Neurobiological underpinnings of macroscale cortical changes related to accelerated and decelerated brain aging

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1. BACKGROUND
- The brain-age gap estimate (brainAGE) is a marker of brain health that quantifies the difference between a person’s chronological and biological “brain age”.¹
- Neurobiological underpinnings of accelerated/decelerated aging are not well understood.
- We used a “virtual histology” approach² to relate interregional profiles of age-related cortical thinning with profiles of gene expression.

2. METHODS
(1) BrainAGE calculation and participant groups
- BrainAGE was computed for 1113 Human Connectome Project³ participants (ages 22-37) by using support vector regression to estimate each participant’s age from their preprocessed T1-weighted structural MRI scan.
- Participants with brainAGE > ±1 SD from the mean were selected for further analyses (positive brainAGE = accelerated aging; negative brainAGE = decelerated aging).

<table>
<thead>
<tr>
<th>Group</th>
<th>Sample size</th>
<th>Mean age (yrs)</th>
<th>Mean brainAGE</th>
<th>% female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accelerated</td>
<td>n = 169</td>
<td>29.22 yrs</td>
<td>+2.14 yrs</td>
<td>59.17%</td>
</tr>
<tr>
<td>Decelerated</td>
<td>n = 162</td>
<td>29.08 yrs</td>
<td>-1.90 yrs</td>
<td>54.32%</td>
</tr>
</tbody>
</table>

(2) Cortical thinning profiles
- Participants’ cortical thicknesses were measured for 34 left regions defined by the Desikan-Killiany atlas⁴.
- Generalized additive models were performed for each region to estimate the rate of thickness change (i.e. slope) at each age.

(3) Gene expression profiles
- Gene expression levels derived from the Allen Human Brain Atlas were mapped to 34 left cortical regions⁵.
- 604 genes were selected based on their associations with 9 brain cell types⁶.

3. RESULTS
Fig. 1: Example cortical thinning profiles for each brainAGE group
- Profiles were acquired for each year of age from 22-37.

Fig. 2: Correlations between thinning & gene profiles for each brainAGE group
- Positive coefficients: higher gene expression is associated with less thinning.
- Negative coefficients: higher gene expression is associated with more thinning.

4. CONCLUSIONS
- In young adulthood, the neurobiological processes underlying age-related cortical thinning is distinct between individuals with accelerated vs. decelerated brain aging.
- Virtual histology is a promising approach to detect the role of cell-specific genes across different brain aging trajectories, and may be extended in future studies to incorporate a wider age range.

REFERENCES
3. humanconnectome.org/study/hcp-young-adult