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Investigating individual variation in microstructural-cognition relationships in aging

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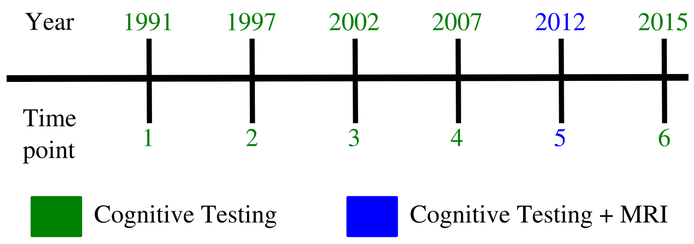
Introduction

We used data-driven, multivariate techniques to investigate microstructural correlates of cognitive performance in an aging population. Using shared patterns of microstructural-cognitive variation, we identify relationships between longitudinal cognitive performance trajectories, from mid to late life, and cortical microstructure in late life.

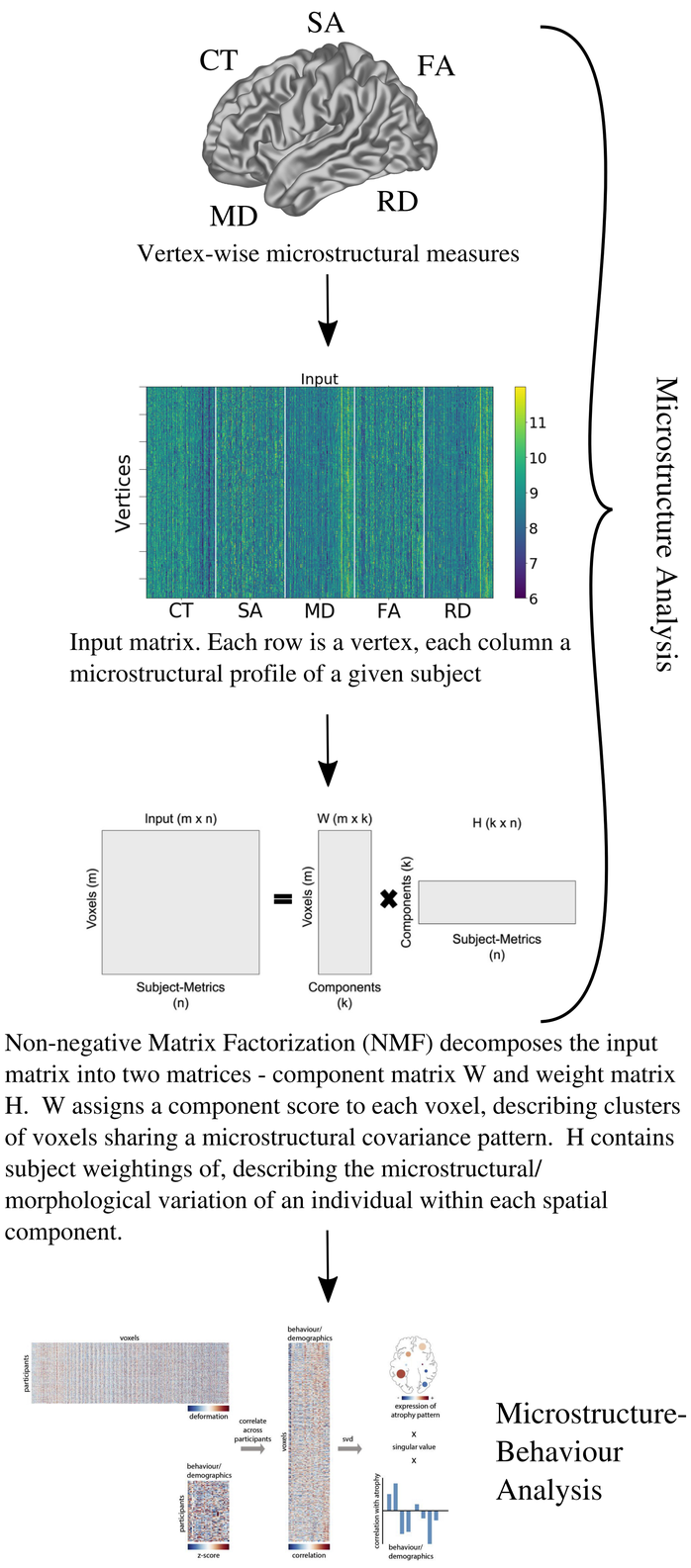
Methods

Data: We analyzed data from 398 subjects (mean age = 69.5 +/- 4.9, 92 females) of the Whitehall II Imaging Sub Study. Cognitive tests of semantic and lexical fluency, crystallized intelligence, verbal memory, and numeric and verbal reasoning were collected longitudinally at 6 time points. **Microstructure was assessed using vertex wise measures of cortical thickness (CT), surface area (SA), mean diffusivity (MD), fractional anisotropy (FA) and radial diffusivity (RD).**

Data Collection Timeline:



Workflow:



Results

A. NMF identified 10 spatially stable components of microstructural variation

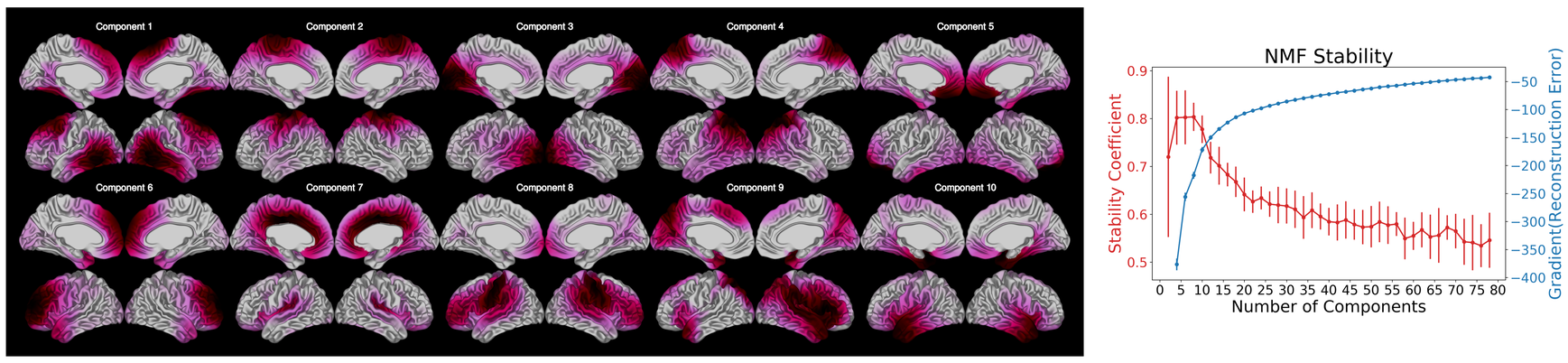


Figure 1: Spatial components of the 10 component NMF decomposition (left). Red areas indicate vertices loading heavily onto a particular component. Each component identifies a selection of vertices sharing a microstructural variance pattern. Together, components cover the entire brain, are largely bilateral and non spatially overlapping. The plot on the right shows split half stability coefficient and change in reconstruction errors for 2-80 component decomposition. To balance high stability (red line) while capturing major changes in accuracy (blue), 10 components was selected for further analysis.

B. Latent variable 1 (LV1) describes low baseline performance, fast memory decline, but stable fluency trajectories in relation to widespread SA decreases, localized decreases in CT and RD, and heterogenuous FA changes

C. LV2 describes slow reasoning decline, and low baseline memory associated with widespread SA increases but typical degeneration of anterior frontal regions

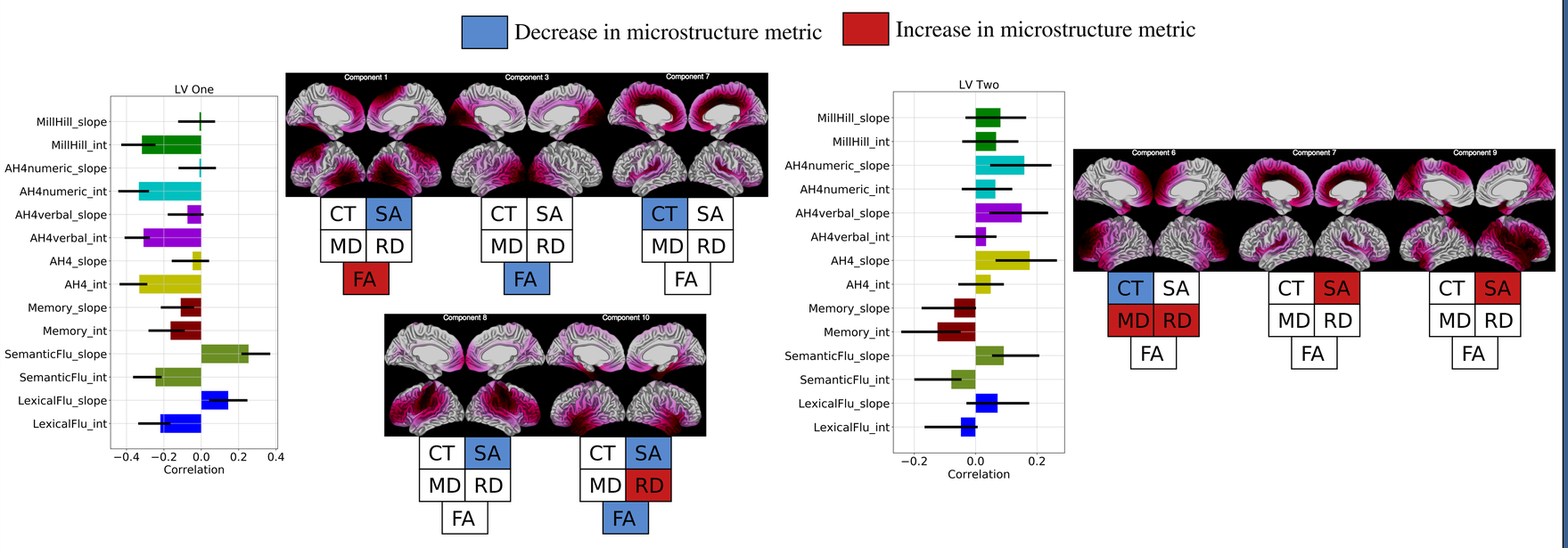


Figure 2: PLS analysis identified two significant latent variables ($p<0.05$), each identifying a pattern of correlation between microstructural NMF weightings, and cognitive intercept and slopes. Bar plots describe the contribution of cognitive intercepts and slopes in each LV. Error bars denote the 95% confidence interval, only variables with a non zero confidence interval are described as contributing to a given LV. For each bar plot, the cortical maps show the spatial patterns of the components contributing to the LV. The fingerprint of each map describes whether a given metric is identified as being decreased (blue), or increased (red) in the spatial component in relation to the cognitive pattern shown in bar plots.

D. LV groupings based on pos/neg splits of LV behaviour scores predict performance at future timepoint, on average 3.2 years post MRI collection. LV1 is the main determinant, with A and B groups performing worse than C and D. For reasoning tests, LV2 distinguishes between A vs B and C vs D.

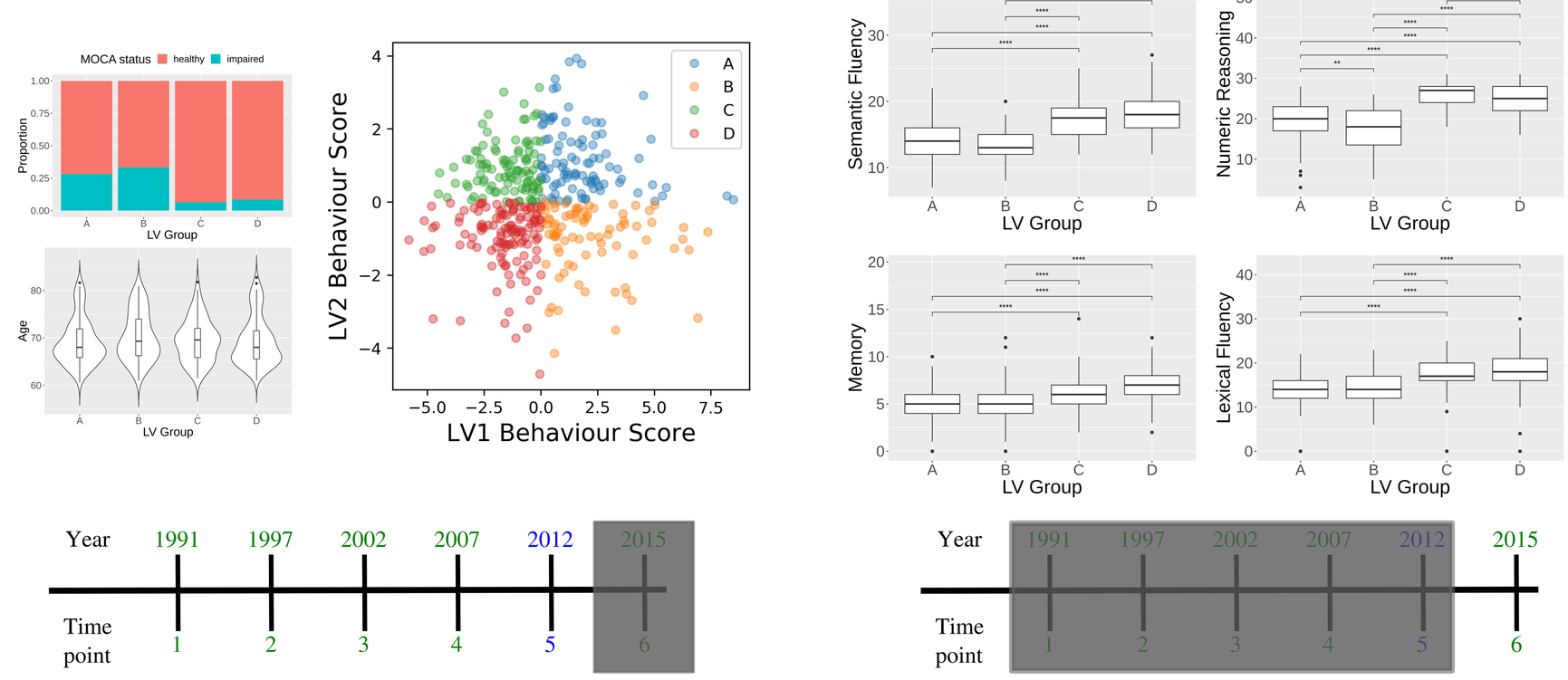


Figure 3: We used individual expression of LV1 and LV2 to predict cognitive performance at a future timepoint. On the left, a plot of LV1 vs. LV2 behaviour score for each individual, describing the degree to which they express the cognitive patterns identified in Results B and C. Using this data, we defined four groups as each pairwise combination of high/low LV1/LV2. These groups differed significantly in terms of MOCA status (X-squared = 35.359, $p<0.01$), but not age. On the right, we show that this data driven group assignment is predictive of future cognitive performance. Each box plot shows the timepoint 6 cognitive performance of each of the four LV groupings for tests of memory, fluency and reasoning. Significance is displayed, covarying for age and sex.

Conclusions

- our analysis identified complex, heterogenuous patterns of brain and behaviour variability
- Desirable microstructural features (eg increased FA) can be associated with undesireable behavioural traits (eg low baseline performance) and vice versa.
- groupings derived from data-driven microstructure-cognition relationships predictive of future (3 years) performance
- baseline performance (ie midlife) strongest predictor of late life performance, and slower decline unable to 'make up the difference'
- variable rates of decline impacted late life reasoning performance, but not other tests
- SA was most prevalent microstrucure feature in microstructure-cognition relationships

Acknowledgements

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