



# Do decreases in cortical thickness or volume relate to cognitive performance in healthy aging?

David A. Ziegler,<sup>1</sup> Olivier Piguet,<sup>1</sup> Keyma Prince,<sup>1</sup> Emily Connally,<sup>1</sup> David H. Salat,<sup>2</sup> Bruce Fischl,<sup>2</sup> Suzanne Corkin<sup>1,2</sup>

<sup>1</sup>Department of Brain and Cognitive Sciences, MIT, Cambridge, MA

<sup>2</sup>Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, MGH, Charlestown, MA



## Background

- Neuropathological studies in older individuals identified a loss of cortical neurons or decreased packing density, but these results are inconsistent and controversial.<sup>1</sup>
- Previous MRI-based studies have shown volumetric loss,<sup>2-5</sup> including:
  - Early and pervasive ventricular enlargement
  - Linear shrinkage of striatum and cerebellum
  - An anterior-to-posterior gradient of cortical loss, with disproportionate vulnerability of association areas, especially prefrontal cortex (PFC)<sup>2</sup>
- In contrast, cortical thinning appears to occur predominantly in primary motor and visual cortices.<sup>7</sup>
- While atrophy of cortical regions, particularly PFC, is believed to underlie age-related cognitive decline,<sup>6</sup> evidence for this association is equivocal.
- Given the discrepancy between results from volumetric and thickness studies, we sought to measure both of these variables in brains of healthy young (YA) and older adults (OA).
- Further, we sought to relate structural changes to performance on behavioral tasks that assess a number of specific cognitive processes.

## Methods

### Participants

Group	N	Age*	Edu*	MMSE*
YA	36	21.9 ± 2.6 (18–30)	15 ± 1.6 (12–18)	29.1 ± 1.3 (27–30)
OA	37	69.7 ± 7.2 (59–86)	17.9 ± 7.4 (14–23)	29.2 ± 1.2 (27–30)

\* Scores are mean ± SD (range);  $p < .05$  for Edu

### Cognitive Testing

All participants performed a series of cognitive tasks to assess:

#### Episodic memory

(delayed recall of word lists and WMS stories)

#### Semantic memory

(Boston Naming, WAIS Vocabulary)

#### Cognitive control processes

(Stroop, letter fluency, backward digit span)

We calculated standardized composite z scores for each measure.

YA performed significantly better than OA on tests of episodic memory ( $p < .0001$ ) and cognitive control ( $p < .002$ ).

OA performed better than YA on semantic memory tasks, but not significantly ( $p = 0.16$ ).

### MRI Acquisition and Preprocessing

We acquired 2 high-resolution T1-weighted anatomical (MPRAGE) scans on each participant using a Siemens 1.5 Tesla Sonata system.

MPRAGE: voxel size 1.0 x 1.0 x 1.33 mm; TR = 2530, TE = 2.6, T1 = 1100, FA = 7°.

Data were processed using FreeSurfer's morphometric analysis tools (<http://surfer.nmr.mgh.harvard.edu>).

We performed motion correction and averaged multiple scans, yielding a single high-contrast and high signal-to-noise volume.

Cortical surfaces were reconstructed using a semi-automated procedure described previously.<sup>8-10</sup>

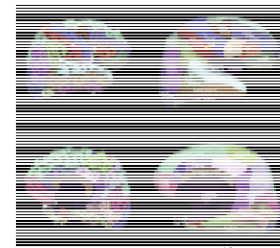
## Analyses of Cortical Thickness & Volume

### Cortical Parcellation

- Performed automatic probabilistic parcellation of the cortical surface into 34 gyral-based units per hemisphere.<sup>11,12</sup>
- Calculated total volume for each parcellation unit
- Tested for differences using a general linear model (GLM), controlling for sex, education and intracranial volume; group contrasts were subject to False-Discovery Rate (FDR) correction.<sup>13,14</sup>

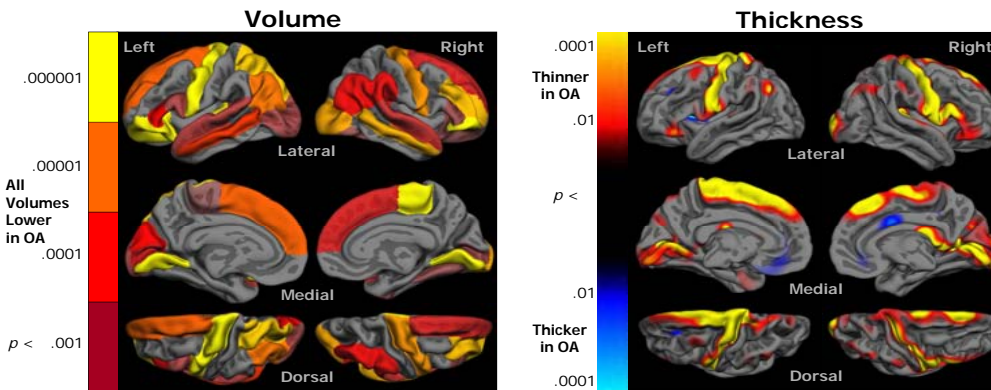
### Surface-based Analyses

- Derived thickness measures at each vertex by calculating the shortest distance from the gray/white border to the outer cortical surface.<sup>15</sup>
- Mapped thickness measures onto each participant's inflated cortical surface and averaged across all participants.
- Performed vertex-wise statistical comparisons using a GLM with FDR correction.



Cortical Parcellation<sup>12</sup>

## Differences Between YA & OA



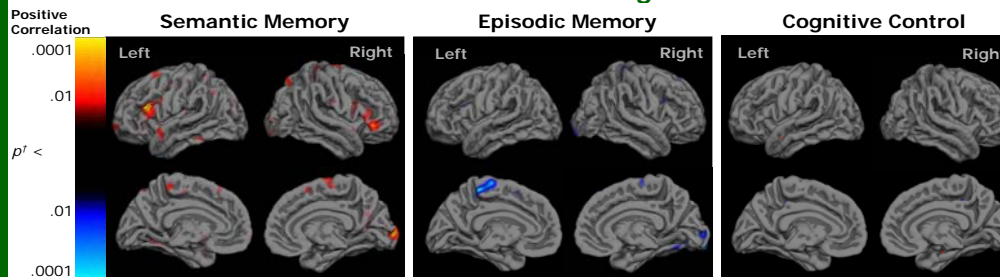
OA showed bilateral reductions in cortical volumes compared to YA. Areas with the greatest differences were:

- superior & inferior frontal gyri (including pars orbitalis)
- precentral gyrus
- middle & superior temporal gyri
- inferior parietal cortex
- calcarine sulcus & lateral occipital lobe

When compared to YA, OA showed bilateral thinning in discrete cortical areas. The greatest degree of thinning occurred in:

- superior frontal gyrus
- lateral PFC & pars orbitalis
- precentral gyrus & central sulcus
- inferior parietal cortex (L > R)
- calcarine sulcus & cuneus

## Correlations Between Thickness & Cognitive Scores in OA

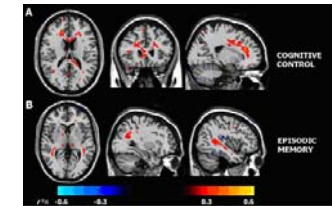


- A robust (FDR corrected) positive correlation was present between semantic memory scores and thickness in inferior prefrontal cortex (pars triangularis).
- A modest negative correlation was observed between episodic memory scores and cortical thickness in the posterior superior frontal gyrus, but this result did not survive FDR correction.
- We found no significant correlations between cortical thickness and cognitive control scores.

<sup>†</sup> uncorrected

## Summary/Conclusions

- Surface-based analyses of cortical thickness revealed large regions of thinner cortex in OA compared to YA.
  - Thinning was greatest in the precentral gyrus and pericalcarine region.
  - Thinning was also found along the superior frontal gyrus and pars orbitalis; other regions of frontal, temporal, and parietal cortices were largely spared.
  - These findings are consistent with a previous study.<sup>7</sup>
- Cortical parcellation results revealed patterns of volumetric loss that overlapped significantly with regions that showed thinning, with the notable addition of extensive volume loss in temporal neocortex.
- Neither surface-based analyses nor parcellation analyses revealed robust patterns of correlation between cognitive scores and measures of thickness or volume.
  - Performance on *semantic memory* tasks showed a moderate positive correlation with thickness in the pars triangularis region of the inferior frontal gyrus.
  - This result is consistent with fMRI evidence that anterior left inferior PFC supports semantic retrieval.<sup>16</sup>
- We previously reported striking age-related reductions of white matter integrity in frontal and temporal regions of these same participants.<sup>17</sup>
  - These DTI-based measures showed strong correlations with performance on *episodic memory* and *cognitive control* tasks (see figure below).
- Thus, age-related impairment in specific cognitive processes may arise from degeneration in components of their respective networks (i.e., the nodes or the connections).



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-Olivier Piguet is now at Prince of Wales Medical Research Inst. Randwick NSW, Australia. Emily Connally is now at the University of Arizona, Tucson, AZ.

Author Contact information:

David A. Ziegler  
MIT, Building 46-5121  
43 Vassar St  
Cambridge, MA 02139  
daz@mit.edu



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