White matter hyperintensities affect activities of daily living differently across dementias-The Sunnybrook Dementia Study

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BACKGROUND

- Loss of functional independence is a feature of all dementia diagnoses.
- White matter hyperintensities (WMHs) are associated with functional impairment in dementia, but this association has mostly been studied in relation to Alzheimer's Disease (AD).

OBJECTIVE

- To investigate if WMHs predict activities of daily living (ADL) in a cohort of dementia patients with AD or Dementia with Lewy Bodies (DLB) combined.
- To test if the association between WMHs and ADLs is influenced by clinical diagnosis of dementia.

METHODS

Setting: the Sunnybrook Dementia Study

Study population:

- Cross-sectional analysis: 277 dementia patients (AD=227, DLB=50)
- Longitudinal analysis ~1.5 years: 164 dementia patients (AD=136, DLB=28)

Predictor variables:

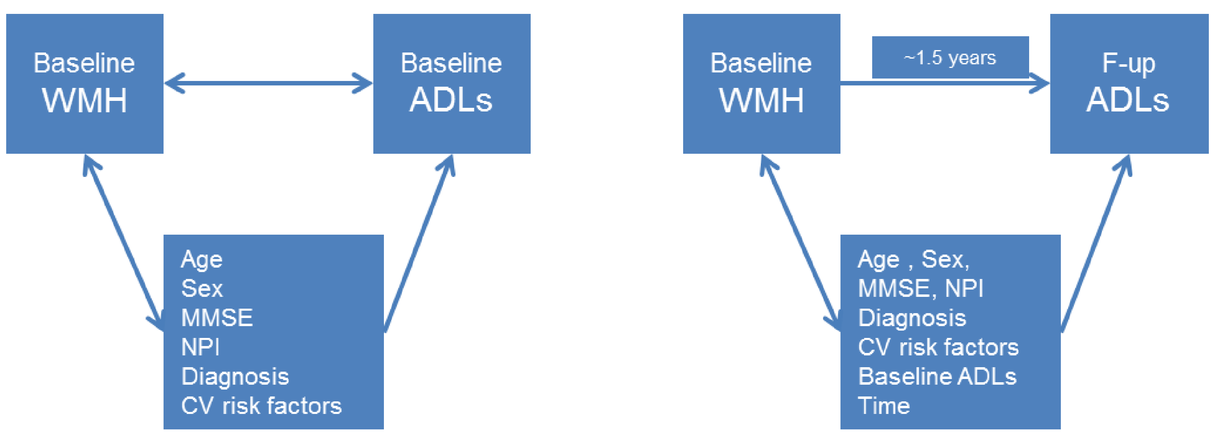
- WMH:
- Standardized volumetric MRI-total (deep and periventricular) WMHs quantified by semiautomatic segmentation using Lesion Explorer.
- Covariates: age, sex, hypertension, diabetes, stroke, hyperlipidemia, global cognition (Mini-Mental-State Examination-MMSE), neuropsychiatric symptoms (Neuropsychiatric-Inventory), and clinical dementia diagnosis (AD and DLB).
- Longitudinal analyses also adjusted for baseline ADLs and time between two ADL assessments.

Outcome variables:

- ADLs:
- Assessed by Disability Assessment for Dementia (DAD) Scale
- Basic ADL (BADL) and Instrumental ADL (IADL)
- Component scores for BADL and IADL: Planning, Initiation, and Action
- Total score (planning, initiation, and action) calculated by taking the score in each category and dividing by the max potential score.

Statistical analysis:

- Multiple linear regression models
- Interaction between WMH and diagnosis tested
- Both cross-sectional and longitudinal analyses repeated stratified for diagnosis, i.e. in AD and DLB groups.



Secondary analyses:

- Associations tested separately for periventricular and deep WMH
- Using component BADL and IADL scores as outcomes

REMARKS

- Despite lower WMH burden in DLB, associations of WMHs with ADLs were stronger in DLB group than in the AD group.
- WMHs possibly interact with DLB pathology differently than with AD pathology consequently influencing functionality.
- Motor deficits and balance problems may have a role in observed associations in the DLB group.
- Preventive strategies for WMHs may result in some preservation of function in dementia patients, particularly in patients with DLB.

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RESULTS

Table 1: Baseline characteristics of the study population.

CHARACTERISTICS	DESCRIPTIVES			
	Total sample	AD	DLB	P-value
	N=277	n=227	n=50	
Age	70.8 (10)	72 (9.6)	65.7 (10.4)	**<0.001**
Women	145 (52.3)	124 (54.6)	21 (42)	0.11
Education, years	14.2 (3.8)	14.1 (3.8)	14.4 (3.9)	0.17
MMSE, score	23.6 (4.2)	23.4 (4.2)	24.6 (4.1)	**<0.001**
NPI, score	12.3 (13.6)	10.7 (12.9)	19.6 (14.1)	**<0.001**
WMH cm3	6.0 (8.3)	6.6 (8.9)	3.2 (4.1)	**<0.001**
Deep	0.76 (1.0)	0.8 (1.0)	0.5 (0.8)	**<0.001**
Periventricular	5.2 (7.8)	5.8 (8.4)	2.6 (3.5)	**<0.001**
Stroke	21 (7.6)	17 (7.5)	4 (8)	0.90
HTN	95 (34.3)	79 (34.8)	16 (32)	0.71
Diabetes	31 (11.2)	26 (11.4)	5 (10)	0.77
Hyperlipidaemia	96 (34.7)	75 (33)	21 (42)	0.23
BADL, score	93.1 (12.6)	93.7 (11.9)	90.8 (14.9)	**0.0004**
IADL, score	70.4 (25.7)	71.3 (26.2)	66.5 (22.8)	**0.003**

Values are means (standard deviation) or counts (percentage)
P-values are based on T-tests for continuous and Chi2 tests for categorical variables

- Interaction between WMH and diagnosis <0.01

TABLE 2: Cross-sectional association of WMH and ADLs.

	ACTIVITIES OF DAILY LIVING			
	ALZHEIMER'S DISEASE n=227		DEMENTIA WITH LEWY BODIES n=50	
	Difference (95% CI)	P-value	Difference (95% CI)	P-value
Basic activities of daily living				
WMH	-0.60 (-1.67,0.46)	0.27	-3.40 (-6.88,0.08)	0.05
Instrumental activities of daily living				
WMH	-0.30 (-2.40,1.81)	0.78	-2.96 (-8.27,2.34)	0.26

TABLE 3: WMH and risk of decline in function.

	ACTIVITIES OF DAILY LIVING			
	ALZHEIMER'S DISEASE n=136		DEMENTIA WITH LEWY BODIES n=28	
	Difference (95% CI)	P-value	Difference (95% CI)	P-value
Basic activities of daily living				
WMH	-0.65 (-2.86,1.56)	0.56	-8.15 (-16.08,-0.23)	**0.04**
Instrumental activities of daily living				
WMH	-0.24 (-3.11,2.63)	0.87	-10.08 (-18.43,-1.71)	**0.02**

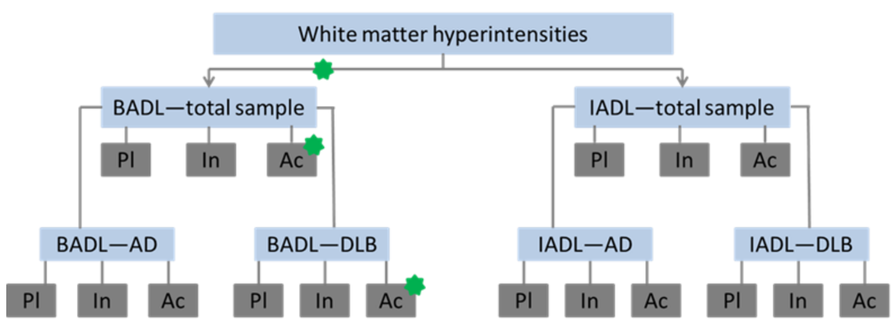
All models are adjusted for age, sex, education, MMSE, NPI, prevalent stroke, hypertension, hyperlipidaemia, and diabetes mellitus type 2. Longitudinal models additionally adjusted for baseline ADL score and time between the two ADL assessments.

POST-HOC RESULTS

- Associations were driven by periventricular WMHs
- Analyses with component ADL scores, i.e. Planning (Pl), initiation (In) and action (Ac) showed that:

- Cross-sectional association between WMH and ADL in DLB group was largely driven by the **Action** component
- Longitudinal association between WMH and ADL in DLB group was driven by all components

Cross-sectional



Longitudinal