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Callosal Hyperintensities and Gait Speed Gain from Two Types of Mobility Interventions in Older Adults

Neelesh K. Nadkarni, MD, PhD, FRCPC¹, Subashan Perera, PhD¹, Stephanie A. Studenski, MD, MPH¹, Caterina Rosano, MD, MPH², Howard J. Aizenstein, MD, PhD³, and Jessie M. VanSwearingen, PhD, PT, FAPTA⁴

¹Division of Geriatric Medicine and Gerontology, Department of Medicine, University of Pittsburgh, Pittsburgh, PA

²Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA

³Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA

⁴Department of Physical Therapy, University of Pittsburgh, Pittsburgh, PA

Abstract

Objective—Corpus callosum, the largest white matter tract in the brain, is prone to small-vessel disease in older adults. White matter hyperintensities (WMH) are neuroimaging markers of small-vessel disease. WMH in the genu and splenium of the corpus callosum are associated with slow gait in older adults. We assessed whether the volume of callosal hyperintensities in the genu and splenium of older adults with mobility impairment are differentially associated with degree of gain in gait speed following two types of gait interventions.

Design—Single-blind randomized control trial of two types of gait exercises in older adults.

Setting—Research center in an academic institution.

Participants—Ambulatory adults aged 65 and older with a slow and variable gait.

Intervention—12-week physical therapist guided trial of a conventional walking, endurance, balance and strength (WEBS) intervention (n=20) vs a timing and coordination of gait (TC) intervention (n=22).

Main outcome measure—Gain in gait speed following intervention and its relationship to callosal hyperintensities in the genu and splenium of corpus callosum.

Results—Gait speed improved in the WEBS (mean change, 0.16m/s) and TC groups (mean change, 0.21m/s), both $p < 0.05$. WMH volume in the genu was differentially associated with gait speed gain (Group x genual WMH interaction, $p = 0.05$). Greater genual WMH volume was related to a smaller gait speed gain in the WEBS ($p = 0.01$) but not in the TC ($p = 0.1$) group. Splenial WMH volume was not differentially associated with gait speed gain (interaction, $p = 0.9$).

Conclusion—Callosal hyperintensities differentially influence gait speed gain by type of gait rehabilitation. Mobility impaired older adults with genual hyperintensities may benefit from a rehabilitation program focused on motor-skill learning rather than on strength and endurance training.

Keywords

corpus callosum; white matter hyperintensities; cognition; mobility; gait rehabilitation

Corpus callosum is the largest white matter tract in the brain that connects both cerebral hemispheres and is important for mobility control. On brain MRI of older adults, small-vessel disease appears as white matter hyperintensities (WMH), which are commonly seen in the corpus callosum and these callosal hyperintensities are of potential clinical significance.^{1, 2} Callosal hyperintensities located in the anterior portion of the corpus callosum, referred to as genu (GCC),^{1, 3} and posterior portion of the corpus callosum, referred to as splenium (SCC),⁴ are independently associated with mobility impairments in older adults. Furthermore, callosal hyperintensities involving the GCC are also implicated in executive functions and processing speed deficits,⁵ which in turn are linked with slow and variable gait in older adults.⁶

Walking is a learned motor skill that integrates bilateral stepping patterns, trunk movements and shifts in the center of body mass across phases of gait in accordance with changes in the environment and intent. This multisystem integration relies on interhemispheric connections. Callosal hyperintensities can disrupt interhemispheric connectivity which can impede walking speed in older adults,^{1, 3, 4} and may interfere with the integration of the bilateral stepping pattern with posture and phases of gait. Callosal hyperintensities in critical areas such as in the genu can impair motor-skill and planning of movement,¹ and might affect the timing and coordination of gait. We examined whether specific callosal hyperintensities were differentially related to response to two types of gait rehabilitation; a traditional program of walking, endurance, balance and strength (WEBS) versus a program of motor-control learning that focuses on timing and coordination of gait (TC).^{7, 8}

METHODS

This is a secondary analysis of a 12-week single-blind randomized controlled trial data of two interventions aimed at improving mobility in community-dwelling older adults with mobility impairment.⁷ The participants were ambulatory adults, 65 years or older, with slow (0.6m/s and 1.0m/s) and variable (coefficient of variation of step-length of greater than 4.5% or step-width less than 7% or greater than 30%) gait.⁷ The interventions were protocol driven and were conducted by trained physical therapists. Gait speed pre- and post-intervention was measured by assessors who were blinded to the intervention arm assignment. All study personnel were blinded to participants' MRI findings. Severity of small-vessel disease was assessed by quantifying WMH volumes, which were normalized to total brain volume (sum of grey matter, white matter and cerebrospinal fluid) to adjust for age-related brain atrophy using previously published methods.⁸ These included separation of brain from skull and underlying soft-tissue and an automated-histogram based WMH

segmentation on T2-FLAIR. We also overlaid a white matter atlas on the WMH segmentation FLAIR images to determine boundaries of the GCC and SCC. This analysis was limited to those participants who completed a brain MRI prior to the intervention. We focused on gait speed as outcome measure because gait speed is associated with fronto-parietal WMH burden and is also linked to adverse outcome in older adults.^{6, 9} Gait speed was averaged over two traverses across a 4m long automated walkway, the GaitMatII (EQ Inc., Chalfonte, PA). All procedures followed standard protocol and in full compliance of the institutional review board of the University of Pittsburgh.

We fit linear models with gait speed change as the dependent variable; intervention type, callosal hyperintensities (each GCC and SCC) and their interaction term as independent variables; and baseline gait speed as a covariate. The statistical significance of interaction term was used as evidence for a differential association. SAS[®] version 9.3 (SAS Institute, Inc., Cary, North Carolina) was used for statistical analysis.

RESULTS

The two groups were similar in demographic, baseline physical and cognitive measures (Table 1). Gait speed improved in both groups (0.21 m/sec in TC and 0.16 m/sec in WEBS group, $p=0.03$). WMH volume in the GCC was differentially associated with improvement in gait speed by type of intervention ($p=0.05$). For every 0.01% difference in the proportion of WMH in the GCC there was a reduction in the gain in gait speed of 0.038 m/sec (regression coefficient $\beta = -388.535$, $p=0.012$, Figure 1a) with the WEBS intervention but not with the TC intervention (regression coefficient $\beta = -80.887$, $p=0.091$). WMH volume in the SCC did not interact with intervention related gait speed gain in WEBS or the TC groups ($p=0.9$, Figure 1b).

As a sensitivity analysis we reanalyzed the data after excluding three outliers and the results did not appreciably change – increasing WMH volume in the GCC was still associated with significant reduction in gain in gait speed in the WEBS intervention ($p=0.014$) but not the TC group ($p=0.119$).

DISCUSSION

In older adults with mobility impairments undergoing gait rehabilitation, callosal hyperintensities in the genu but not the splenium are differentially associated with gait speed gain depending on type of gait rehabilitation. In those with greater callosal hyperintensities in the genu, a gait intervention based on timing and coordination rather than endurance and strength, may be particularly beneficial to improving walking speed.

The anterior and posterior parts of the corpus callosum play a differential role in the interhemispheric integration of stimuli. The fibers in the GCC include those connecting frontal lobes involved in motor planning^{3, 10} while the SCC includes those connecting occipito-parietal lobes involved visuo-perceptual functions,^{4, 10} which are together crucial to limb positioning, guidance and trajectory of the body while walking. In older adults with genual hyperintensities, rehabilitation of mobility using a motor-skill learning approach may

influence timing and coordination of gait and may benefit gait speed more than an endurance and strength training approach.

Study limitations

A limitation of this study is that the range of WMH in the GCC was smaller in the WEBS group as compared to the TC group. However, their physical performance measures including baseline gait speed and cognitive measures were comparable in both groups. Another limitation of the methodology is that we could not account for WMH in interweaving fibers that could potentially lie at the boundaries of GCC and SCC. Finally, the original study was powered to test for differences in gait variability measures.⁷ Despite the potentially low power for this analysis the findings that interventions outcomes may relate to small-vessel disease burden in the genu that connects bilateral frontal lobes are interesting and worthy of further research.

CONCLUSION

The results suggest that the location and burden of callosal hyperintensities in older adults may need to be considered while choosing the type of gait rehabilitation in this populations. These findings provide new information that small-vessel disease in interhemispheric tracts that carry fibers connecting frontal brain regions are of relevance to rehabilitation of mobility impairments in older adults. Such studies open avenues for individualized gait therapy in older adults and may provide some insight as to why outcomes of gait rehabilitation may differ between older individuals. These findings should be confirmed in larger studies targeting older adults who have mobility limitations associated with callosal small-vessel disease.

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- Figure 1a: Genu of corpus callosum **- Figure 1b: Splenium of corpus callosum** **Figure 1.**

Differential association between improvement in gait speed and location of callosal hyperintensities burden for the two mobility intervention arms (Timing and Coordination (TC): closed circles, Walking, endurance, balance, strength (WEBS): open diamonds).

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Table 1

Baseline group characteristics (WEBS: walking, endurance, balance strength training; TC: timing and coordination training).

	WEBS group	TC group	P value/chi-square
N	20	22	
Age, years	78 ± 5	76 ± 6	0.2
Female, n (%)	11 (55%)	19 (82%)	0.1
Black, n (%)	2 (10%)	4 (17%)	0.7
Comorbidities, Index (mean ± (SD))	2 ± 1	3 ± 1	0.2
Geriatric Depression Scale, 0 to 15 (mean ± (SD))	1.9 ± 1.4	1.5 ± 1.3	0.6
Mini-Mental Status Examination, 0 to 30 (mean ± (SD))	29 ± 1	29 ± 1	0.3
Trails B time, (sec, mean ± (SD))	129 ± 56	122 ± 73	0.9
Short Physical Performance Battery, 0 to 12, mean ± (SD))	8 ± 2	9 ± 2	0.3
Pre-intervention gait speed (m/sec, mean ± (SD))	0.82 ± 0.12	0.87 ± 0.12	0.1