ASYMMETRY OF WHITE MATTER HYPERINTENSITY BURDEN AND POTENTIAL DIFFERENTIAL RELATIONSHIPS WITH COGNITION

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BACKGROUND

White matter hyperintensities (WMH) are a prominent feature in normal aging, dementia and Alzheimer's disease [1].

WMH are thought to be a downstream effect of small vessel disease and reflect pathological changes that may affect cognitive functioning [2].

Generally speaking, WMH tend to form symmetrically over time in the human brain. However, in certain individuals, there appears to be substantial asymmetry of WMH burden.

PURPOSE & HYPOTHESIS

The aim of this study was to examine differential cognitive deficits seen with highly asymmetrical lesions.

We hypothesized that asymmetrical lesions would result in greater cognitive deficits in function relating to the affected hemisphere.

METHODS

Fifty-five subjects from the Sunnybrook Dementia study have been included from a variety of neurodegenerative vascular disease states.

- 19 subjects with Left (L) > Right (R) WMH burden (mean volume difference = 6.36cc)
- 9 subjects with R>L WMH burden (mean volume difference = 8.45cc)
- 27 subjects with symmetric WMH burden (L/R volumes did not differ by more than +/- 1cc, mean volume difference = 0.27cc)

Neuropsychological Testing [3]:

Visuospatial: (predominantly right lateralized function) Benton Judgement of Line Orientation (BJLO) test

Language: (predominantly left lateralized function) Boston Naming (BN) test

Non-verbal abstract reasoning: (predominantly non-lateralized function) Ravens Progressive Matrices (RPM) test

MRI-derived volumetrics:
WMH burden and regional volumetrics were obtained using the previously validated pipelines Semi-Automatic Brain Region Extraction (SABRE) [4] and Lesion Explorer [5].

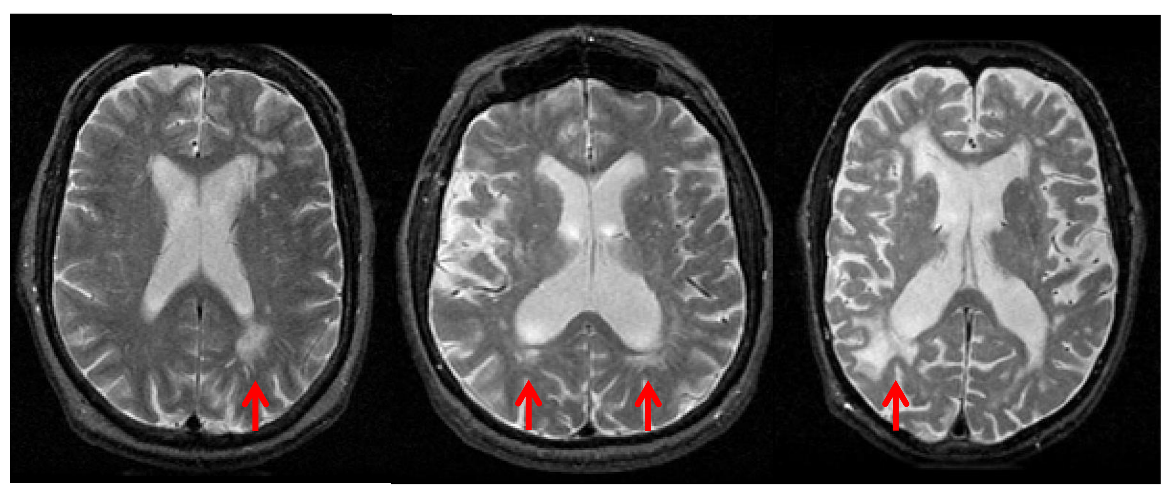

Figure 1. T2 MRI depicting left lateralized WMH burden, (left), symmetric WMH burden (middle), right lateralized WMH burden (right).

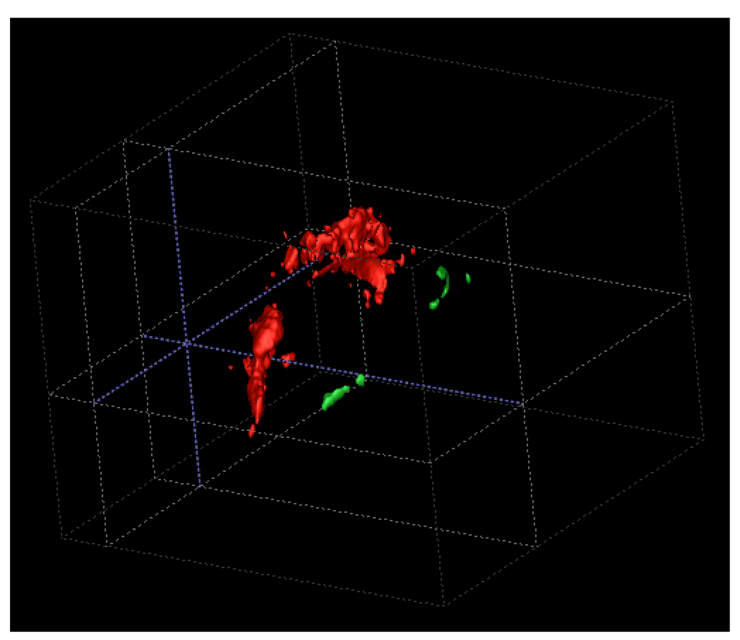

Figure 2. 3D rendering of WMH in right lateralized subject (69 year old male, NC).
Left hemisphere=green, right hemisphere=red
Note: Image is displayed in neurological convention and rotated obliquely.

ANALYSIS

Brain behaviour relationships were analyzed using bivariate Spearman's correlation. All WMH volumes were corrected by supra-tentorial intracranial capacity (STIC).

RESULTS

There was no significant difference between groups for years of education, sex or STIC.
L>R group was significantly older (p<0.05).

Table 1. Demographics: L>R, R>L and symmetric groups

	L>R (n=19)	R>L (n=9)	Symmetric (n=27)	p
Demographics				
Age (years)	80.0±6.0	76.1±9.5	74.2±7.3	*
Education (years)	13.8±3.9	13.2±2.2	13.7±3.4	ns
Sex (males)	10	5	15	ns

Data is presented as Mean±SD
*p<0.05

The L>R group had significantly more WMH (p=0.000), while the R>L group had significantly larger WMH asymmetry (p=0.000).

Table 2. Volumetrics and neuropsychological testing scores: L>R, R>L and symmetric groups

	L>R (n=19)	R>L (n=9)	Symmetric (n=27)	p
Volumetrics				
STIC (cc)	1292.6±111.5	1238.4±156.2	1269.5±124.6	ns
WMH (cc)	38.2±18.5	33.5±13.9	19.1±11.1	***
Left Hemisphere WMH (cc)	22.3±9.0	12.5±6.6	9.5±5.5	***
Right Hemisphere WMH (cc)	15.9±9.6	21.0±7.5	9.5±5.6	***
Frontal lobe WMH (cc)	14.1±6.8	11.9±7.0	8.0±5.5	**
WMH asymmetry (cc)	6.4±2.6	8.4±2.7	0.01±0.4	***
Cognition				
BJLO	18.1±9.0	17.0±8.9	19.9±10.3	ns
BN	19.3±7.8	22.0±5.4	21.1±7.8	ns
RPM	22.9±9.7	21.6±5.3	26.3±8.4	ns

Data is presented as Mean±SD
Raw volumes are presented for illustrative purposes
**p<0.01, ***p<0.001

The L>R group showed significant negative correlations between L (Spearman ρ=-0.54, p<0.05), R (Spearman ρ=-0.59, p<0.05), and total (Spearman ρ=-0.58, p<0.05) WMH volume and RPM performance.
The R>L and the symmetric groups showed no significant correlations with neuropsychological testing.

Table 3. Group analysis, correlation between L>R, R>L and symmetric groups and neuropsychological testing

	L>R (n=19)			R>L (n=9)	Symmetric (n=27)
	L WMH	R WMH	WMH		
Cognition					
BJLO	ns	ns	ns		
BN	ns	ns	ns	ns	ns
RPM	*	*	*		

Data is presented as Mean±SD
Raw volumes are presented for illustrative purposes
*p<0.05

DISCUSSION

Asymmetric WMH burden does not appear to selectively impact language and spatial cognition in this preliminary sample.

Those with greater left hemisphere WMH burden had a more significant correlation with overall cognition, but this could potentially relate to their overall greater global WMH burden.

The relationship between the L>R group and RPM may be explained by the overall greater WMH burden when compared to the R>L group.
The L>R group has more frontal lobe WMH than the R>L group (ns), which may contribute to the poor RPM performance.

It is possible that with a larger sample size the relationship between other cognitive functions and lateralized WMH may become significant.

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