

Data-driven functional decline trajectories correspond to distinct brain perfusion imaging patterns

Sofia Michopoulou^{1,2}, Dave Evenden², Angus Prosser², John Dickson³, Jessica Teeling², Christopher Kipps^{1,2}

¹University Hospital Southampton NHS Foundation Trust, ²University of Southampton, ³University College London Hospitals

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Study Background and Aim

- Cognitive decline is heterogeneous, limiting prognosis and care planning.
- Clinical tools such as CDR-SB track functional decline but provide limited biological insight.
- Perfusion SPECT provides a physiological marker of regional synaptic dysfunction, often before structural change.

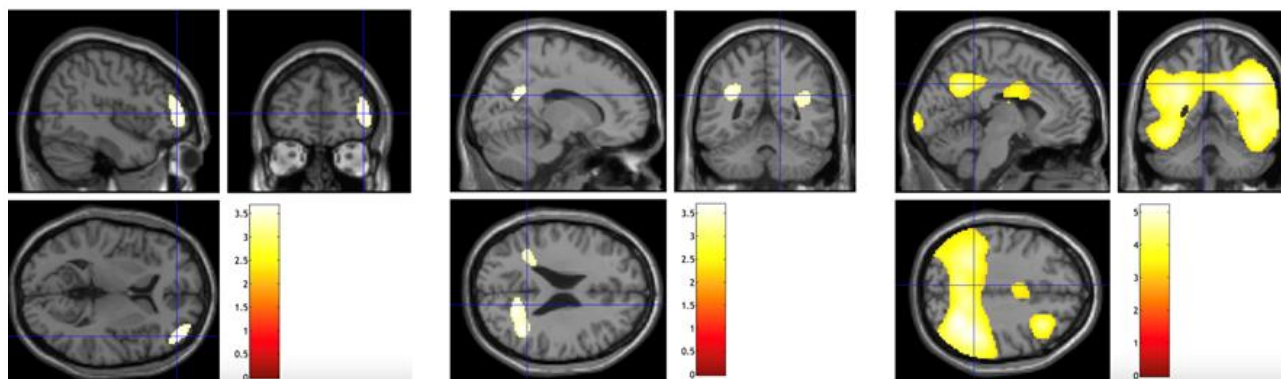
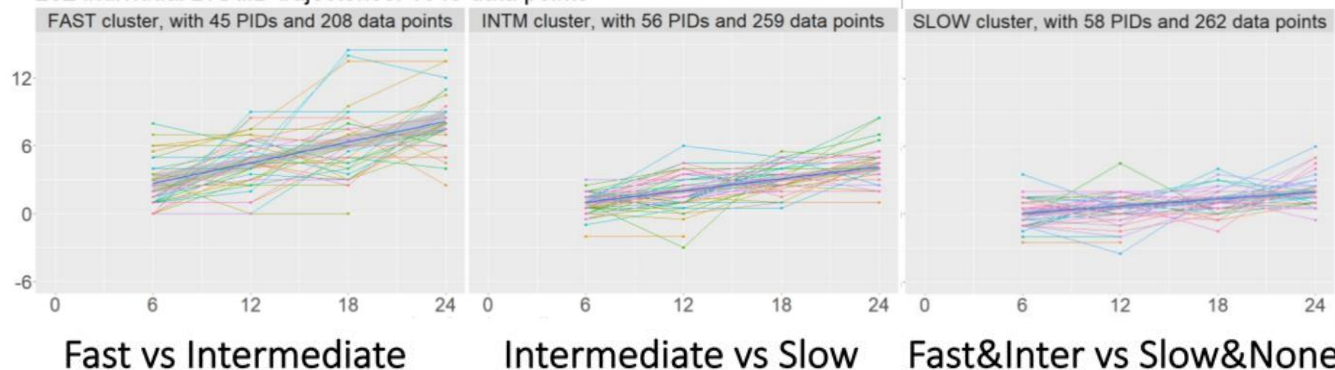
Aim: To assess whether cerebral perfusion distinguishes individuals with different functional decline trajectories.

Methods

- Design:** Brain Imaging in Dementia (BRAID) longitudinal cohort (n = 232).
- Clustering:** Longitudinal CDR-SB change grouped using curveRep() into four decline trajectories. See poster [#2615](#) on hierarchical clustering.
- Imaging:** Baseline brain perfusion SPECT analysed using SPM to provide voxel-wise comparisons across different decline trajectories

BRAID clustering progression groups

232 individual BRAID trajectories: 1049 data points



Results:

- Data-driven clustering identified four distinct CDR-SB trajectories. Fast progressors showed the steepest decline: 4.02 units/year. Slow progressors declined 1 unit/year.
- Perfusion maps reveal that faster decline is associated with more extensive hypoperfusion in posterior cortical areas.

Conclusion and Clinical Impact

- Functional decline trajectories mapped onto distinct brain perfusion profiles in a real-world clinical cohort.
- Faster progression was associated with greater posterior hypoperfusion, particularly within the default mode network.
- Findings support network-based models of neurodegeneration, where dysfunction spreads across interconnected posterior hubs.
- Progression speed appears to reflect underlying biological heterogeneity, not only baseline clinical severity.
- Perfusion SPECT may support early risk stratification by identifying individuals at higher risk of rapid decline, improving patient stratification for therapy.

Contact sofia.michopoulou@uhs.nhs.uk