Imaging Markers of Cerebral Small Vessel Disease are Associated with Slower Gait and Cognitive Complaints in Older Adults

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BACKGROUND

- Gait disturbances reliably predict dementia and mobility disability in older adults[1].
- Cerebral small vessel disease (CSVD) affects the small arteries, venules, and capillaries of the brain – and is common in older adults.
- Motoric cognitive risk (MCR) syndrome is defined as having slow gait and subjective cognitive complaints and is a strong predictor of all-cause dementia, especially vascular dementia[2].
- Imaging markers of CSVD include white matter hyperintensities (WMH) and lacunes. These markers are associated with poor outcomes such as cognitive and gait decline.
- To date, what brain regions affected by CSVD are associated with these outcomes is poorly understood.

OBJECTIVES

- To identify brain regions affected by CSVD that are associated with gait speed, cognitive complaints, and MCR.
- To test whether those with more severe WMH burden are more likely to have slow gait, cognitive complaints, and MCR.

METHODS

This study included multiple cohorts of older, community-dwelling adults without dementia from 4 countries. Images were rated by two independent raters, JV and GA. Multivariable linear regression was used to calculate regression coefficients and logistic regression was used to obtain adjusted odds ratio for the risk of having CSVD markers and cognitive complaints, slow gait, and MCR. Finally, Pearson's chi square test was used to measure the association between confluent-diffuse WMH and the above-mentioned outcomes. All models were adjusted for cohort, age, sex, history of diabetes, hypertension, and stroke and p-values from the chi-square analyses were corrected for multiple comparison testing.

RESULTS

Table 1. Cohort Demographics. M=mean. SD=standard deviation.

	All Cohorts	USA	Australia	India	Japan
N	1772	122	383	179	1088
Age, years M±SD	71.1±6.8	78.7±6.4	72.2±7.1	68.9±5.5	70.3±6.4
Sex, male	50.1%	54.1%	43.3%	63.7%	51.2%
Hypertension	45.88%	29.8%	49.6%	51.9%	45.4%
Diabetes	16.3%	9.1%	12.5%	43.6%	13.9%
Stroke	5.6%	0%	7.8%	7.8%	4.4%
Gait velocity, cm/s M±SD	107.6±24.1	102.6±19.7	113.2±22.4	74.6±23.0	111.6±20.1
Presence of WMH	69.5%	69.5%	48.0%	86.6%	72.2%
Presence of Lacunes	13.3%	21.3%	14.1%	8.4%	13.0%
Slow Gait	15.2%	10.3%	12.0%	21.2%	15.8%
Cognitive complaints					
iADLs	22%	4.9%	4.2%	12.9%	31.7%
GDS memory item	31.8%	4.1%	9.4%	38.6%	41.5%
Any Cognitive Complaint	41.4%	9.0%	11.5%	44.7%	55%
MCR					
MCR/iADLs	4.6%	0%	1.6%	6.7%	5.9%
MCR/GDS memory item	4.8%	0%	1.6%	8.4%	5.8%
Any MCR	7.3%	0%	2.4%	10.1%	9.4%

Table 2. Associations between regional and global WMH score and gait speed, slow gait, cognitive complaints, and MCR.

	Gait Speed β*, (95% CI), p-value	Slow Gait (aOR*), (95% CI), p-value	Cognitive Complaints, (aOR), (95% CI), p-value	MCR (aOR), (95% CI), p-value
Frontal	**-1.40 cm/s, (-2.19, -.61), <0.001**	1.08, (0.98, 1.22), 0.12	1.07, (0.98, 1.16), 0.14	**1.25, (1.08, 1.44), 0.003**
Parieto-occipital	-.71 cm/s, (-1.41, -.002), 0.050	1.03, (0.94, 1.14), 0.52	1.03, (0.95, 1.11) 0.51	1.11, (0.97, 1.26), 0.12
Temporal	**-1.57 cm/s, (-2.80, -.33), 0.013**	0.98, (0.83, 1.71), 0.89	1.14, (0.99, 1.33) 0.054	1.05, (0.84, 1.33) 0.63
Basal Ganglia	-1.14 cm/s, (-2.31, .02), .054	1.05, (0.90, 1.24), 0.48	**1.17, (1.03, 1.33), 0.019**	1.22, (.99, 1.49) 0.065
Infratentorial	-.29 cm/s, (-2.27, 1.67), 0.77	0.91, (0.68, 1.21) 0.52	**1.38, (1.10, 1.73) 0.005**	1.29, (0.85, 1.97) 0.23
Global	**-.46 cm/s, (-.75, -.17) 0.002**	1.02, (0.98, 1.06), 0.38	**1.04, (1.01, 1.07), 0.028**	**1.07, (1.01, 1.12), 0.015**

Table 3. Associations between regional and global lacune score and normal pace walking (NPW) velocity, slow gait, cognitive complaints, and MCR.

	Gait Speed β*, (95% CI), p-value	Slow Gait (aOR*), (95% CI), p-value	Cognitive Complaints, (aOR), (95% CI), p-value	MCR (aOR), (95% CI), p-value
Frontal	0.92 cm/s, (-2.88, 4.73), 0.64	0.92, (0.56, 1.51), 0.74	1.38, (0.85, 2.24), 0.20)	1.06, (0.60, 1.88), 0.84
Parietal	**-6.78 cm/s, (-12.3, -1.25), 0.016**	1.50, (0.84, 2.67) 0.17	0.96, (0.54, 1.70), 0.89	1.69, (0.93, 3.07) 0.087
Temporal	-1.53 cm/s, (-11.75, 8.69), 0.77	0.71, (0.10, 5.14), 0.74	1.24, (0.34, 4.57), 0.75	**N/A**
Occipital	-4.25 cm/s, (-12.00, 3.50), 0.28	1.62, (0.65, 3.99), 0.29	1.30, (0.55, 3.07), 0.55	1.39, (0.42, 4.61), 0.59
Total Cortical	-1.60 cm/s, (-4.29, 1.08), 0.24	1.13, (0.84, 1.54), 0.43	1.18, (0.87, 1.62), 0.28	1.24, (0.88, 1.14), 0.22
Basal Ganglia	-1.24 cm/s, (-3.99, 1.51), 0.38	1.26, (0.92, 1.75), 0.16	**1.43, (1.04, 1.97) 0.028**	**1.57, (1.08, 2.27), 0.018**
Total Deep	-.35 cm/s, (-1.93, 1.23), 0.71	1.11, (0.91, 1.39), 0.31	**1.28, (1.05, 1.56), .012**	1.28, (0.99, 1.67), 0.059
Infratentorial	-1.34 cm/s, (-7.46, 4.77), 0.94	0.97, (0.41, 2.31), 0.95	1.16, (0.52, 2.60), 0.71	0.54, (0.088, 3.31), 0.51
Global	-.73 cm/s, (-1.77, .31), 0.17	1.05, (0.92, 1.99), 0.47	**1.21, (1.06, 1.38) 0.004**	1.16, (0.98, 1.38), 0.077

*β=regression coefficient. aOR=adjusted odds ratio. Linear and logistic regression models were adjusted for age, sex, cohort (study site), hypertension, diabetes, and stroke history.

Figure 1. Parietal and basal ganglia lacunes on FLAIR imaging. Figure on the left shows a left- sided parietal region lacune. Figure on the right shows a left-sided basal ganglia lacune. Indicated by blue arrows.

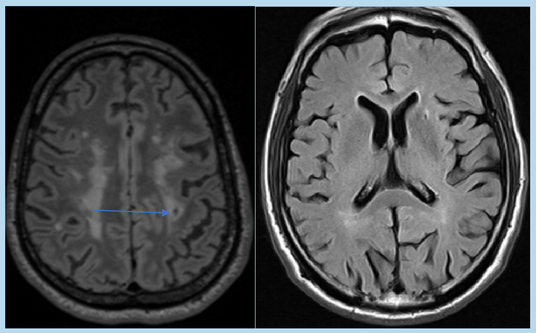

Figure 2. Representative images of bilateral frontal and parieto-occipital confluent-diffuse WMHs on FLAIR imaging indicated by blue arrows.

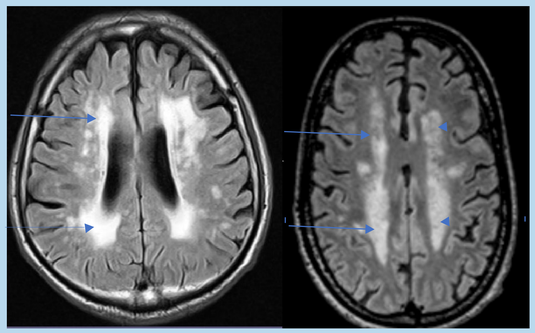

Table 4. Presence of severe WMH score (total rating>10), global and regional confluent-diffuse WMH and slow gait, cognitive complaints, and MCR.

	Slow Gait		p-value*	Cognitive Complaints		p-value*	MCR		p-value*
	Yes	No		Yes	No		Yes	No	
N	268	1497		730	1035		129	1643	
Presence of Confluent-Diffuse WMH	**25.8%**	**19.0%**	**0.012**	**23.1%**	**17.9%**	**0.008**	**30.2%**	**19.2%**	**0.003**
Frontal	16.0%	11.4%	0.03	**14.7%**	**10.2%**	**0.004**	**20.2%**	**11.4%**	**0.003**
Parieto-occipital	19.0%	14.2%	0.04	17.1%	13.4%	0.03	22.5%	14.4%	0.01
Temporal	2.6%	1.9%	0.47	2.3%	1.8%	0.47	3.9%	1.9%	0.12
Basal Ganglia	3.4%	2.6%	0.49	3.0%	2.5%	0.52	3.9%	2.6%	0.40
Infratentorial	0%	0.47%	0.26	0.4%	0.4%	0.94	0%	0.43%	0.46
Overall Severe	7.1%	4.8%	0.13	6.1%	4.5%	0.13	**10.1%**	**4.8%**	**0.009**

*Pearson's chi-square test for categorical variables. Bonferroni correction for multiple testing (corrected alpha=.05/3=.017).

CONCLUSIONS

- Frontal WMHs associated with slower gait speed
- Basal ganglia and infratentorial WMHs associated with increased risk of cognitive complaints
- Frontal and basal ganglia WMHs associated with increased risk of MCR
- Lacunes in basal ganglia associated with increased risk of cognitive complaints and MCR
- Those with confluent-diffuse WMH in the frontal lobes more likely to have cognitive complaints and MCR
- CSVD may underlie pathogenesis of MCR in some older individuals
- Those with slow gait and cognitive complaints may benefit from interventions aimed at reducing CSVD risk

REFERENCES

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