Discovering heterogeneous patterns of advanced brain aging: a BLSA study

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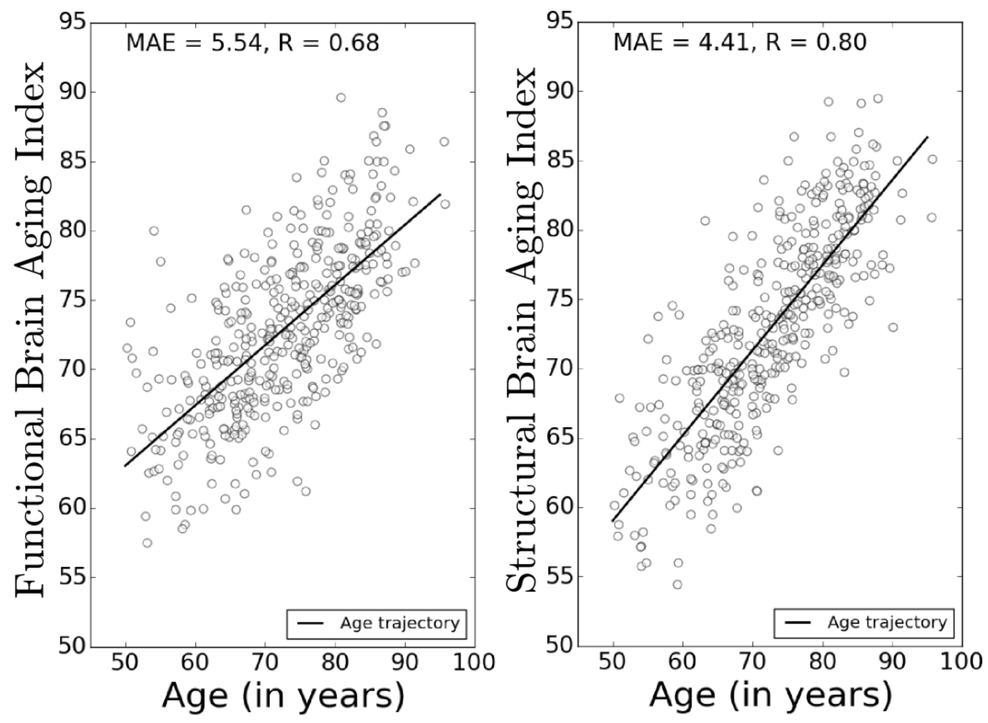
Objectives

- Compute imaging-based functional and structural *Brain Aging Trajectories*, which can be used to identify *resilient* and *advanced* agers
- Identify heterogeneous patterns of structural and functional brain change among the advanced agers, relative to resilient agers, using *Mixture of Experts* [1]

Data

- Data: T1- MRI and rsfMRI acquired as part of Baltimore Longitudinal Study of Aging (BLSA), 400 subjects, age range **50 – 96** years, Mean Relative Displacement (MRD) $<$ **0.2**mm
- Pre-processing: Confound regression, Band-pass filtering, registration to MNI template, data-driven parcellation using GraSP [3], yielding 596 parcels
- Functional connectivity: Using **596x596** correlation matrices as input, we identified a total of **500** Sparse Connectivity Patterns (SCPs) [2] and associated coefficients
- Functional coherence: Within each parcel, we computed the regional homogeneity, which summarizes the local connectivity within the parcel
- Grey matter density: Within each parcel, we computed average tissue density, computed using sMRI data

Brain Aging Trajectories



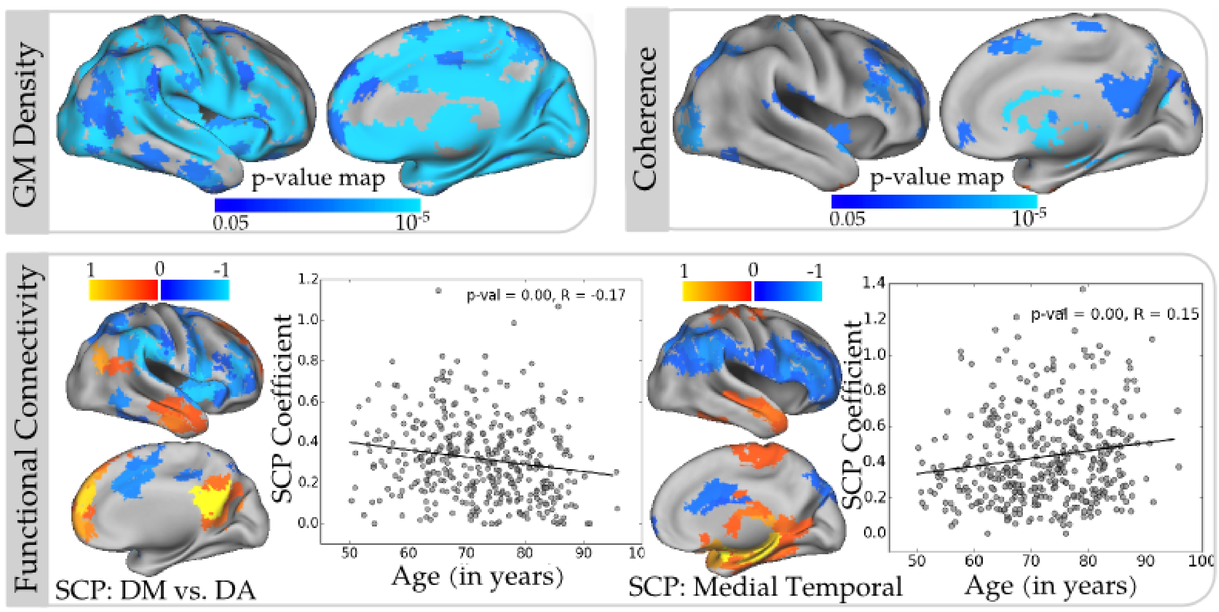
Functional and structural Brain Age Indices (BAIs) plotted against each individual's age. Functional BAI was computed from SCP coefficients and local functional coherence measures; structural BAI was computed from average GM density values. The aging trajectories (solid lines) show the expected BAI, corresponding to an individual's age.

Define *resilient* and *advanced* agers as follows:

- Resilient: BAI $\leq$ Expected BAI (below the trajectory), in both structure and function
- Advanced: BAI $>$ Expected BAI, in either structure or function

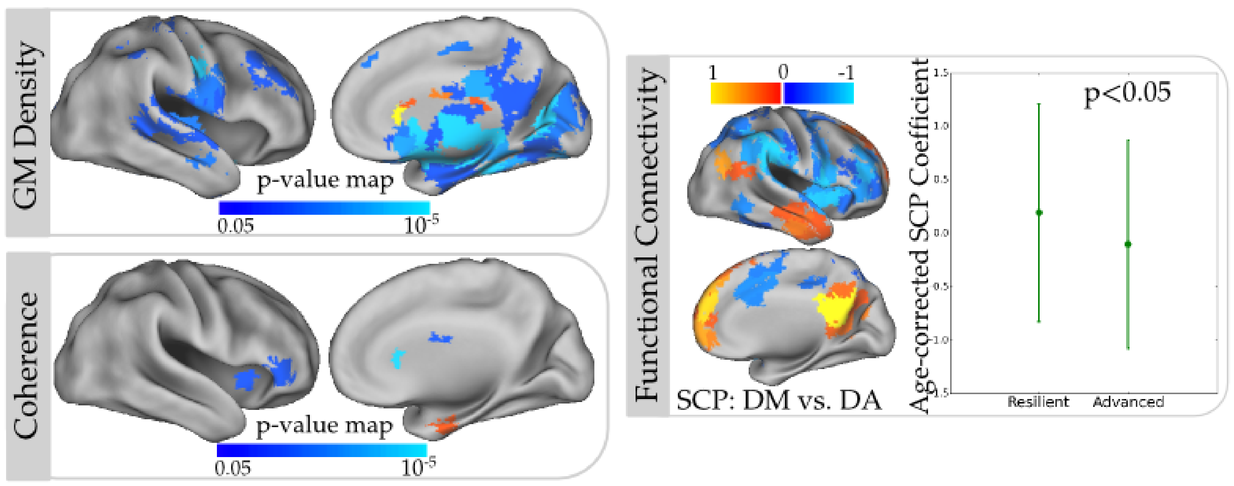
Heterogeneity in advanced aging

Effects of aging on structure and function



Top two panels show p-value maps where GM density and functional coherence significantly decreased with age, in Blue-Light blue. Bottom panel shows two SCPs whose associated coefficients are significantly correlated with age. SCPs are shown to the left - overlays indicate a spatial pattern of correlated regions, opposing colors (Red-Yellow vs. Blue - Light Blue) reflect anti-correlated regions.

Advanced aging vs. Resilient aging

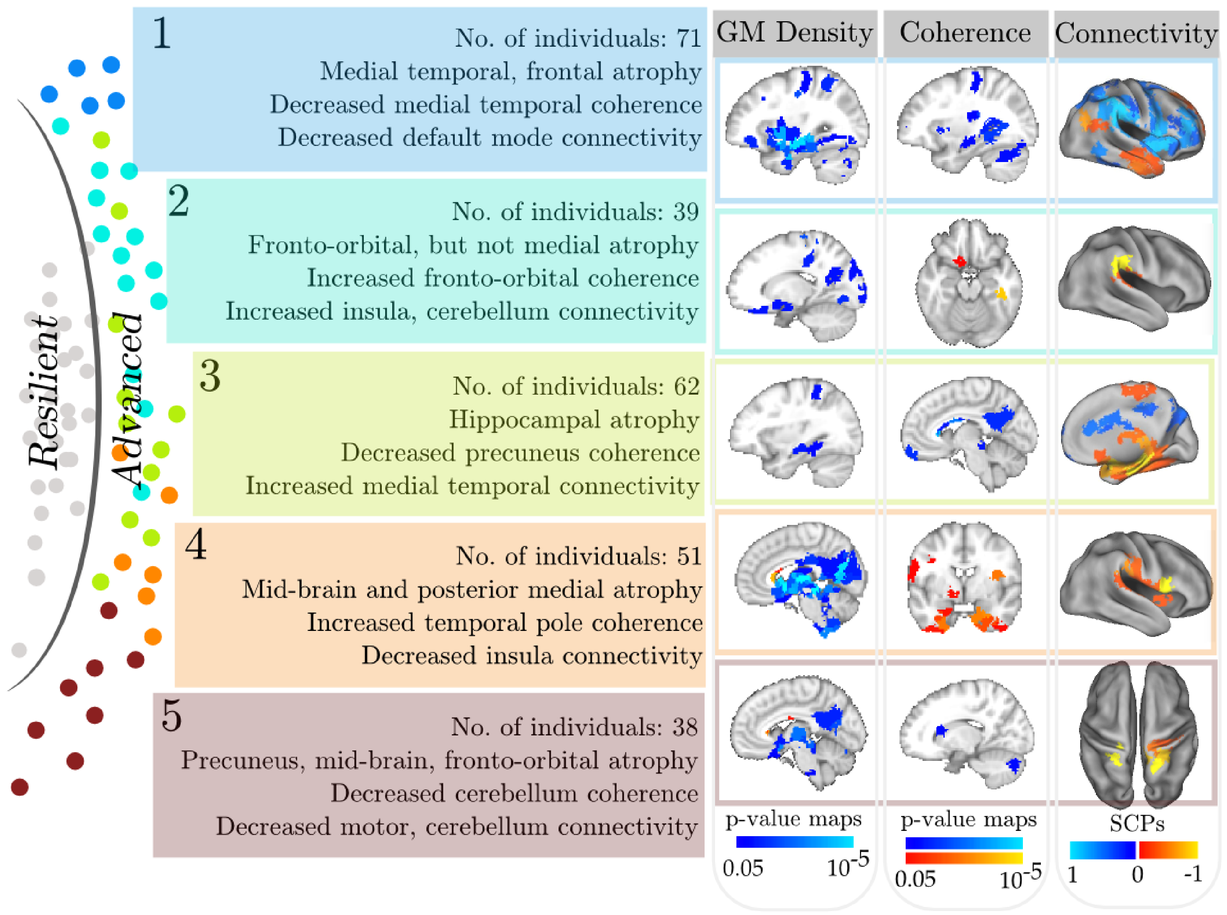


Panels to the left show p-value maps of differences between groups ($\mathbf{p < 0.05}$, corrected for multiple comparisons) across individuals are shown in Blue-Light blue. Right panel shows the DM vs. DA SCP - overlay indicates a spatial pattern of correlated regions, opposing colors (Red-Yellow vs. Blue - Light Blue) reflect anti-correlated regions. The mean and standard deviation of the associated SCP coefficient for both groups is plotted to the right.

Differences in cognitive performance and lesion load

- Group 1 has significantly lower cognitive performance in measures of verbal fluency and attention relative to resilient agers
- Group 1,5 had significantly higher lesion load, Group 3 has lower lesion load compared to the resilient group

Heterogeneity found using Mixture of Experts



Summary of changes to GM density, functional coherence and connectivity for all five groups of advanced agers. Changes to GM density and coherence are shown using p-value maps (first two columns on right). SCPs whose connectivity was significantly altered are shown in the last column. Note that the color overlay for SCPs indicates patterns of correlated (or anti-correlated) regions, and is not related to statistical significance.

Discussion

- We discovered remarkable heterogeneity in structural and functional changes, summarized by five imaging phenotypes
- Group 1: Significant GM atrophy, reduced functional coherence as well as connectivity, higher lesion load and cognitive decline was observed. These patterns are consistent with changes previously reported in aging and AD studies.
- Group 3: Focal hippocampal GM atrophy and reduced posterior cingulate/precuneus coherence suggests early stage of AD. However, it is likely that increased functional connectivity of MTL and lower levels of lesion load, implies high brain reserve allowing them to compensate both functionally and cognitively for the hippocampal and precuneus pathology.

References

[1] Harini Eavani et al. "Capturing heterogeneous group differences using mixture-of-experts: Application to a study of aging". In: *NeuroImage* 125 (2016).
[2] Harini Eavani et al. "Identifying Sparse Connectivity Patterns in the brain using resting-state fMRI". In: *NeuroImage* 105 (2015).
[3] N Honnorat et al. "GraSP: Geodesic Graph-based Segmentation with Shape Priors for the functional parcellation of the cortex". In: *NeuroImage* 106 (2015).