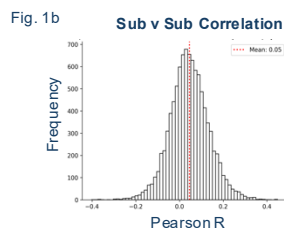
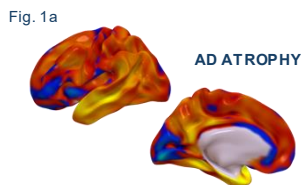


Visuospatial-related Atrophy in Alzheimer's Disease Predicts Functional Decline in an Independent Cohort

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Introduction

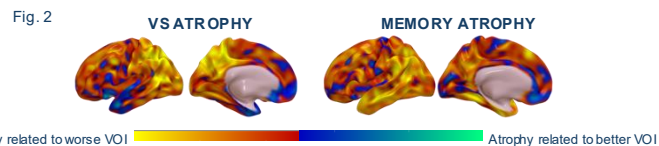


Functional decline and lack of independence in Alzheimer's Disease (AD) are frequently attributed to global disease burden or memory impairment^{1,2}.

- AD is highly heterogeneous¹, and visuospatial dysfunction may more specifically drive this loss of independence.
- Early intervention has shown that visuospatial deficits are potentially modifiable^{2,3}, yet their structural correlates remain under-utilized in prognosis⁴.

This study investigates the predictive value of a visuospatial-specific atrophy profile compared to standard markers of disease burden and memory loss in determining patient outcomes.

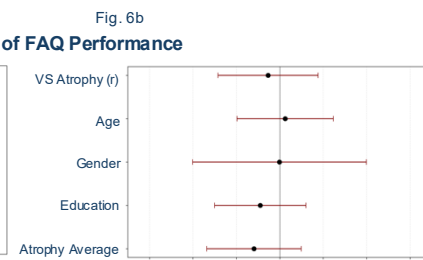
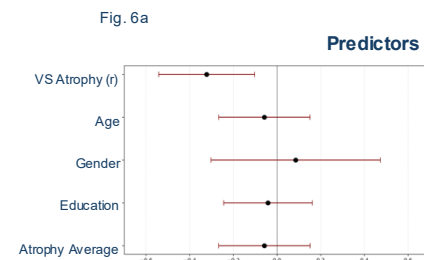
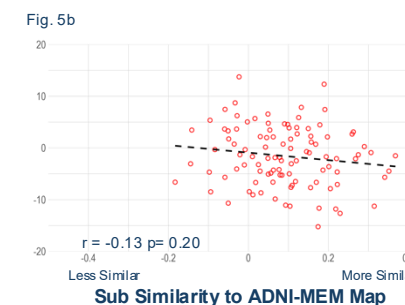
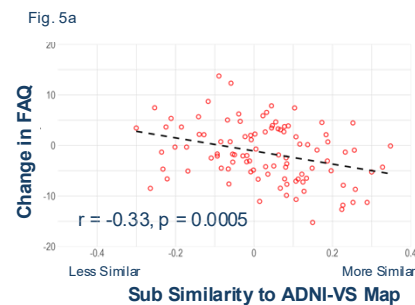
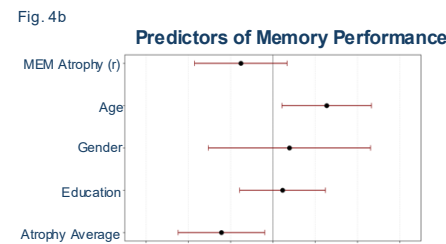
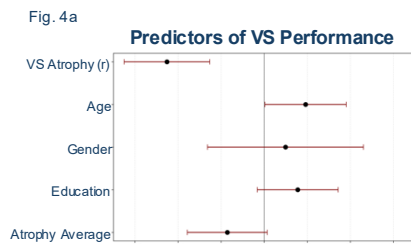
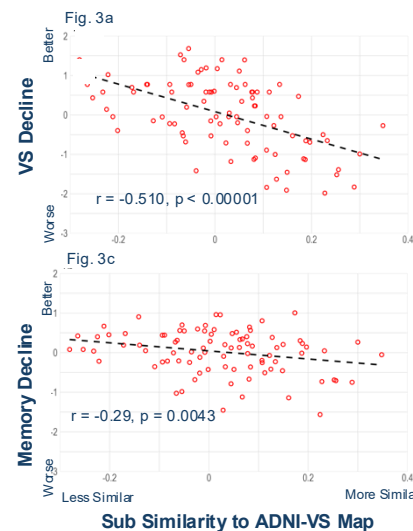
Methods



Using Alzheimer's Disease Neuroimaging Initiative ADNI2 data (n = 139), we mapped atrophy patterns causing deficits in visuospatial construction (VS) and verbal memory (MEM). These maps were then spatially correlated with individual subjects from an independent ADNI1 cohort (n = 92). We ran a linear regression to determine the relationship between each subject's spatial correlations and their two-year decline in visuospatial, memory, and functional (Functional Activities Questionnaire or FAQ) scores, while controlling for age, sex, education, and total atrophy burden.

Two-year decline was measured by regressing baseline scores from individual's two-year scores.

Results



- An individual's correlation to the group visuospatial map is significantly correlated to their change in FAQ total score, while this relationship is not captured by their correlation to the group memory map.
- Mixed effects model reveals that visuospatial-related atrophy is the only significant indicator of FAQ ($p < 0.05$).

Conclusions

- Visuospatial construction and FAQ scores serve as direct indicators of critical functional outcomes, including driving ability, independence, and safety. Our results reveal real-world functional metrics are best explained by visuospatial-related atrophy patterns, rather than general amnesic markers.
- While memory decline tracks closely with overall global disease burden, visuospatial-specific atrophy acts as a much more precise, frequently overlooked predictor of practical behavioral change.

References

- Phillips, M. L., Stage, Jr., E. C., Lane, K. A., et al. (2019). Neurodegenerative Patterns of Cognitive Clusters of Early-Onset Alzheimer's Disease Subjects: Evidence for Disease Heterogeneity. *Dementia and Geriatric Cognitive Disorders*, 48, 131–142.
- Cacho, J., García-García, R., Fernández-Calvo, B., et al. (2005). Improvement Pattern in the Clock Drawing Test in Early Alzheimer's 4 Disease. *European Neurology*, 53, 140–145.
- Katsumi, Y., Eckbo, R., Chapleau, M., et al. (2024). Greater baseline cortical atrophy in the dorsal attention network predicts faster clinical decline in Posterior Cortical Atrophy. *Alzheimer's Research & Therapy*, 16.

- While subjects' correlation to both the visuospatial ($r = -0.51$) and memory ($r = -0.33$) map showed significant relationships to visuospatial decline ($p < 0.05$), a Williams' test confirmed the **ADNI-VS map is a significantly better predictor of visuospatial decline than the ADNI-MEM map ($p = 0.04$)**. Conversely, individuals' decline in memory was correlated to both memory map correlation ($r = -0.32$) and visuospatial map ($r = -0.29$) correlation with no significant difference ($p = 0.96$).
- Mixed effects model reveals the atrophy correlation is the only significant predictor for visuospatial decline while total atrophy burden is the only significant indicator for memory decline