

# DECREASED WHITE MATTER TRACT INTEGRITY IN ALZHEIMER'S DISEASE WITH SMALL VESSEL DISEASE BURDEN

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## BACKGROUND

- Subcortical White Matter Hyperintensities (WMH) on MRI are commonly used biomarkers of cerebral small vessel disease (SVD) burden that is linked to the progression of dementia and cognitive decline [1-3].
- WMH are typically observed in Alzheimer's disease (AD) and as such are considered an indicator of vasculopathy in AD [1-3].
- Previous studies indicate that decreased activation of the default mode network (DMN) can be used a biomarker for AD, the main WM tract connecting brain regions involved being the cingulum tract (Fig. 2) [4-6].

## PURPOSE & HYPOTHESIS

**Purpose:** To investigate the regional features of WM microstructural integrity and the potential relationship with co-morbid SVD in AD using diffusion tensor imaging (DTI) metrics.  
**Hypothesis:** Microstructural integrity will be impaired within DMN tracts of AD patients with high WMH burden.

## 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).

## PARTICIPANTS

Participants were selected from Sunnybrook Dementia Study (see Table 1). AD (n=62) patients were dichotomized from the median value of global WMH in the sample (Fig. 1). Normal controls (NC: n=45) were also collected for comparison. Groups were divided as follows:

- AD *low* WMH (WMH: 0.0-3.3cc; n=31) Fig. 1a
- AD *high* WMH (WMH: 3.8-53.3cc; n=31) Fig. 1b

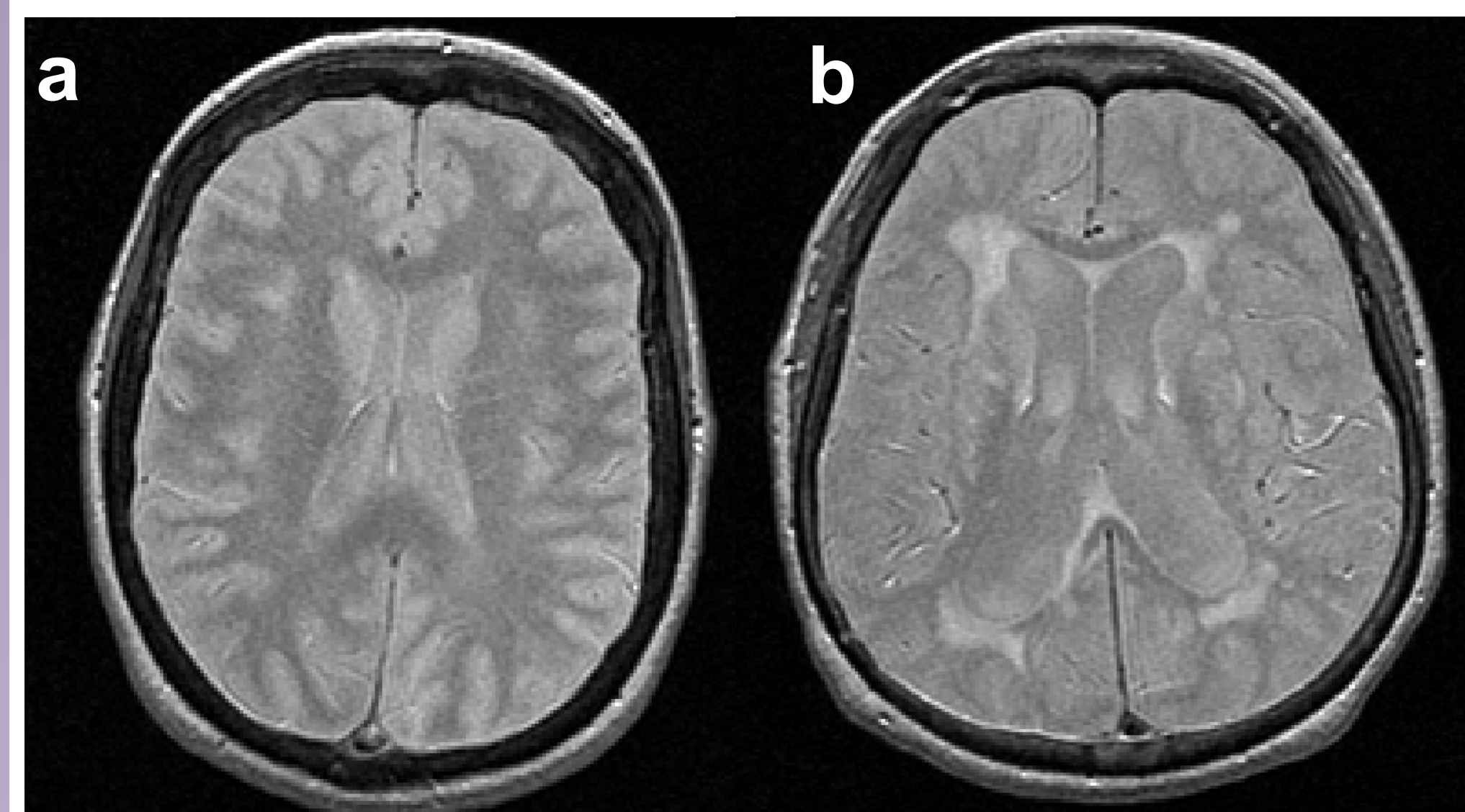


Fig 1: WMH of the AD groups (a) AD low WMH (b) AD high WMH

## IMAGE PROCESSING & ANALYSIS

**DTI processing:** Tools from the FMRIB Software Library (FSL) was used for all DTI processing [7]. Pre-processing was performed using FDT (FMRIB's Diffusion Toolbox) for eddy current correction, brain extraction and diffusion tensor fitting. Tract Based Spatial Statistics (TBSS) was used to visualize significant differences ( $p > 0.05$ ) in white matter tract integrity [8]. Alignment of white matter and FA maps were visually inspected by user. White matter tracts were located using the John Hopkins University White Matter Tractography Atlas [9].  
**WMH Volumetric Data:** Tissue and lesion segmentation were obtained using the semi-automated brain region extraction (SABRE) method and Lesion Explorer [10].

## RESULTS

Table 1 – Participant demographics and imaging volumetric data

	NC	AD low WMH	AD high WMH	p	significance
<b>Demographics<sup>1</sup></b>					
n	45	31	31	--	--
Age, y	69.9(8.0)	68.0(9.5)	76.8(8.6)	0.000	***
Sex, n (%) m	19.0(42.0)	17.0(54.8)	14.0(45.2)	0.448	n.s
Education, y	16.2(3.3)	13.7(3.6)	13.7(3.8)	0.002	**
MMSE/30	26.7(3.3)	25.1(4.6)	25.9(4.1)	0.243	n.s
<b>WMH Volumetrics<sup>1,2,3</sup></b>					
WMH	4.7(6.8)	1.3(1.0)	15.6(14.0)	0.000	***
pWMH	3.9(6.3)	0.9(0.8)	14.0(13.6)	0.000	***
dWMH	0.7(0.7)	0.4(0.3)	1.6(1.4)	0.000	***

Key: WMH=global WMH, pWMH=periventricular WMH, dWMH=deep white WMH;

<sup>1</sup> Values reported as mean(SD).

<sup>2</sup> All reported volumes are raw for illustrative purposes; analysis was performed on transformed data.

<sup>3</sup> Values reported in cubic centimetres.

\* $p > 0.05$ , \*\* $p > 0.01$  \*\*\* $p > 0.001$

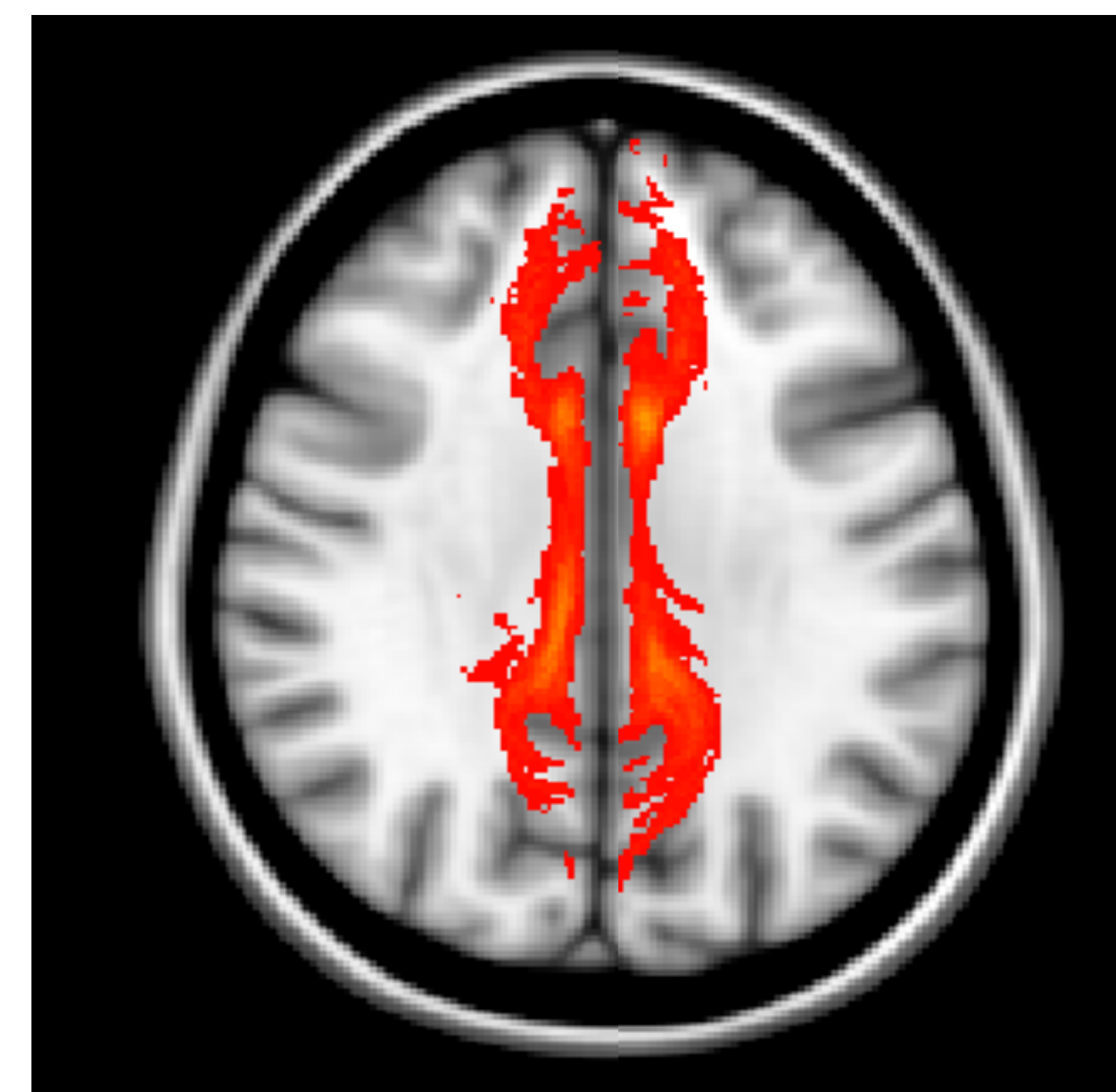


Fig. 2- The cingulum tract pictured in the John Hopkins University White Matter Tractography Atlas in FSLView 4.0.1

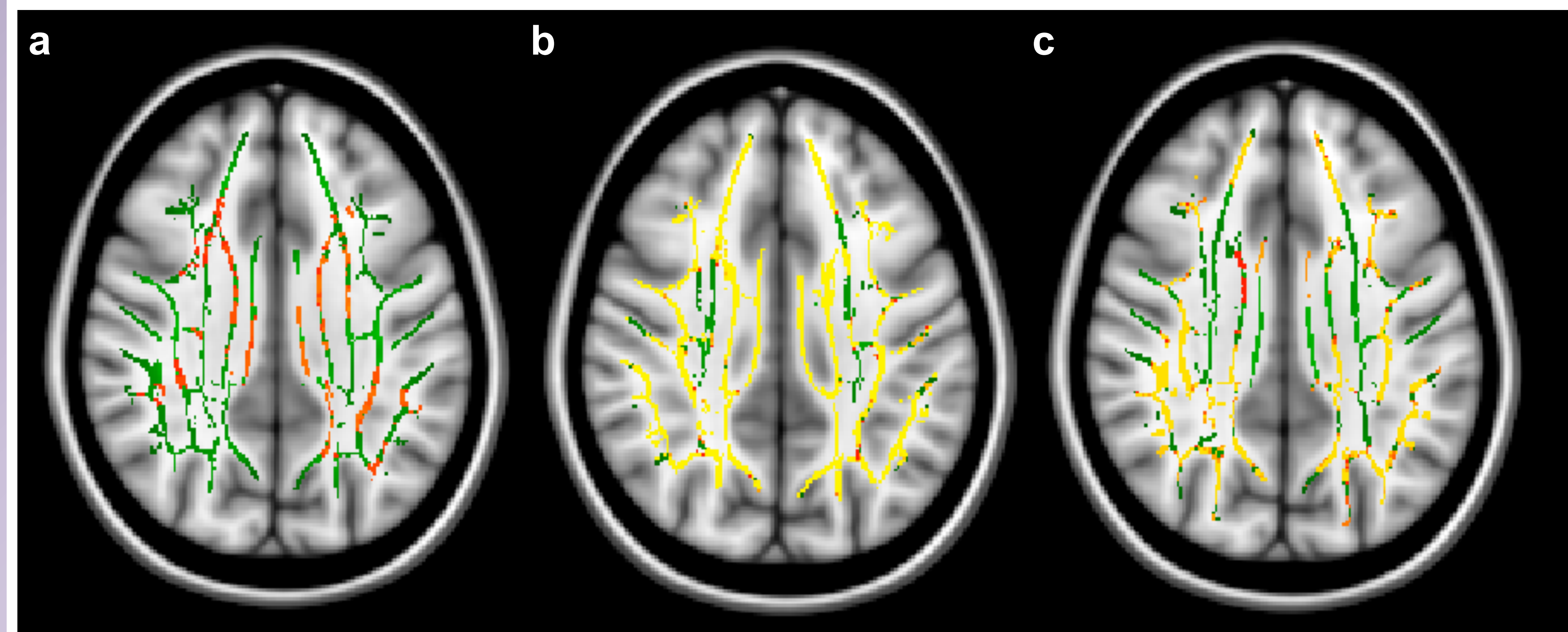


Fig. 3 - FA significance maps between the three groups. Green = non-significant difference in FA. Red-Yellow = significant difference in FA ( $p > 0.05$ ).

## DISCUSSION

- The cingulum tract showed a decrease in FA when comparing NC to both AD groups (Fig 3a and 3b).
- Furthermore, a significant decrease in FA of the cingulum tract was observed between AD *low* WMH and AD *high* WMH (Fig 3c)
- These results may suggest SVD burden in combination with AD could further contribute to decreased microstructural integrity of the cingulum tract and therefore be a potential correlate of decreased activation of the DMN.
- Future research will examine microstructural integrity longitudinally in AD patients with varying SVD burden to examine relationship integrity.

## LIMITATIONS

- Though the cingulum tract is spared from overlapping WMH that may influence FA other nodes of the DMN, such as anterior portions of the superior longitudinal fasciculus, may be affected.
- Future research would be required to examine all white matter tracts of the DMN individually.

## ACKNOWLEDGEMENTS

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