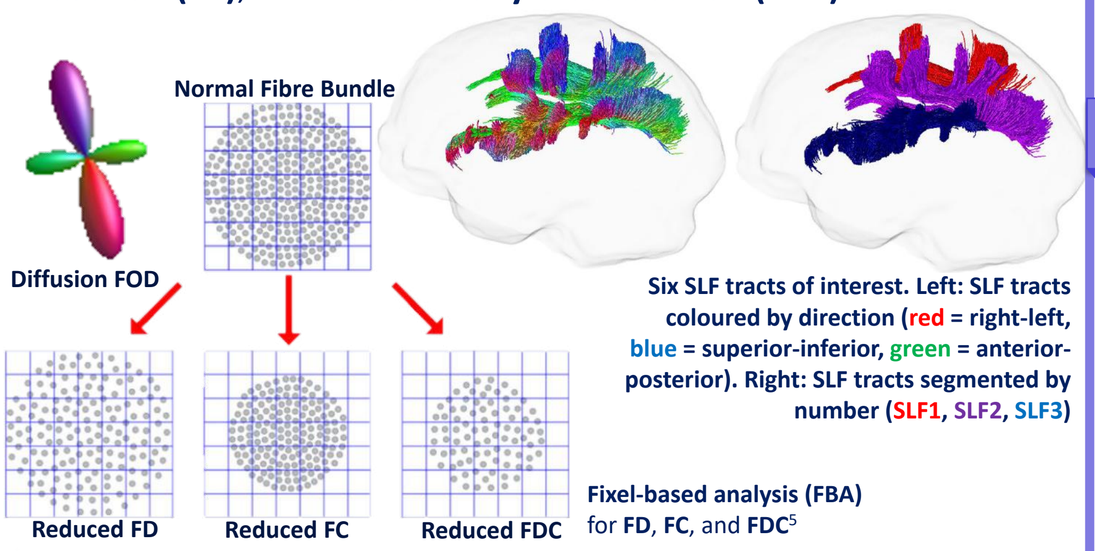
Poorer executive function is associated with lower white matter fibre density in the superior longitudinal fasciculus in groups at risk of Alzheimer's disease

Lenore T Tahara-Eckl[1,2], Reece Roberts[1,2], Catherine Morgan[1,2], Flavio Dell'Acqua[3], Ian Kirk[1,2], Tracy R Melzer[4,6], John C Dalrymple-Alford[4,5], Tim J Anderson[4,6], Nicholas J Cutfield[7], Lynette Tippett[1,2]

[1]School of Psychology, University of Auckland, New Zealand; [2]Centre for Brain Research, University of Auckland, New Zealand; [3]Forensic and Neurodevelopmental Sciences, King's College, London, England; [4]NZ Brain Research Institute, Christchurch, New Zealand; [5]School of Psychology, Speech and Hearing, University of Canterbury, Christchurch, New Zealand; [6]Department of Medicine, University of Otago, Christchurch, New Zealand; [7]Department of Medicine, University of Otago, Dunedin, New Zealand

Background

- **Alzheimer's disease (AD)** risk increases with:
  - age
  - **subjective cognitive decline (SCD)**[1]
  - **mild cognitive impairment (MCI)**
  - white matter (WM) degeneration[2]
- **Executive dysfunction**[3] and WM degeneration[2,4] may be early markers of AD
- The **superior longitudinal fasciculus (SLF)** tract modulates attention and executive function in ageing [5,6], but its role is not fully understood in AD
- Recently, WM tracts modeled through **fibre orientation density (FOD)**, can derive three properties: **fibre density (FD)**, **fibre cross-section (FC)**, and **fibre density cross-section (FDC)**[7].



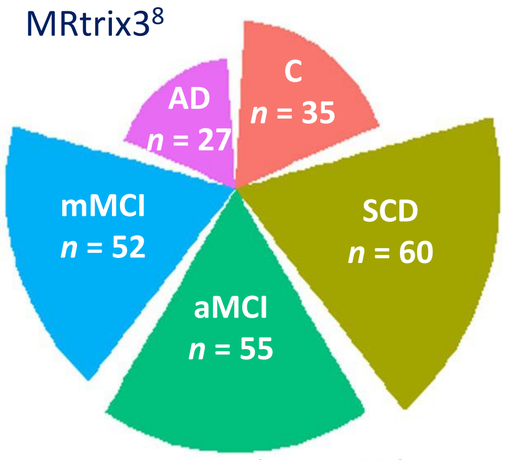
Methods

Participants. *n* = 229 (122 F, 69.75 ± 8.25 years), recruited from the **Dementia Prevention Research Clinic (DPRC)** over three sites: Auckland, Christchurch, Dunedin

Neuropsychological assessment.

Processing Speed	Inhibition
Hayling's Congruent Sentence Set 1	Hayling's Incongruent Sentence Set 2
Stroop Colour Naming	Hayling Category A Error
Stroop Word Reading	Hayling Category B Error
Trail Making Test A	Stroop Inhibition
	Category Switching
	Trail Making Test B

Image acquisition and preprocessing. Diffusion-weighted MRI (100 directions, b = 1000, 2000 s/mm^2). FOD estimation with multi-tissue constrained spherical deconvolution and FBA processed with MRtrix3[8]



C = Control; **SCD** = Subjective Cognitive Decline; **aMCI** = single-domain amnestic MCI; **mMCI** = multiple-domain amnestic MCI; **AD** = Alzheimer's disease

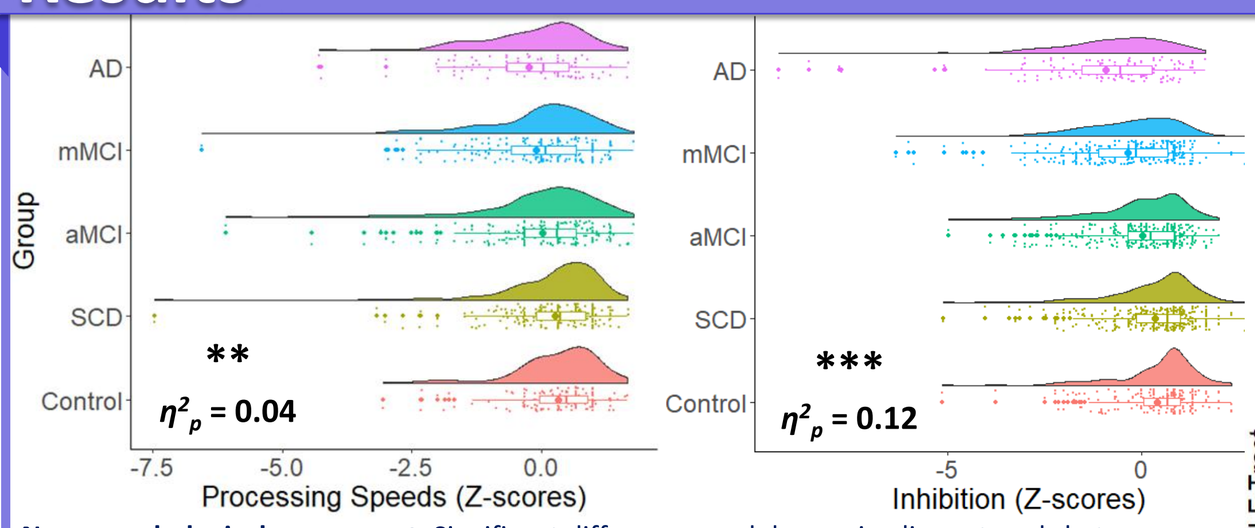
Five participant groups (total *n* = 229)

Research Questions

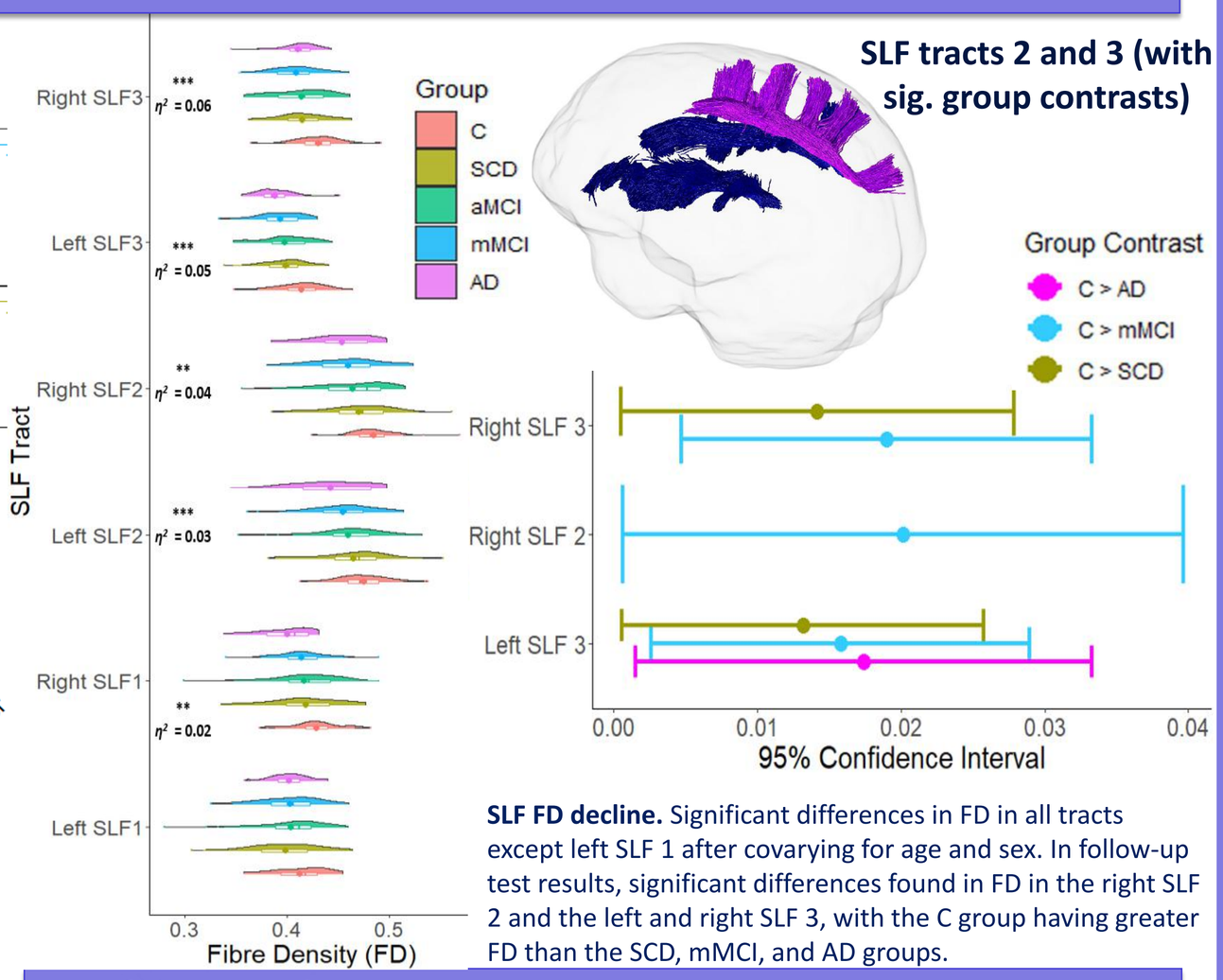
In groups at different levels of risk of AD…

1. Do measures of **processing speed** and **inhibition differ**?
2. Do **SLF fibre properties differ**?
3. Do the **SLF tracts correlate** with **processing speed** and **inhibition** measures?

Results



Neuropsychological assessment. Significant differences and decreasing linear trends between groups in processing speed and inhibition (accounting for age, sex, and education). Groups significantly differed in all individual tests except for Stroop Word Reading and Hayling's Congruent, Incongruent Sentences. Significant follow-up tests results were evident between most groups, but none were found between C and SCD.



SLF FD decline. Significant differences in FD in all tracts except left SLF 1 after covarying for age and sex. In follow-up test results, significant differences found in FD in the right SLF 2 and the left and right SLF 3, with the C group having greater FD than the SCD, mMCI, and AD groups.

Partial Least Squares. Significant association between FD in left SLF 2 and 3 tracts and inhibition but not processing speed after covarying for age and sex. All inhibition measures except Total Category Errors significantly contributed to the latent variable.

Discussion

1. **Inhibition** and **processing speed** impaired in MCI and AD groups
   - Standardised tests detect cognitive changes in impaired groups, and more so in inhibition than processing speed
2. **WM fibre density (FD)** in **SLF** differed between groups, but not FC, and little for FDC
   - Density, rather than volume of the fibre, steadily decreased between groups
   - While **C** and **SCD** groups had similar cognitive performance, the **SLF FD differed**. The **C** group had greater **SLF FD**, while the **SCD** group's **SLF FD** was more similar to the **MCI** and **AD** groups
3. **Inhibition**, and *not processing speed* significantly correlated with **FD** in the **left SLF 2** and **3**
   - The SLF plays a critical role in inhibition processes in AD risk cohorts

Conclusion

Our findings suggest that specific microstructural changes in the SLF, namely FD, may provide a very early biomarker of changes occurring in AD. Chiefly, individuals with subjective memory impairments showed FD changes before objective impairments were evident.

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