

Longitudinal Clustering Identifies Different Rates of Cortical Aging in Healthy Older Adults

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SUPPLEMENTARY DATA

Supplementary Material S1: Outlier handling

Table S1: Distribution of imputed values across the 68 Desikan–Killiany ROIs at baseline and follow-up.

Number of imputed values per ROI	ROIs at baseline	ROIs at follow-up
0	27	24
1	32	32
2	6	10
3	3	2
Total ROIs	68	68
Total imputed values/total values	53/11 968	58/11 968

To assess the robustness of the two-cluster solution to the choice of outlier-handling strategy, we repeated the analysis using winsorization instead of mean imputation. Values with a z-score exceeding +3 or below −3 at either timepoint (per ROI) were capped at the corresponding z-score boundary rather than replaced with the ROI-specific cohort mean, and APC and hierarchical clustering were recomputed from these winsorized values. This reproduced the two-cluster solution, with 85.2% of participants (150/176) assigned to the same cluster as in the main analysis (adjusted Rand index=0.49), comparable to the agreement observed for the other control analyses (Supplementary Material S2–S4).

Supplementary Material S2: Cluster number selection and algorithm comparison

To further evaluate the robustness of the two-cluster solution, we computed the Calinski–Harabasz (CH) index across $k=2$ to 8 and compared the Ward partition with K-means clustering ($k=2$, 20 random initializations) using the adjusted Rand index. The CH index was highest for $k=2$ (CH=18.73) and decreased monotonically for higher k ($k=3$: 13.09; $k=4$: 10.81; $k=5$: 9.66; $k=6$: 9.00; $k=7$: 8.54; $k=8$: 8.16), supporting the two-cluster solution over further subdivisions. K-means clustering with $k=2$, averaged across 20 random initializations, assigned 87.0% of participants (on average 153/176) to the same cluster as Ward's linkage (adjusted Rand index=0.55), indicating that the two-cluster structure is not specific to the Ward criterion.

Supplementary Material S3: Feature scaling

To assess the robustness of the two-cluster solution to feature scaling, we repeated the hierarchical clustering after z-scoring each of the 68 regional APC values. In this control analysis, 81.8% of participants (144/176) were assigned to the same cluster as in the main analysis (adjusted Rand index=0.40). We further compared the regional APC profile of each cluster obtained from the z-scored clustering solution with the corresponding cluster from the main (raw-value) analysis (Cluster 1 vs. Cluster 1, and Cluster 2 vs. Cluster 2), expressing both profiles in the original (raw APC) units for comparability. These profiles were highly correlated ($r=0.99$ for both clusters), indicating that the regions distinguishing the clusters are essentially unchanged by feature scaling, even though a subset of individual (borderline) participants shift cluster assignment. The two-cluster structure and its spatial characterization were therefore preserved.

Supplementary Material S4: Baseline dependence of APC

SUPPLEMENTARY DATA

To assess whether the identified clusters depend on the definition of cortical change, we repeated the hierarchical clustering using (i) absolute annualized change in cortical thickness (mm/year) instead of annualized percent change, and (ii) change residualized for baseline cortical thickness (per-ROI residuals from a linear regression of APC on baseline CTh). The two-cluster solution was reproduced in both analyses, with 81.8% (144/176) and 72.2% (127/176) of participants assigned to the same cluster as in the main analysis, respectively. The somewhat lower agreement for the residualized version reflects a modest negative correlation between baseline CTh and APC across ROIs (mean $r=-0.25$); removing this baseline-related variance shifts a subset of borderline assignments, but a two-cluster partition was consistently recovered in both control analyses.