NORMAL APPEARING WHITE MATTER MICROSTRUCTURAL CHANGES AND NEUROPSYCHIATRIC SYMPTOMS IN ALZHEIMER'S DISEASE

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BACKGROUND

- Neuropsychiatric symptoms (NPS) are common in Alzheimer's Disease (AD) [1-2]
- Increases in NPS lead to lower functional outcome, faster progression of the disease, and increased cost of care [2-5]

PURPOSE & HYPOTHESIS

Purpose: To investigate the relationship between NPS and white matter microstructural integrity while accounting for concomitant small vessel disease (SVD)

METHODS

MRI imaging was acquired on 1.5T GE Signa scanner

- 12 direction DTI (3mm)
- T1-weighted (AX 3D SPGR, 1.2-1.4mm)
- Proton density (PD) and T2-weighted (T2) (interleaved axial dual-echo spin echo, 3mm)

Neuropsychological measures:

- Dementia Rating Scale (DRS) – to measure global cognitive function
- Neuropsychiatric Inventory (NPI)
- Behavioural Pathology in Alzheimer's Disease (BEHAVE-AD)

PARTICIPANTS

- Participants with AD (n=38) were selected from Sunnybrook Dementia Study
- Participants completed a comprehensive battery of cognitive tests
- Sample had less

IMAGE PROCESSING

DTI processing: Tools from the FMRIB Software Library (FSL) was used for all DTI processing [6] Pre-processing was performed using FDT (FMRIB's Diffusion Toolbox) for eddy current correction, brain extraction, and diffusion tensor fitting

WMH Volumetric Data: Tissue and lesion segmentation were obtained using the semi-automated brain region extraction (SABRE) method and Lesion Explorer [7]

RESULTS

Demographics	**Mean**	**SD**
Age	69.4	11
Education, years	13.9	3.7
Sex, n (% male)	19 (50)	--
Dementia Rating Scale, total score	116.6	16.3
MRI Volumetrics (cc)	**Median**	**IQR**
Normal appearing white matter	352.9	60.7
Normal appearing grey matter	513.2(40.0)	40.0
White matter hyperintensities	2.6(7.8)	7.8
Sulcal cerebrospinal fluid	255.9(88.4)	88.4
Ventricular volume	43.6(27.9)	27.9
NPS-DTI Sig. Correlations (p<0.05)	**Mean FA**	**Mean MD**
BEHAVE-AD Activity Disturbances	-0.332	0.338
BEHAVE-AD Overall Rating	-0.414	0.259
NPI Aberrant Motor Behaviour	-0.332	0.350

Table 1. Demographics, MRI volumetrics in cubic centimeters (cc) and NPS-DTI significant spearman correlations

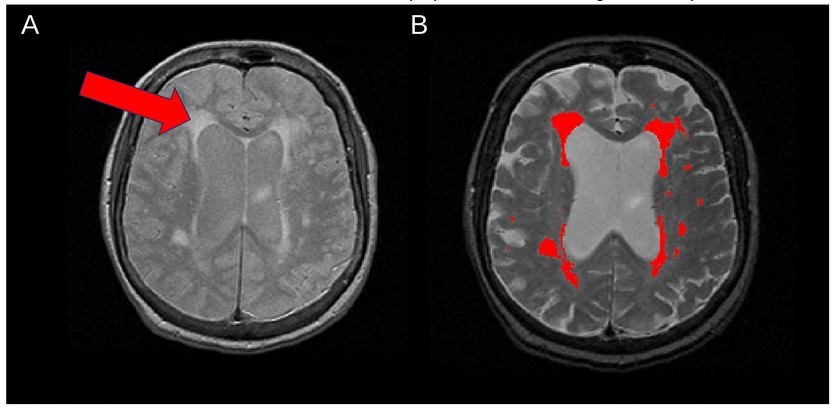

Fig. 1 – Coregistered MRIs of an Alzheimer's disease patient with moderate degree of SVD. (A) Shows an axial image of PD with red arrow pointing to WMH (B) Shows an axial image of T2-weighted with the WMH segmentation overlayed in red

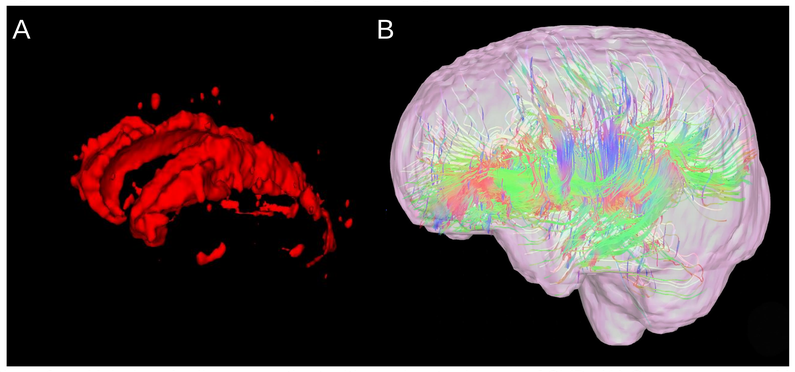

Fig. 2- 3D visualization of an Alzheimer's disease patient with moderate degree of SVD. (A) Shows a saggital image of a 3D volume of WMH. (B) Shows DTI microstructural integrity of white matter tracts with a 3D overlay of the cortex

DISCUSSION

- Previous studies have found that SVD burden is associated with deficits in executive and motor function [8]
- Results suggest that degradation of the brain's white matter tracts results in decreased overall connectivity, potentially disrupting normal motor behaviour and activity in AD patients
- Future studies examining region specific white matter tracts may reveal additional relationships with other NPS in AD patients with small vessel disease
- Future findings may yield potential therapeutic targets to improve the functional outcomes and reduce the various NPS that are common in AD
- The sample used in this study had 2.6cc of WMH compared to the average WMH in the SDS which is 10.4cc. These results may represent a sample with mild SVD burden

LIMITATIONS

- DTI was limited to 12 directions.
- We did not examine specific tracts. Region specific analyses should yield valuable information
- Due to the nature of AD, NPS data was only obtained from informants

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