MRI White-Matter Hyperintensities and Neuropsychological Performance in a Young Adult Clinical Sample

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Introduction

- White matter hyperintensities (WMH) are patchy areas of increased signal intensity in cerebral white matter detected on MRI[1].
- WMH tend to proliferate with age, and although more common in older adults, they are also identified in young, non-demented and normal aging individuals[2]
- Findings regarding the cognitive sequela associated with WMH in younger samples are mixed.
- Some studies have found decreased performance on measures of processing speed/attention, memory, working memory, and some aspects of executive functioning in young adults with WMH, though typically with less severity than older adults[3,4]
- Other researcher has found that WMH were not associated with cognition in those aged 20-59[5].
- The purpose of this study is to investigate the clinical significance of WMH and neuropsychological performance in a young adult clinical sample.

Method

- Dataset included 607 patients that underwent comprehensive neuropsychological evaluation at OHSU Hillsboro Health in Hillsboro, OR
- Two groups were selected based on MRI results: 1) normal (*n* = 50 (30 females), M_{age} = 46.20, M_{edu} = 15.16) and 2) WMH without other MRI abnormality (*n* = 35 (20 females), M_{age} = 47.83, M_{edu} = 14.24)
- Exclusion criteria included dementia, other brain neuropathology (e.g. stroke, neurodegeneration, traumatic brain injury, multiple sclerosis, etc.), below normal scores on performance validity tests, & age >59.
- Neuropsychological index scores were calculated for five cognitive domains. See table 1.

Table 1. Neuropsychological Tests and Cognitive Domains

Domain	Measures
Language	Boston Naming Test; Controlled Word Association Test: FAS & Animals; WAIS-Vocabulary, Complex Ideational material
Visual Spatial/ Construction	WAIS-Block Design; Rey-Osterrieth Complex Figure (RCFT)
Attention/ Processing Speed	Digit Span Forward & Backward; WAIS-Arithmetic; WMS-III Spatial Span Forward & Backward; D-KEFS Trails Number & Letter
Memory	WMS-Logical Memory I & II; WMS Visual Reproduction I & II; CVLT-II Total & Long Delay Free Recall; RCFT Delayed Recall
Executive Functions	WAIS-Matrix Reasoning; WAIS Similarities; Wisconsin Card Sorting (% persev errors percentile & % errors percentile); D-KEFS Trails Switching

Main Measures

Table 2. Base Rate Clinical Range Performance

Domain		*Well Below Average*	*Below Average*	*Low Average*	*Average*	*Above Average*	*χ2*	*p-value*
Language	WMH	0%	6%	9%	59%	26%	1.11	.78
	Non-WMH	0%	6%	16%	50%	28%		
Visual-spatial/construction	WMH	3%	11%	9%	54%	23%	4.07	.40
	Non-WMH	0%	6%	6%	48%	40%		
Attention/Processing Speed	WMH	3%	9%	14%	71%	3%	8.07	.09
	Non-WMH	0%	4%	10%	63%	22%		
Memory	WMH	0%	20%	14%	46%	20%	5.64	.13
	Non-WMH	0%	4%	16%	58%	22%		
Matrix Reasoning	WMH	3%	15%	15%	27%	39%	8.37	.08
	Non-WMH	0%	4%	4%	32%	60%		
Similarities	WMH	0%	9%	15%	24%	53%	1.59	.66
	Non-WMH	0%	6%	9%	34%	51%		
D-KEFS Trails Switching	WMH	10%	7%	13%	47%	23%	3.43	.49
	Non-WMH	5%	7%	14%	33%	42%		
WCST Composite	WMH	15%	10%	5%	30%	40%	4.68	.32
	Non-WMH	5%	14%	5%	52%	24%		

Table 3. Odds Ratios

Domain	Z-score cut-off -1.67 OR (95% CI)	*p-value*	Z-score cut-off -1.00 OR (95% CI)	*p-value*
Language	4.52 (0.18-114.36)	.36	0.56 (0.10-3.08)	.51
Visual-spatial/Construction	6.19 (0.66-58.03)	.11	2.81 (0.75-10.49)	.12
Attention/Processing Speed	2.97 (0.26-34.10)	.38	3.93 (0.94-16.39)	.06
Memory	1.45 (0.20-10.85)	.71	2.13 (0.71-6.40)	.18
Similarities	0.26 (0.01-5.67)	.39	1.80 (0.50-6.47)	.37
Matrix Reasoning	4.60 (0.46-46.32)	.20	8.44 (1.69-42.22)	.01*
D-KEFS Trails Switching	1.95 (0.48-7.97)	.35	1.59 (0.52-4.86)	.41
WCST Composite	1.06 (0.28-4.05)	.93	1.22 (0.35-4.27)	.75

Results

- Independent samples t-test revealed statistically significant group differences at $p < .05$ for: Block Design, $t(81) = 2.47$, $p = .02$, $d = .55$; Spatial Span Backward, $t(80) = 2.16$, $p = .03$, $d = .49$; Digit Span Backward, $t(69) = 2.04$, $p < .05$, $d = .49$; DKEFS Trails Number, $t(53) = 3.19$, $p < .001$, $d = .78$; DKEFS Trails Letter, $t(72) = 2.53$, $p = .01$, $d = .59$; and Matrix Reasoning, $t(54) = 2.15$, $p = .04$, $d = .52$. Effect sizes were small to medium and ranged from .49 – .78.
- Neuropsychological index scores were calculated for five cognitive domains (Table 1) and then categorized in the following clinical ranges: well below average = z-score $\leq$ -2.35; below average = z-score -2.34 to -1.3; low-average = z-score -1.29 to -0.67; average = z-score -0.66 to 0.66; above average = z-score $\geq$ 0.67. A chi-square analysis was run comparing base rates across these clinical ranges for the WMH and normal groups., No significant differences were found in any cognitive domain (table 2).
- Odds ratios for each cognitive domain were calculated to determine the odds of a person with WMH having an impaired score relative to a person without WMH, using z-score cut-offs of -1.67 and -1.00. Results indicated that individuals with WMH were eight times more likely of having an index z-score $\leq$-1.00 on Matrix Reasoning, a visually presented test of reasoning (*OR* = 8.44, *p* = .01, 95% CI: 1.69-42.22). Odds ratios were not significant at the -1.67 or -1.00 z-score cut-offs for any other cognitive domain, though a trend was nearing statistical significance at the -1.00 z-score cut-off on attention/processing speed tests (p = .06). See table 3.

Conclusions

- Similar to prior research, the WMH group's neuropsychological test performance differed, with effect sizes ranging from .49-.78.
- However, mean scores were within the average range for both groups on virtually all tests, suggesting differences have limited clinical applicability to the individual patient with WMH on MRI.
- Base rate comparisons showed no statistically significant differences among the proportion of these two groups within any clinical ranges. However, a trend was observed in the proportion of the WMH group in low average to below average ranges on attention/processing speed tests (*p* = .09), and on an executive function test of reasoning (*p* = .08).
- Odds ratios indicate individuals with WMH are 8 times more likely to have a score below average, in the 5th-16th percentile range, on a visually presented test of reasoning. However, they are no more likely than normals to have substantially below average scores less than the 2nd percentile
- Taken together, these findings indicate that even in young adult clinical samples, WMH may represent subtle decline in attention/processing speed, and an increased probability of mild inefficiency/decline on some aspects of executive functioning.

References

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