Detailed shape analysis of healthy brains and brains with Alzheimer's disease

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Summary

This work constitutes the most detailed shape analysis of human brains ever conducted. The results provide information about the variation in different shape measures computed on MRI-derived brain structures, focusing on healthy brains and brains with Alzheimer's disease (AD). We intend for this effort to drive future comparisons with similarly processed image data of patients with different neuropsychiatric conditions.

Methods

We processed brain MR images from 101 healthy [1] and hundreds of ADNI participants [2] (N_{AD}=126, N_{HC}=199) by FreeSurfer [3] and ANTs [4]. Mindboggle [5] extracted labeled regions and sulci and measured their shapes: area, thickness, volume, curvature, depth, Laplace-Beltrami spectra, and Zernike moments.

To assess the importance of subject and hemisphere, we fitted a linear mixed model for each shape measure and brain region. To select top structures implicated in AD, we used the average of the ranks of the following tests: (1) Kolmogorov-Smirnov test to see if there was a difference between distributions at baseline and at 3 years, (2) Correlation of change in shape and change in ADNI-MEM cognitive scores.

Results

- Care must be taken when comparing differently defined shape measures.

- For all shapes and regions, most of the variability is concentrated in the residual (not the hemisphere or individual).

- AD and healthy control brains have similar shape statistical summaries.

- After a 3-year interval, ADNI-MEM scores are estimated best by changes in volume, thickness, curvature in various regions.

Next steps

We have generated data to do the following:

- ➔ Include all covariates and shape measures.
- ➔ Include a volume analysis of non-cortical regions.
- ➔ Look at interactions among shape measures.
- ➔ Compare shapes of FreeSurfer vs. ANTs labels.
- ➔ Compare shapes of automated vs. manual labels.

We will also try to infer the heritability of brain shape variation, by analyzing MRI data from monozygotic and dizygotic twins, using data from the Human Connectome Project [6].

Acknowledgments and References

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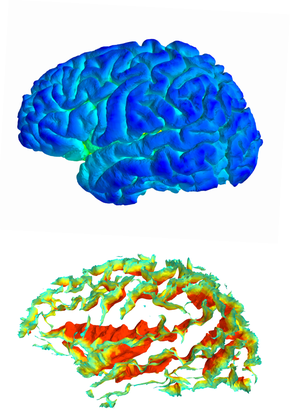
ADNI investigators provided data but did not participate in the analysis or writing of this report.

[1] Klein, A, Tourville, J. (2012). 101 labeled brain images and a consistent human cortical labeling protocol. Frontiers in Brain Imaging Methods. 6:171. http://mindboggle.info/data.html
[2] http://adni.loni.usc.edu
[3] https://surfer.nmr.mgh.harvard.edu/
[4] http://stnava.github.io/ANTs/
[5] http://mindboggle.info/
[6] http://www.humanconnectomeproject.org/

Example shape measure

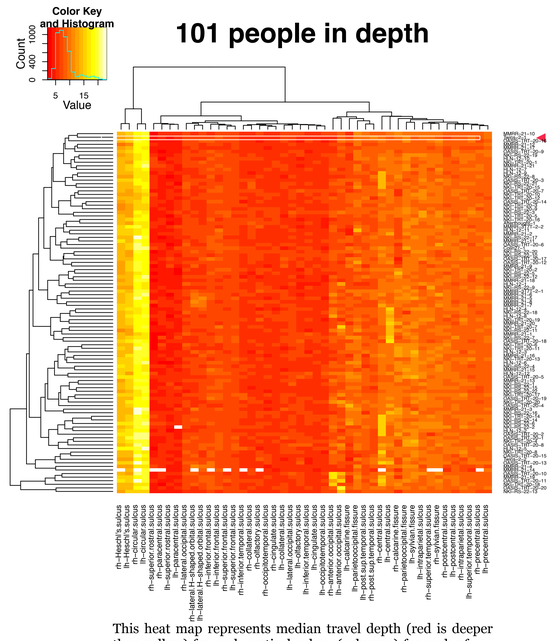
One person in depth



Here we show an example shape measure (travel depth) computed for the 140,000+ vertices of a surface mesh of a whole cortical hemisphere of a single healthy subject (top) [1], or just for the sulcus folds (bottom).

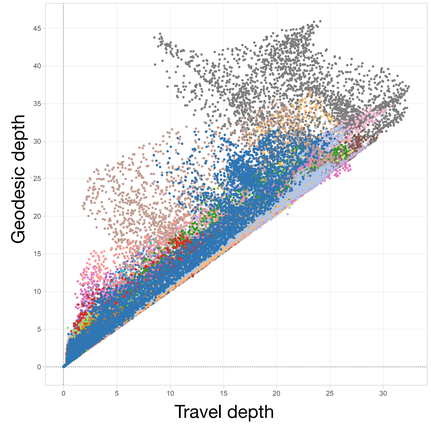
Color indicates depth (red is deeper than blue).

101 people in depth



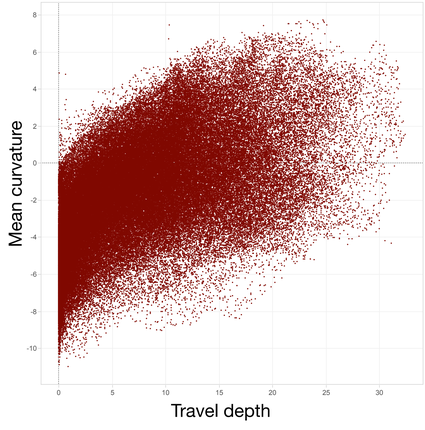
This heat map represents median travel depth (red is deeper than yellow) for each cortical sulcus (columns) for each of 101 healthy individuals (rows; example on left highlighted). Similar colors along a column indicate consistent shapes for a given sulcus.

Two kinds of depth



Here we plot one measure of depth (geodesic depth) versus another (travel depth) for every vertex of the sulcus folds for one cortical hemisphere of a single subject, and assign a unique color to each brain region. We can see that geodesic depth is higher than travel depth, and may exaggerate depth, such as in the insula (gray markers).

Curvature vs. depth



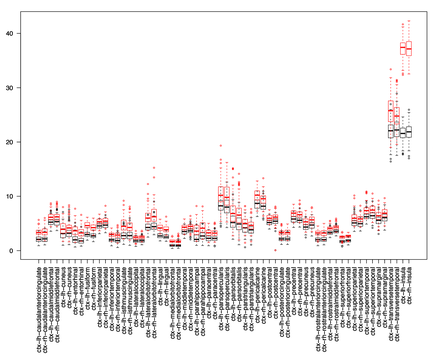
Shape measures are not independent of one another.

Here we plot mean curvature versus travel depth, again for every vertex of the sulcus folds for the same subject.

As one might expect, we see greater curvature at greater depth.

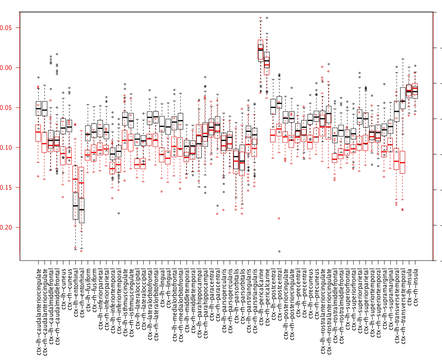
Shapes of 101 healthy brains

travel / geodesic depth



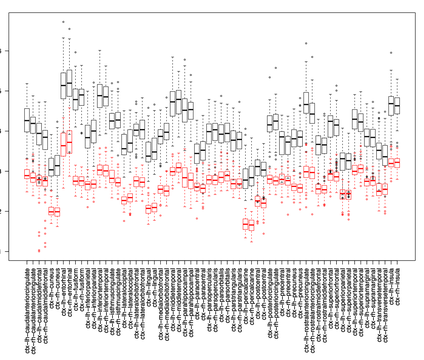
These box plots represent the distributions of median travel depth (black) and median geodesic depth (red) for each labeled region across all 101 manually labeled healthy brains.

mean / FreeSurfer curvature



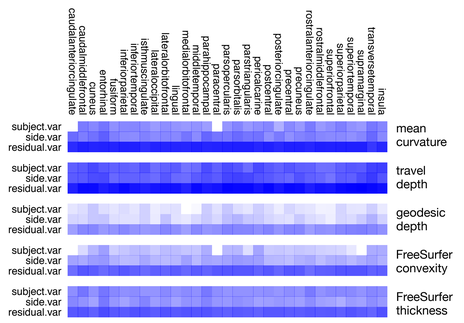
These box plots represent the distributions of the median values of Mindboggle's mean curvature (black) and of FreeSurfer's curvature measure (red), using different scales.

thickinthehead / FreeSurfer thickness



These box plots represent the distributions of Mindboggle's thickinthehead volume-based thickness measure (black) and FreeSurfer's surface-based thickness measure (red).

Sources of shape variability



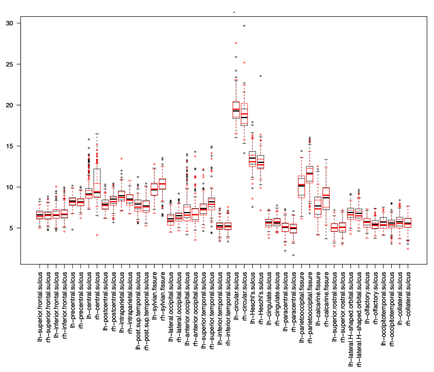
The above heatmap shows the relative contributions of subject/hemisphere/residual to describe the variability for each shape measure.

Total variance of each shape measure =
variance between subjects +
variance between brain hemispheres within a subject +
variance within brain hemisphere

Most of the variability is in the residual.

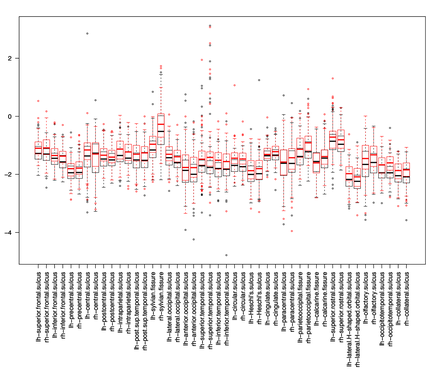
Shapes of brains with Alzheimer's

travel depth



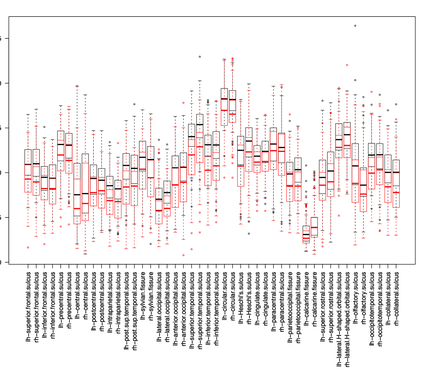
Median travel depth for healthy (black) and Alzheimer's (red) sulci.

mean curvature



Median values of mean curvature for healthy (black) and Alzheimer's (red) sulci.

FreeSurfer thickness



Median FreeSurfer thickness for healthy (black) and Alzheimer's (red) sulci.

Shape biomarkers of AD

Changes in shape measures after a 3-year interval were significantly correlated with changes in ADNI-MEM cognitive score:

Volume for right caudal anterior cingulate and left: entorhinal, inferior parietal, (middle/superior) temporal, superior frontal, precuneus, supramarginal

FreeSurfer thickness for left and right: entorhinal, fusiform, inferior parietal, (inf/mid/sup) temporal, superior frontal, precuneus, supramarginal;
left: (caudal middle/lateral orbito/rostral middle) frontal, pars triangularis;
right: lingual.

Mean curvature for left and right rostral middle frontal;
left (middle/superior) temporal;
right inferior temporal.