z-value within each cluster. White regions represent the masks used to analyze the correlations. The orange regions represent clusters of voxels (within each mask) that correlate with gait speed. Analysis was performed using FSL feat models with defined masks described in the text (see Imaging Processing).

Figure 3.

Scatter plots showing the relationship between task-related brain activation measured using BOLD fMRI and preferred pace (upper panel) and fast pace (lower panel) gait speed when adjusted for age using partial correlation, thus residuals are shown.

Table 1.

Participant characteristics (N=20).

	Mean $\pm$ SD	Range
Age (y)	71 $\pm$ 5	63–80
Height (cm)	169 $\pm$ 8	152–184
Weight (kg)	68 $\pm$ 13	43–90
Body mass index (kg/m ²)	23 $\pm$ 2	16–27
Blood glucose (mg/dL)	94 $\pm$ 8	79–110
<i>Spatial Simon/Stroop Task</i>		
Incongruent accuracy (%)	77 $\pm$ 30	7–100
Incongruent reaction time (ms)	1234 $\pm$ 183	950–1505
Left middle frontal gyrus (%)	10 $\pm$ 16	–9–39
Right superior parietal lobe (%)	8 $\pm$ 8	–4–24
Bilateral precuneus (%)	14 $\pm$ 19	–15–61
Bilateral superior lateral LOC (%)	16 $\pm$ 14	–12–43
<i>Gait Speed (m/s)</i>		
Preferred pace	1.38 $\pm$ 0.20 ^a	1.03–1.76
Preferred pickup object	1.11 $\pm$ 0.14 ^b	0.83–1.42
Fast pace	1.88 $\pm$ 0.22	1.49–2.26
Fast over obstacles	1.61 $\pm$ 0.20 ^a	1.25–1.98
400m walk time (s)	251 $\pm$ 23	210–286

Brain regions are BOLD percent signal change during incongruent trials over bars. LOC, lateral occipital cortex.

^a, slower than fast pace gait speed (p<0.001)

^b, slower than preferred pace gait speed (p<0.001)

Table 2.

Unadjusted Pearson correlation coefficients for the relationship between gait performance and neurocognitive function.

	Preferred Pace	Preferred Pickup Object	Fast Pace	Fast Over Obstacles	400m Walk Time
Accuracy	0.40	0.40	0.59 *	0.61 *	-0.73 *
Reaction time	-0.06	0.01	0.20	-0.05	-0.23
<i><u>Regional BOLD</u></i>					
Left middle frontal gyrus	0.50 *	0.25	0.27	0.44 *	-0.31
Right SPL	0.34	0.07	0.47 *	0.48 *	-0.39
Bilateral precuneus	0.26	0.19	0.45 *	0.40	-0.44 *
Bilateral superior LOC	0.25	0.11	0.47 *	0.46 *	-0.46 *

BOLD, blood oxygen level-dependent; SPL, superior parietal lobe; LOC, lateral occipital cortex.

*, $p < 0.05$.