Mindboggle:
A scatterbrained approach
to automate brain labeling

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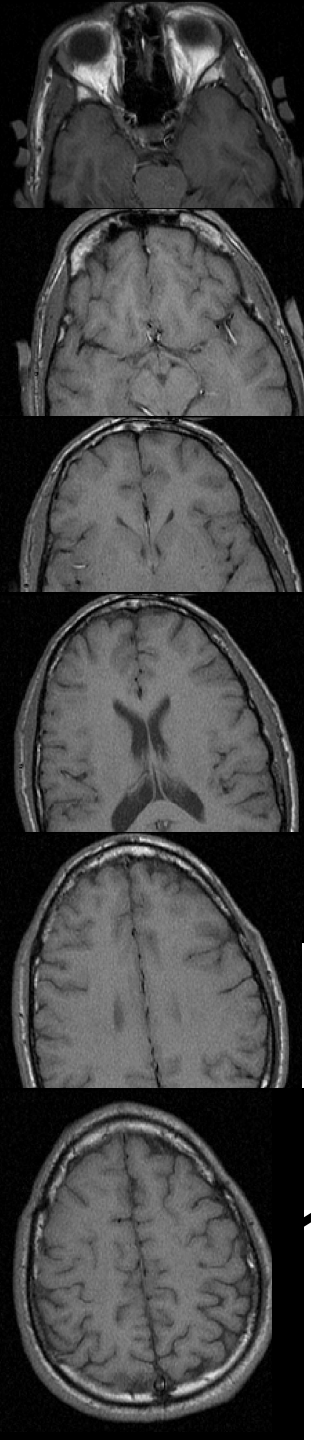
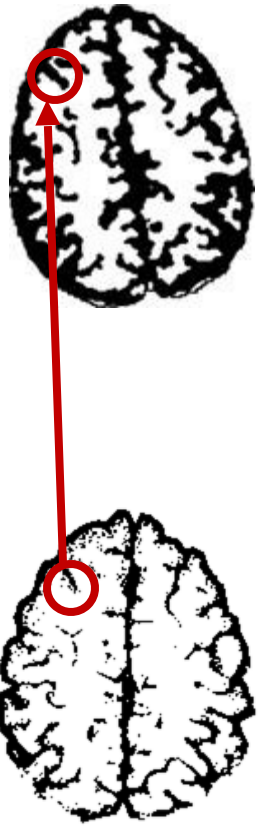
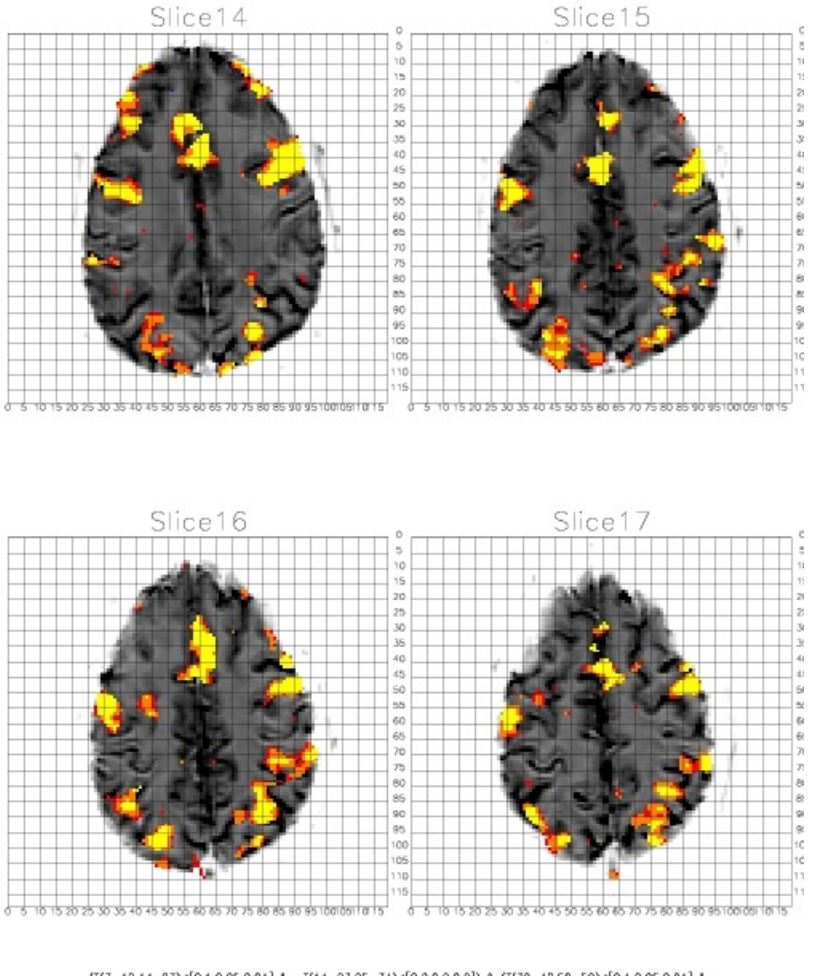
Unlabeled brain image data



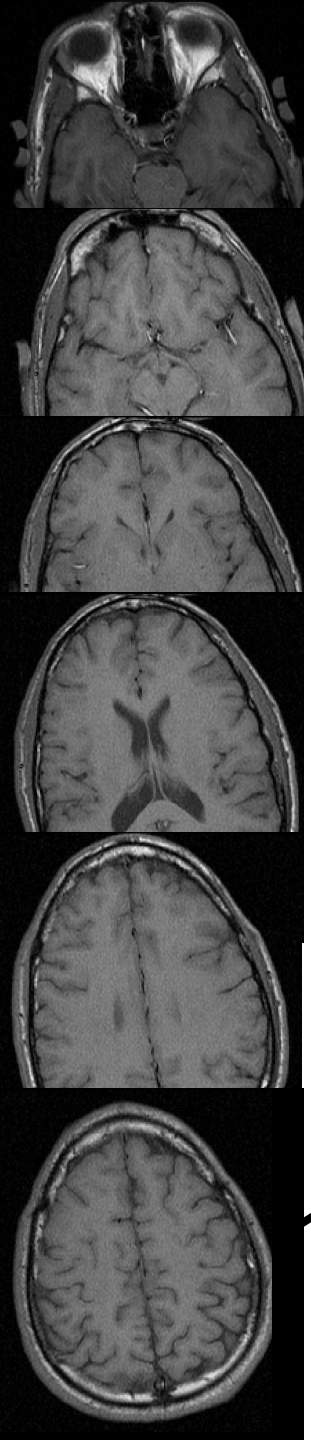
Morphometric data



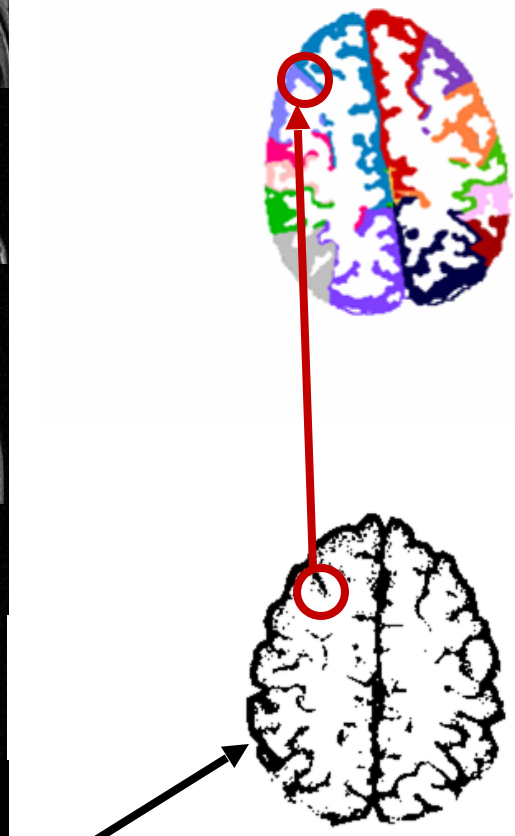
fMRI BOLD data



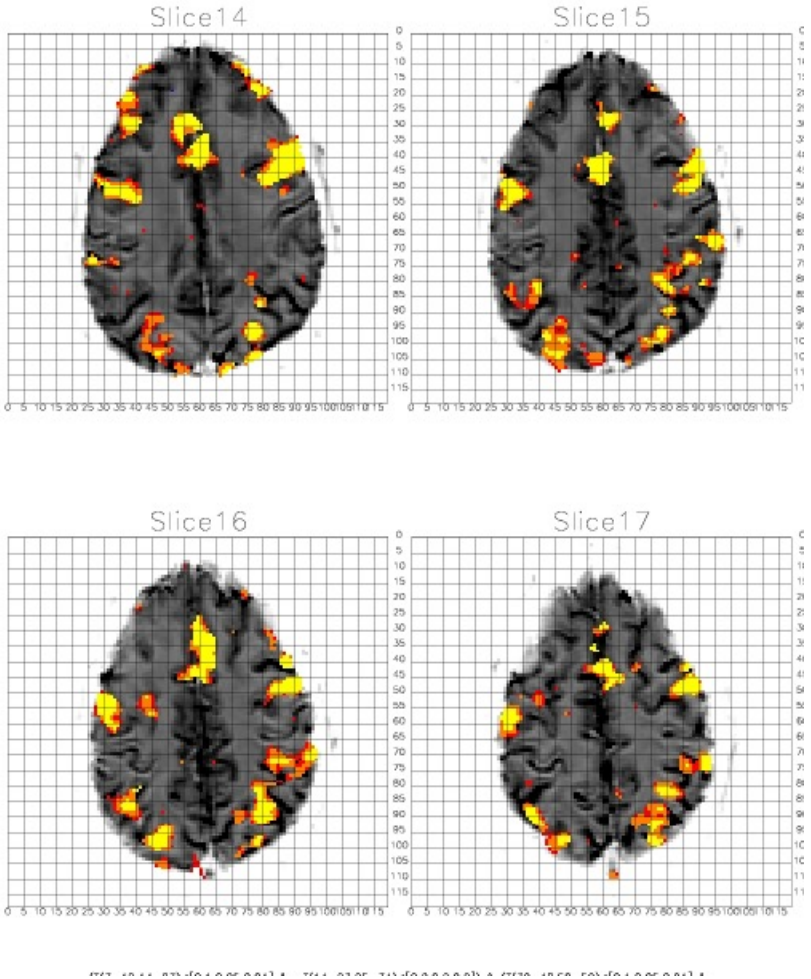
Manually labeled structural data



Morphometric data

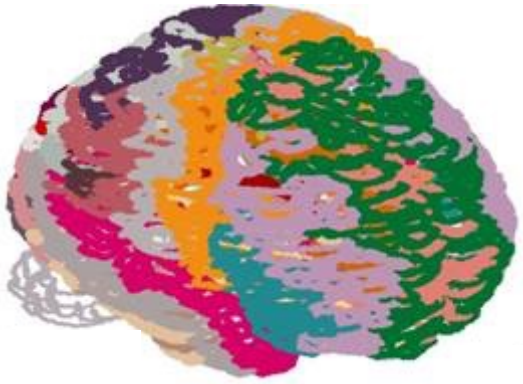


fMRI BOLD data

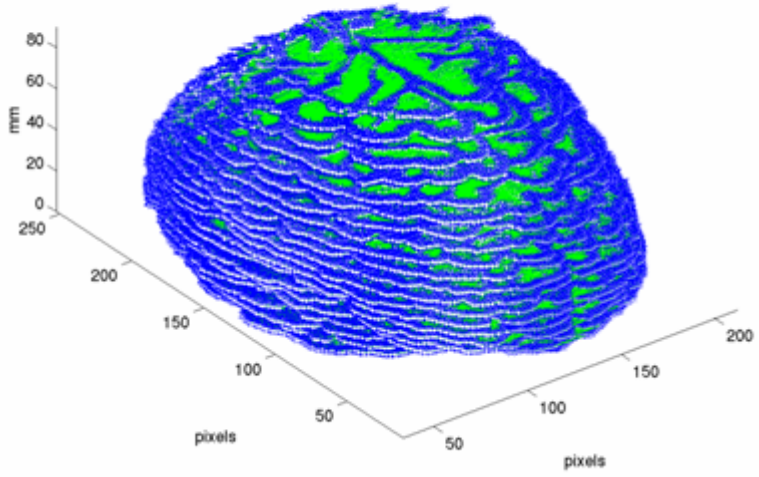


Manually labeled activity data

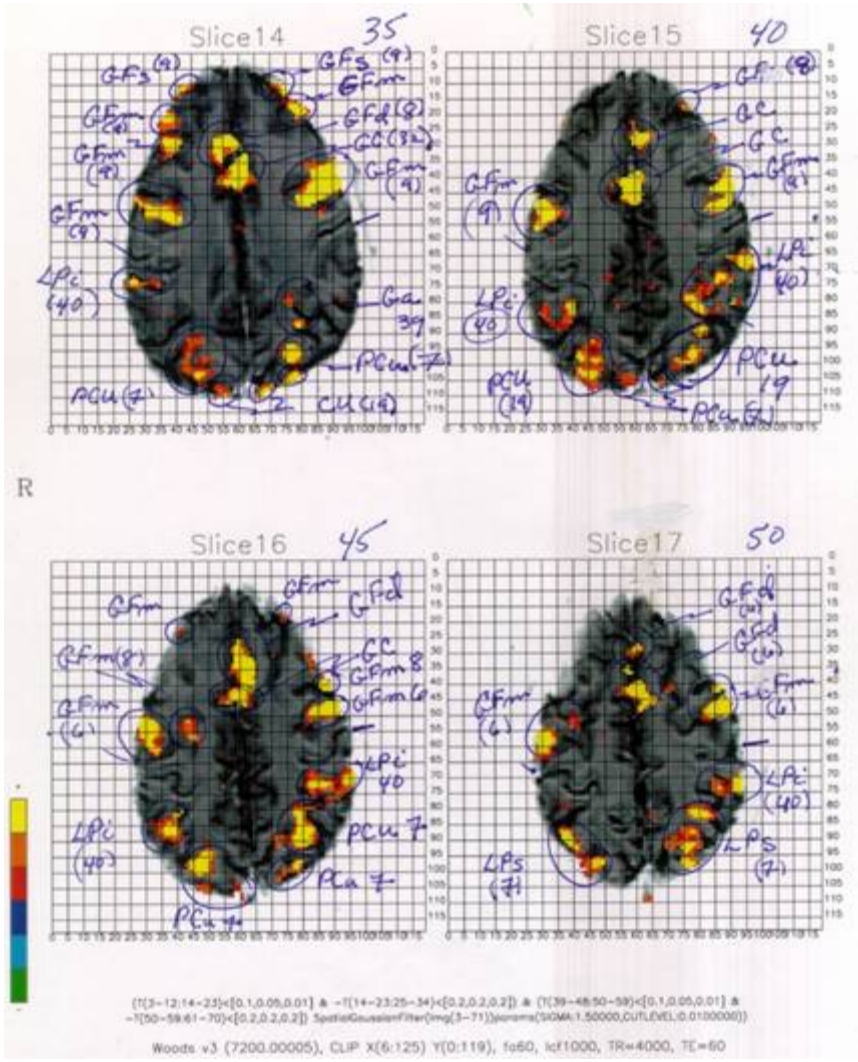
Talairach Atlas



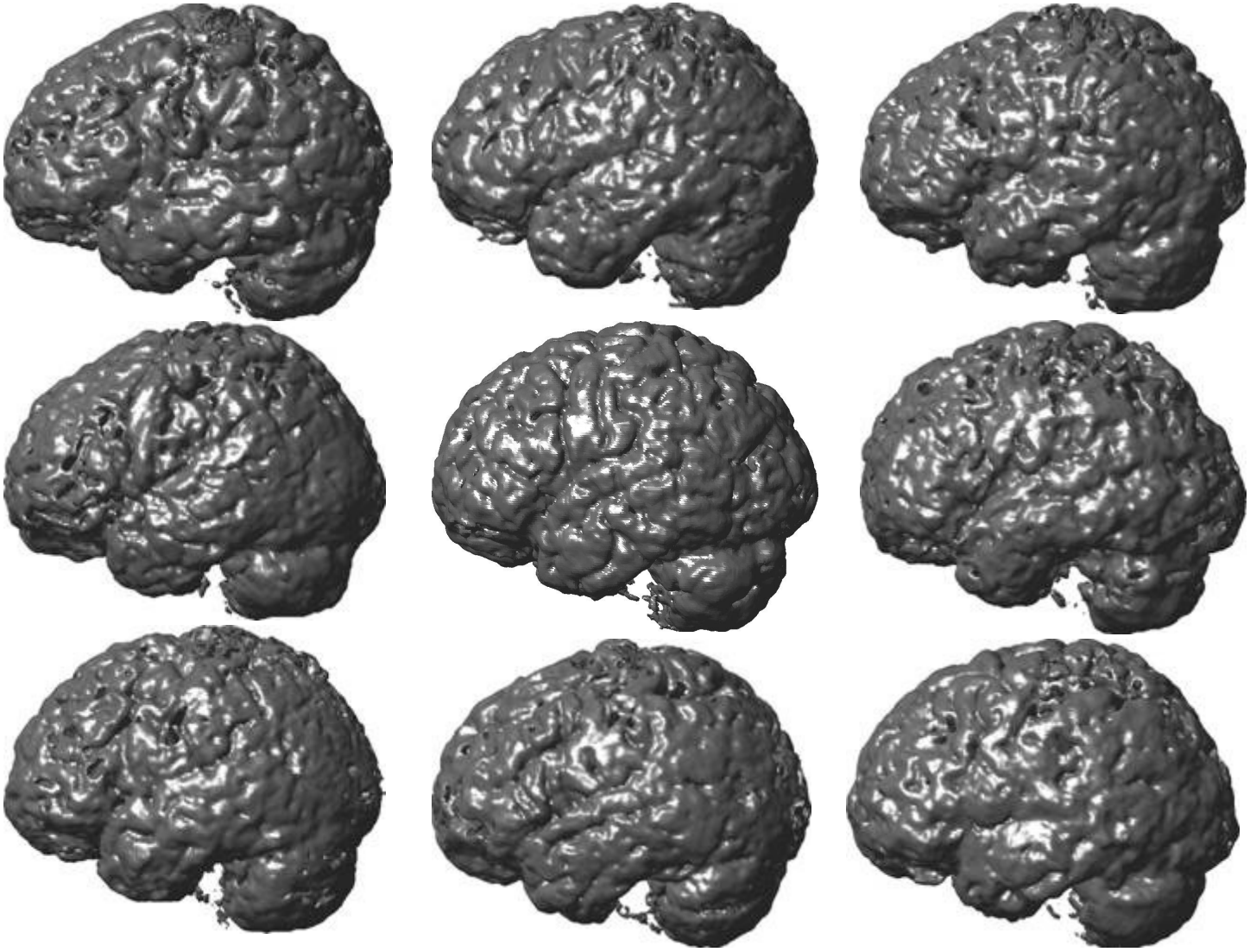
Corresponding subject slices



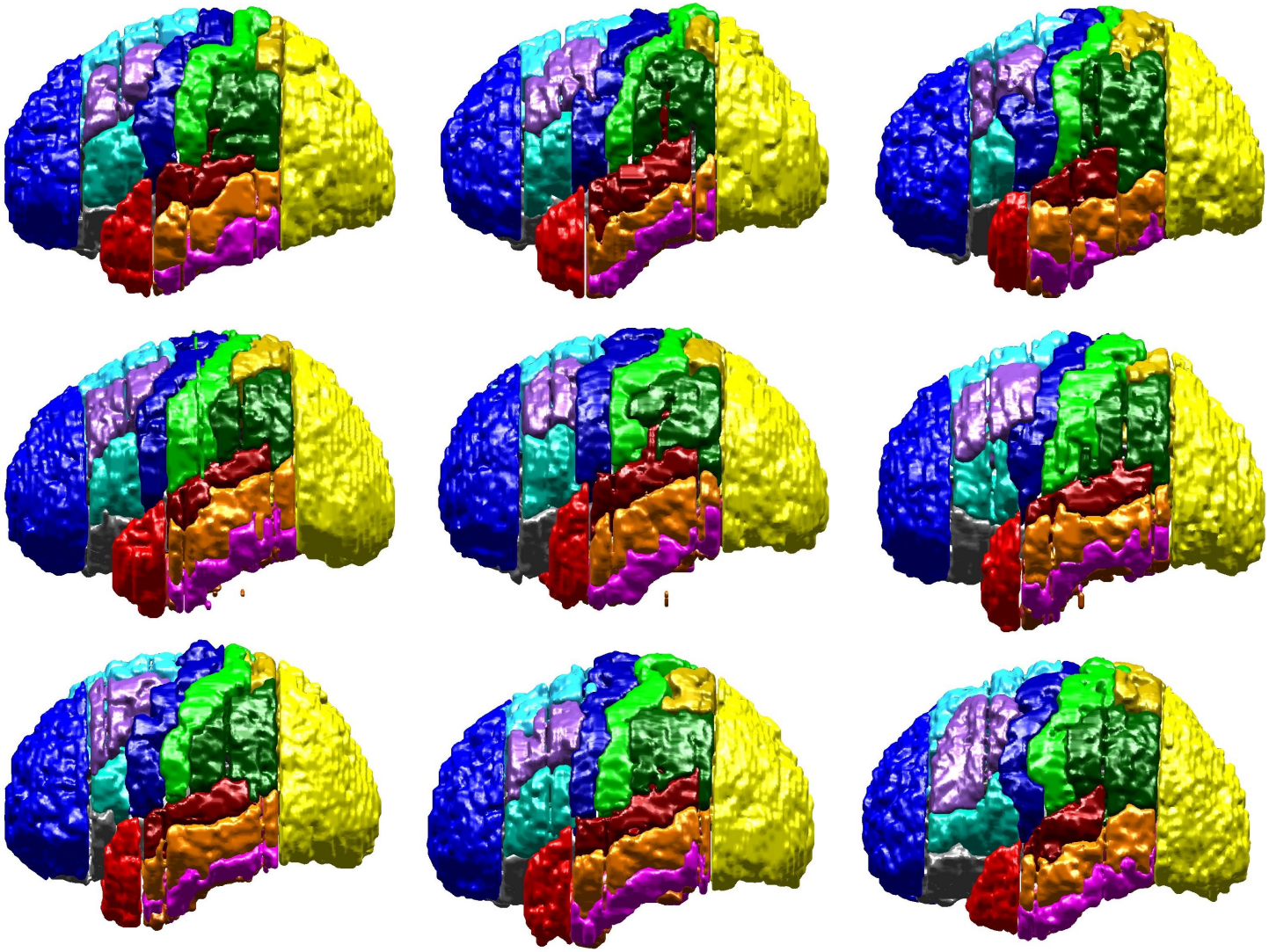
fMRI BOLD data



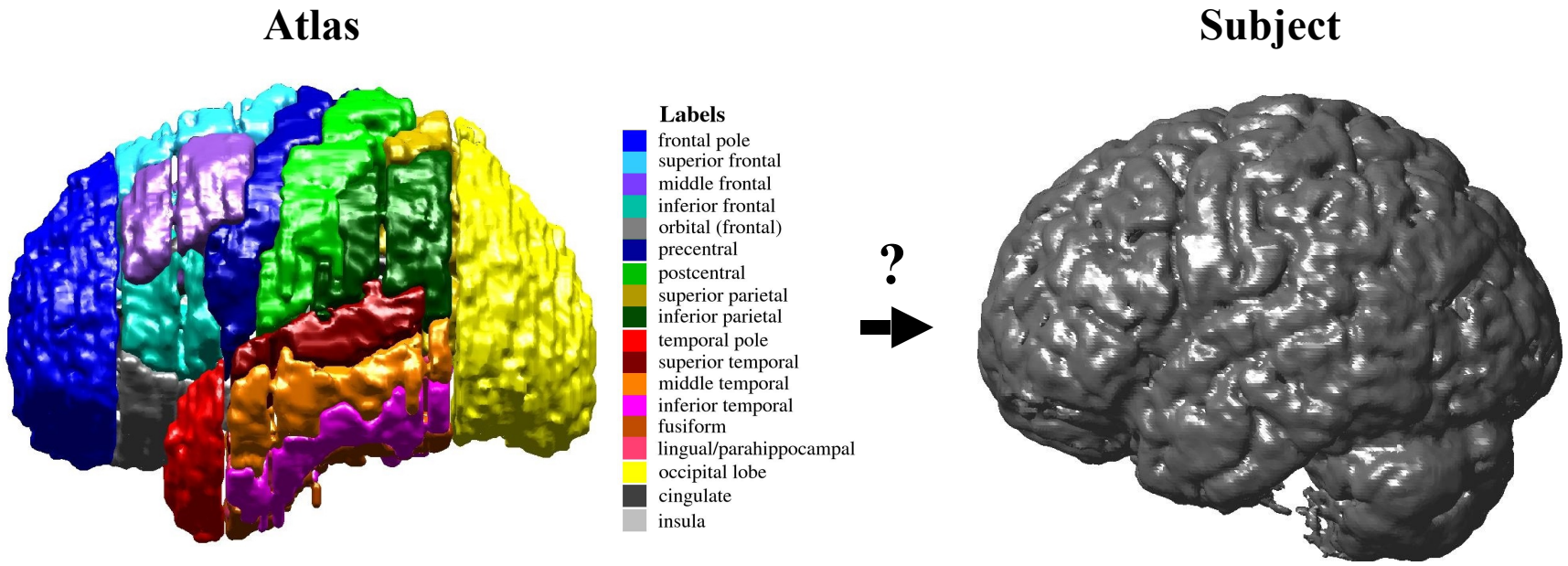
Unlabeled brains



Atlases (manually labeled brains)



The correspondence problem

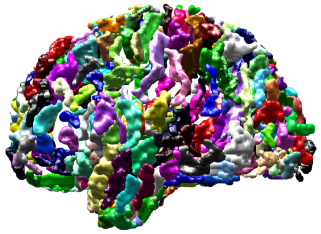


Standard approaches

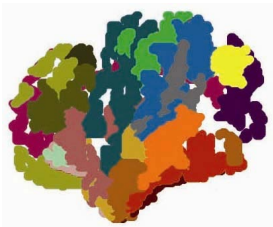
Methods	**Examples**
Linear registration:	Talairach-type spaces
Piece-wise linear registration:	Talairach (original)
Warping with landmarks:	Thin-plate splines
Unsupervised warping:	SPM, AIR, ANIMAL
Feature matching:	Watershed basins, parametric curves/surfaces

Mindboggle

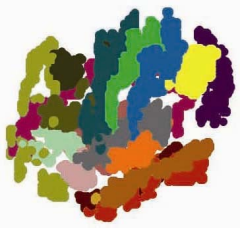
Extract pieces



Match pieces

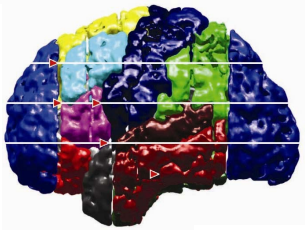


Transform boundaries



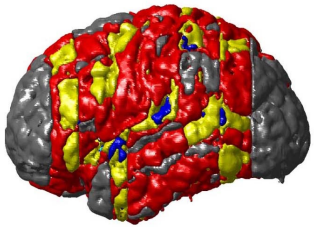
Warp labels

Evaluate



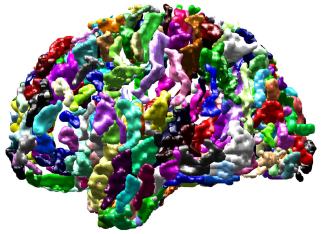
Use multiple atlases

Evaluate



Mindboggle

Extract pieces



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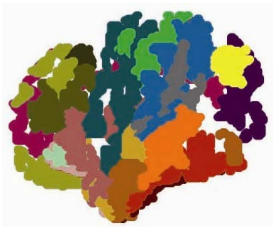
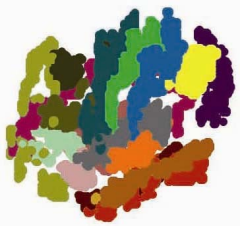


Transform boundaries



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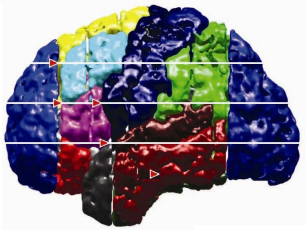
Evaluate



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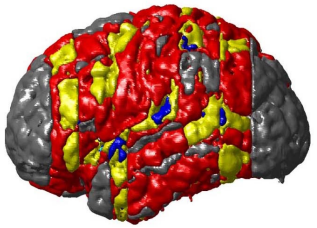
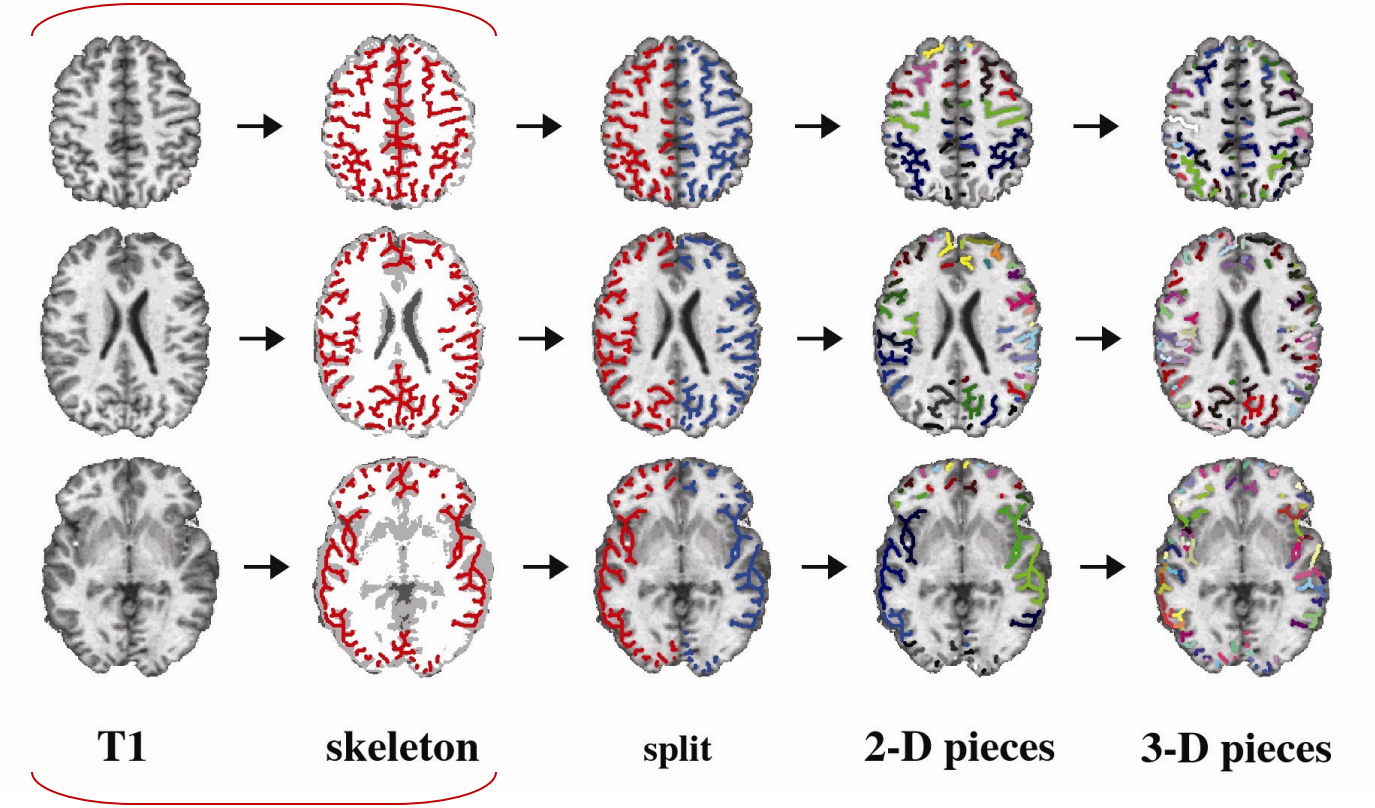
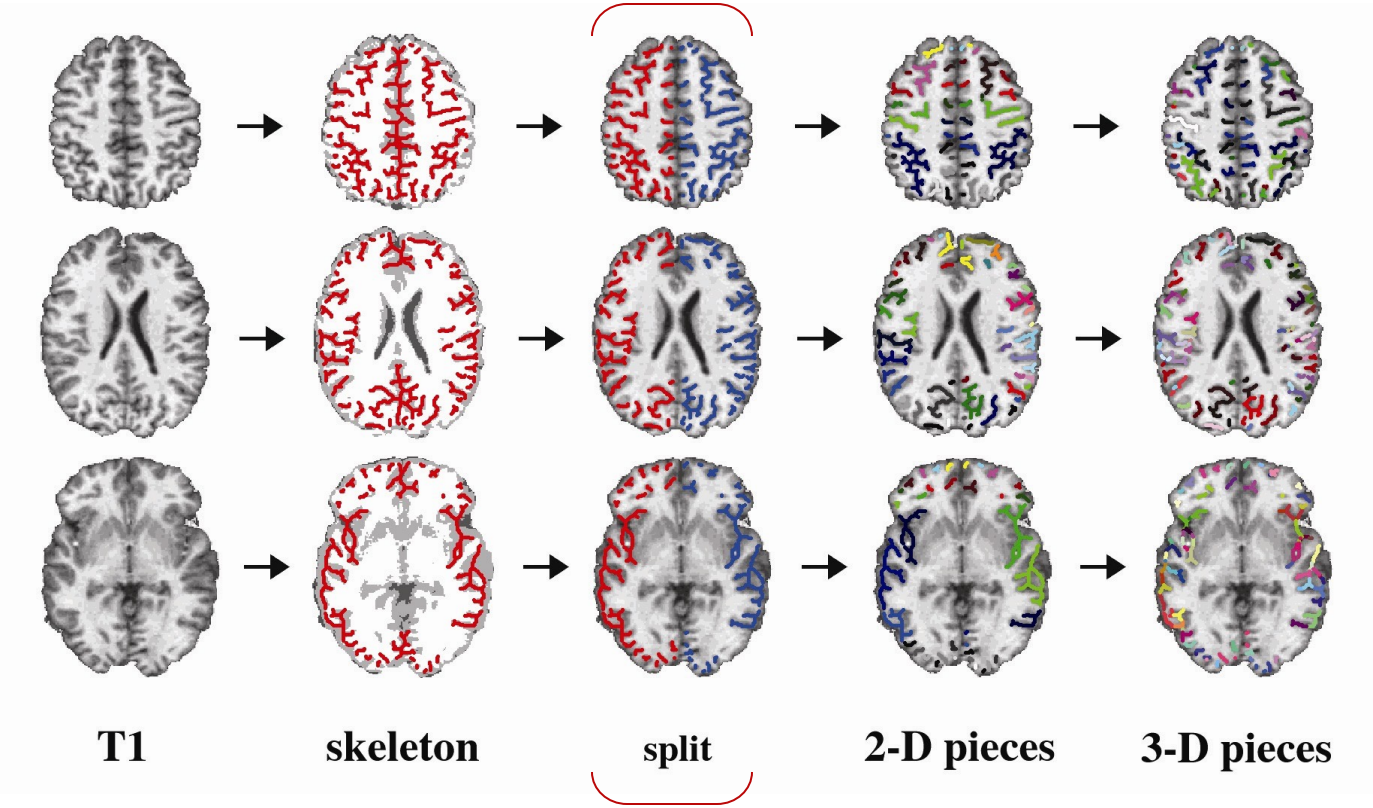


Extract pieces



- **Skeletonize** each slice of segmented non-white matter (only step in 2-D).
- **Split** the resulting sulcus skeleton into left and right **hemispheres**.
- **2-D** pieces in adjacent slices are grouped to make **3-D** pieces.

Extract pieces



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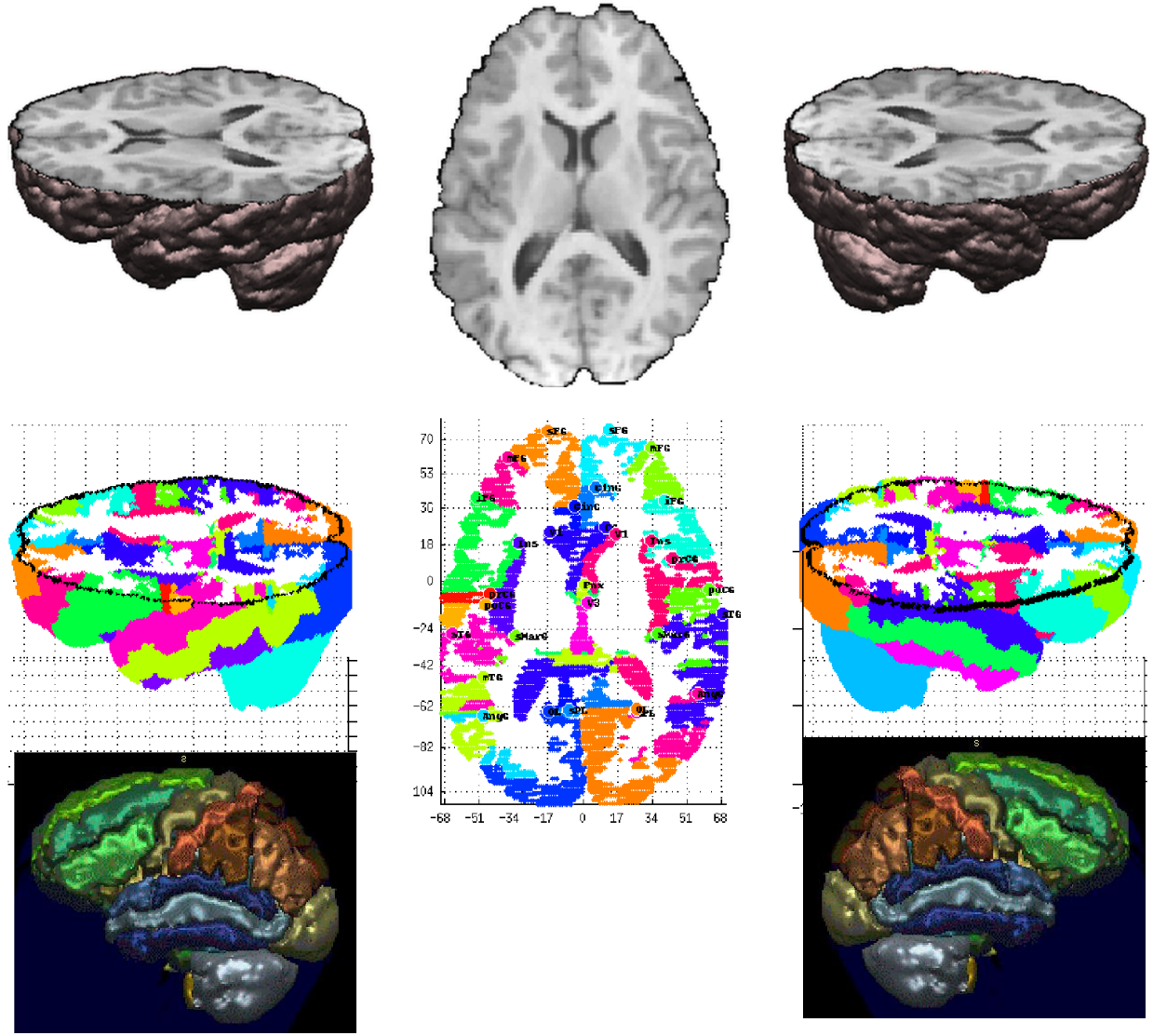

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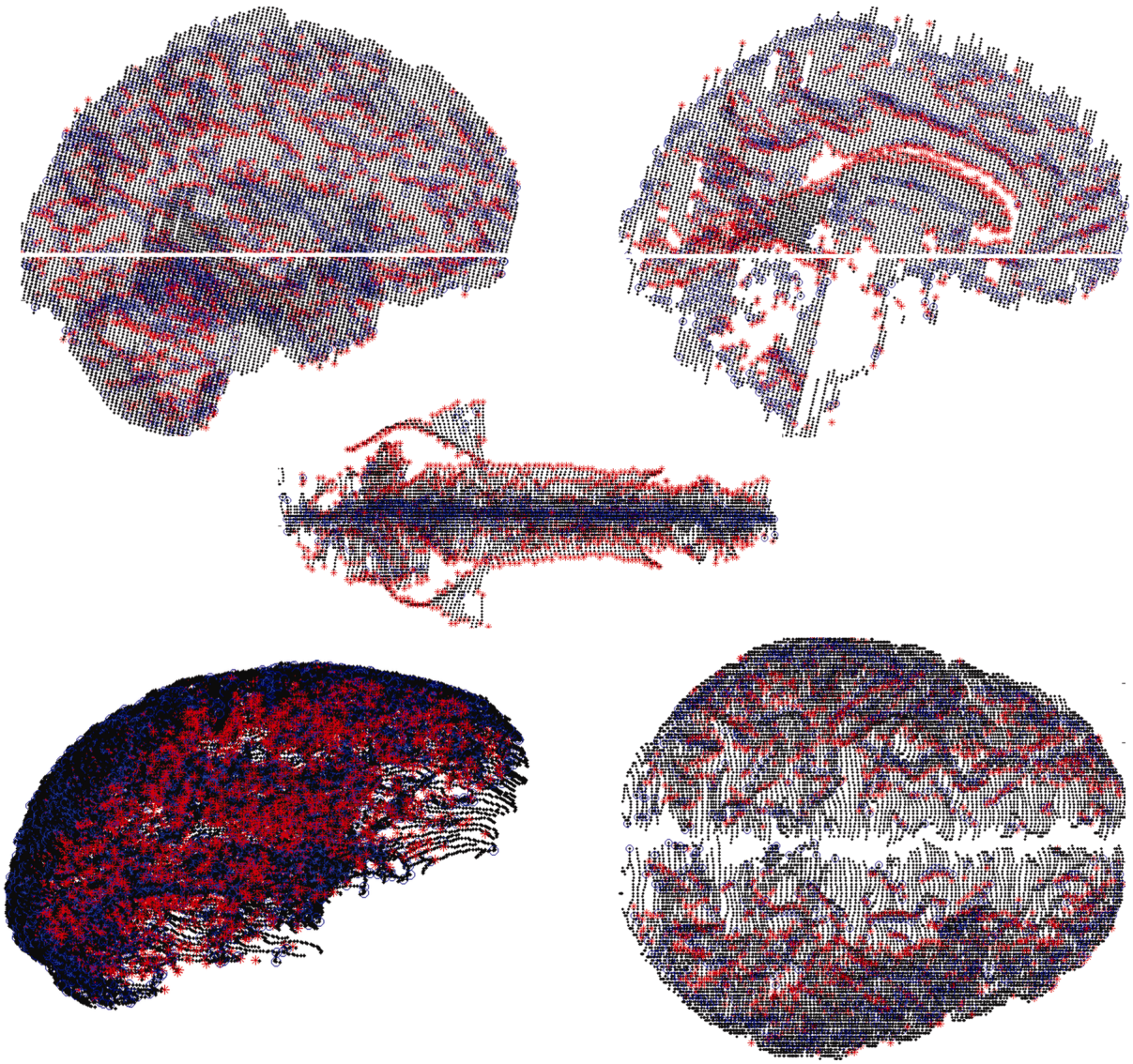
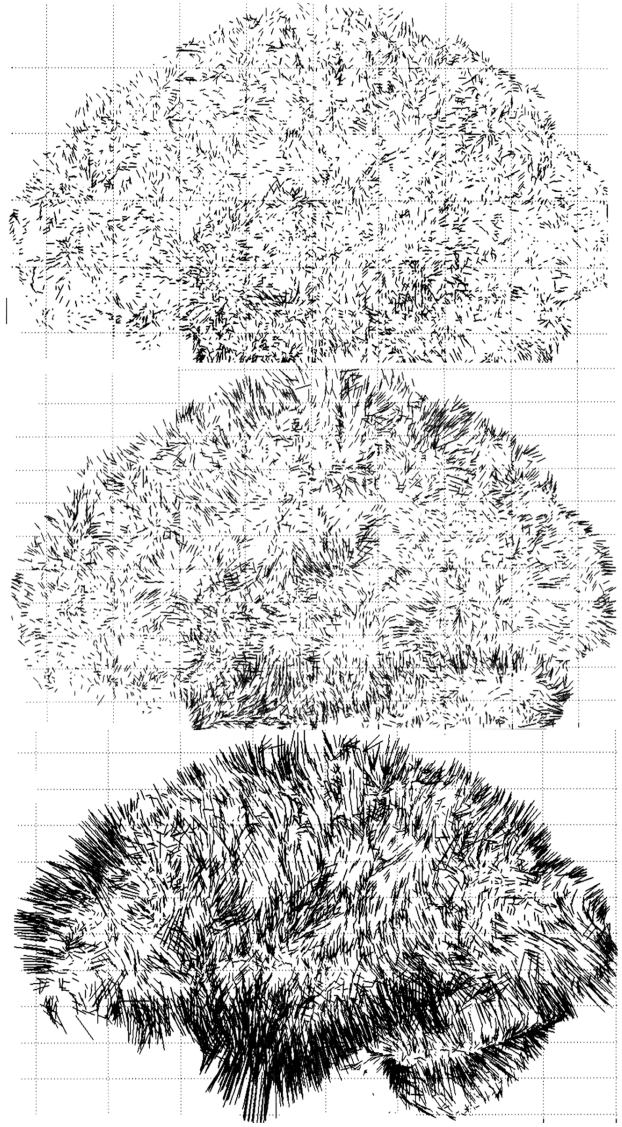
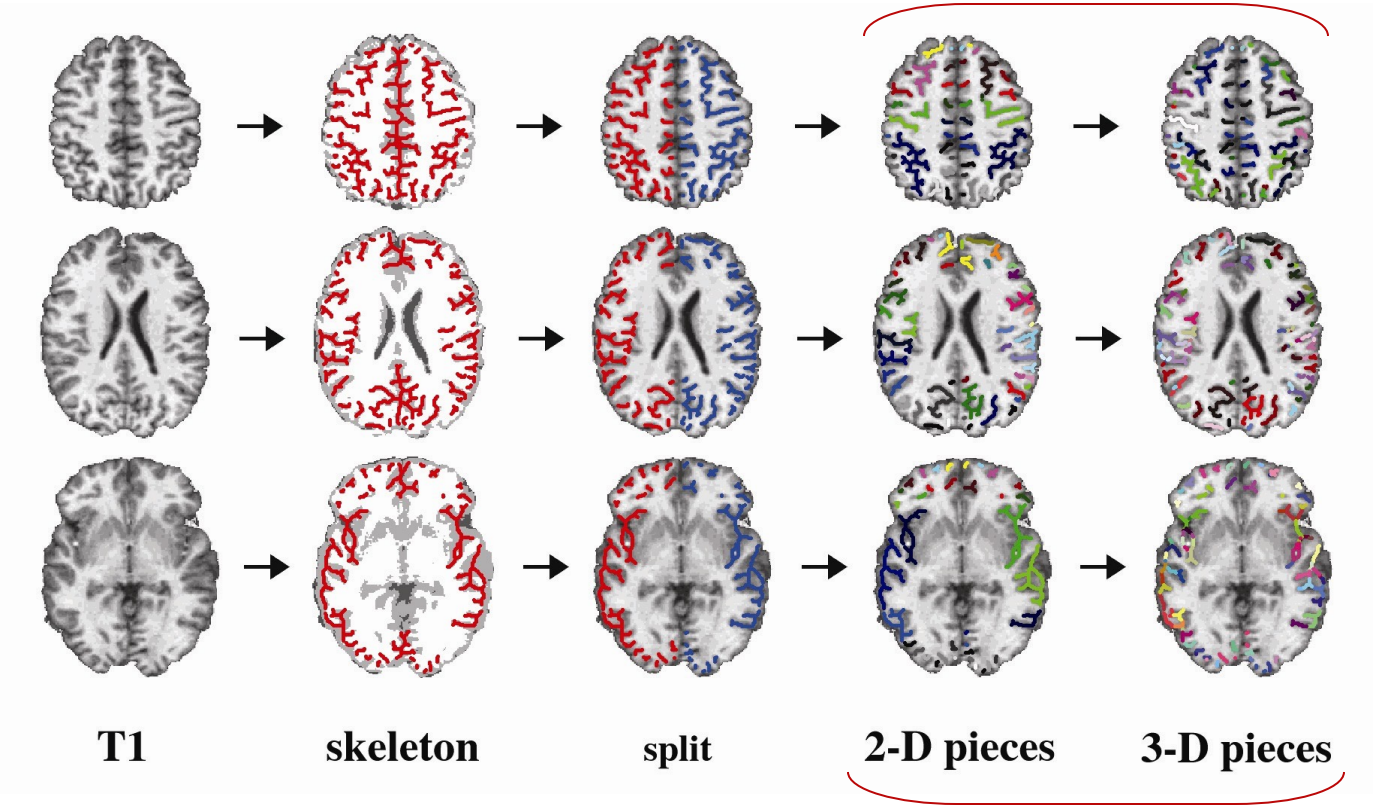


Extract pieces



Extract pieces



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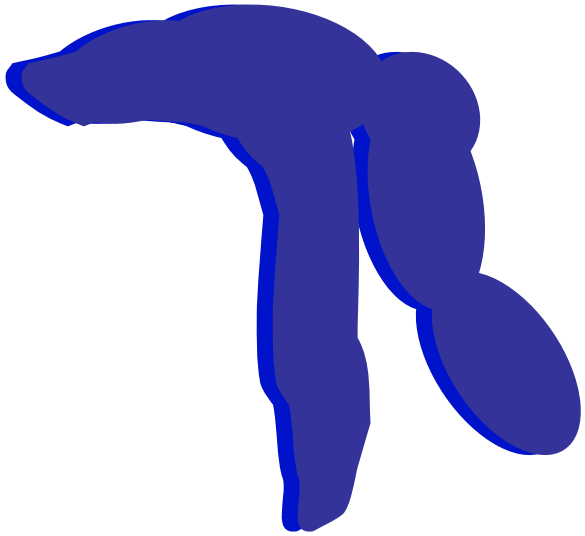
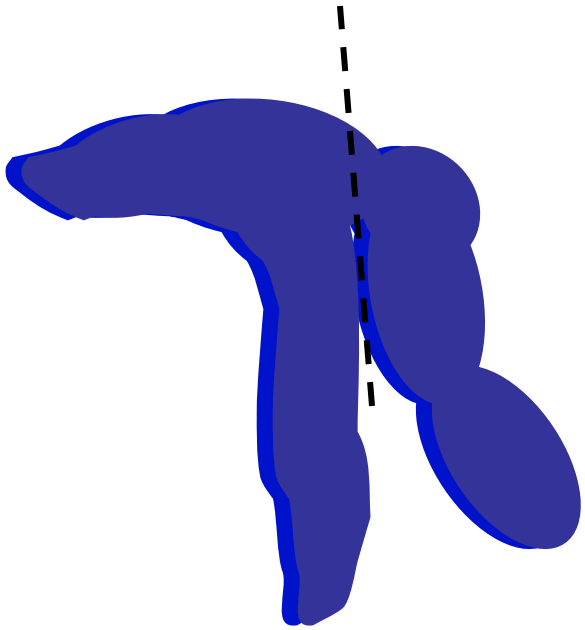
Extract pieces

One sulcus piece:



- **Divide** the resulting 3-D sulcus pieces along vertical bifurcations.
- **Fragment** into smaller clusters with a k-means algorithm.
- **Recombine** pairs of fragments if they share extensive borders.

Extract pieces



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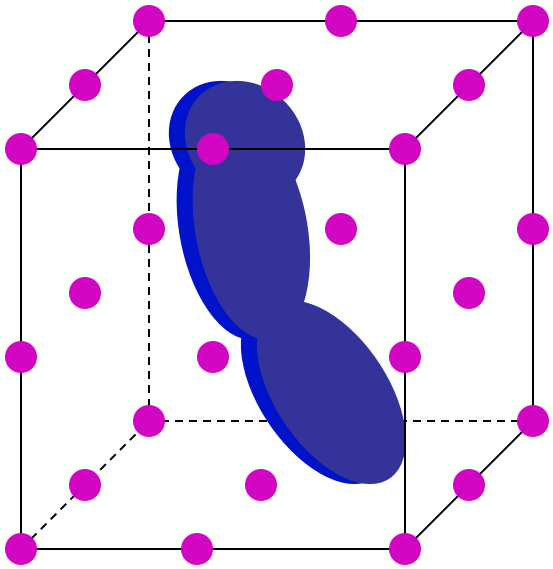

27 initial means (bounding box)

- **Divide** the resulting 3-D sulcus pieces along vertical bifurcations.
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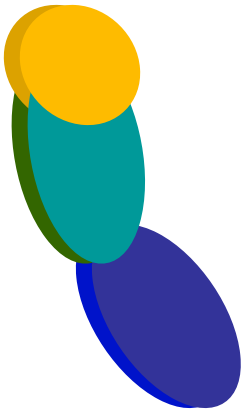
Extract pieces



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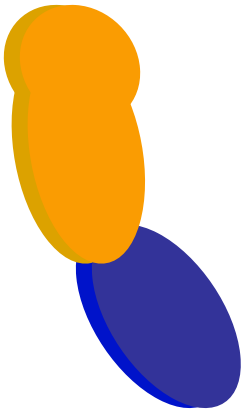

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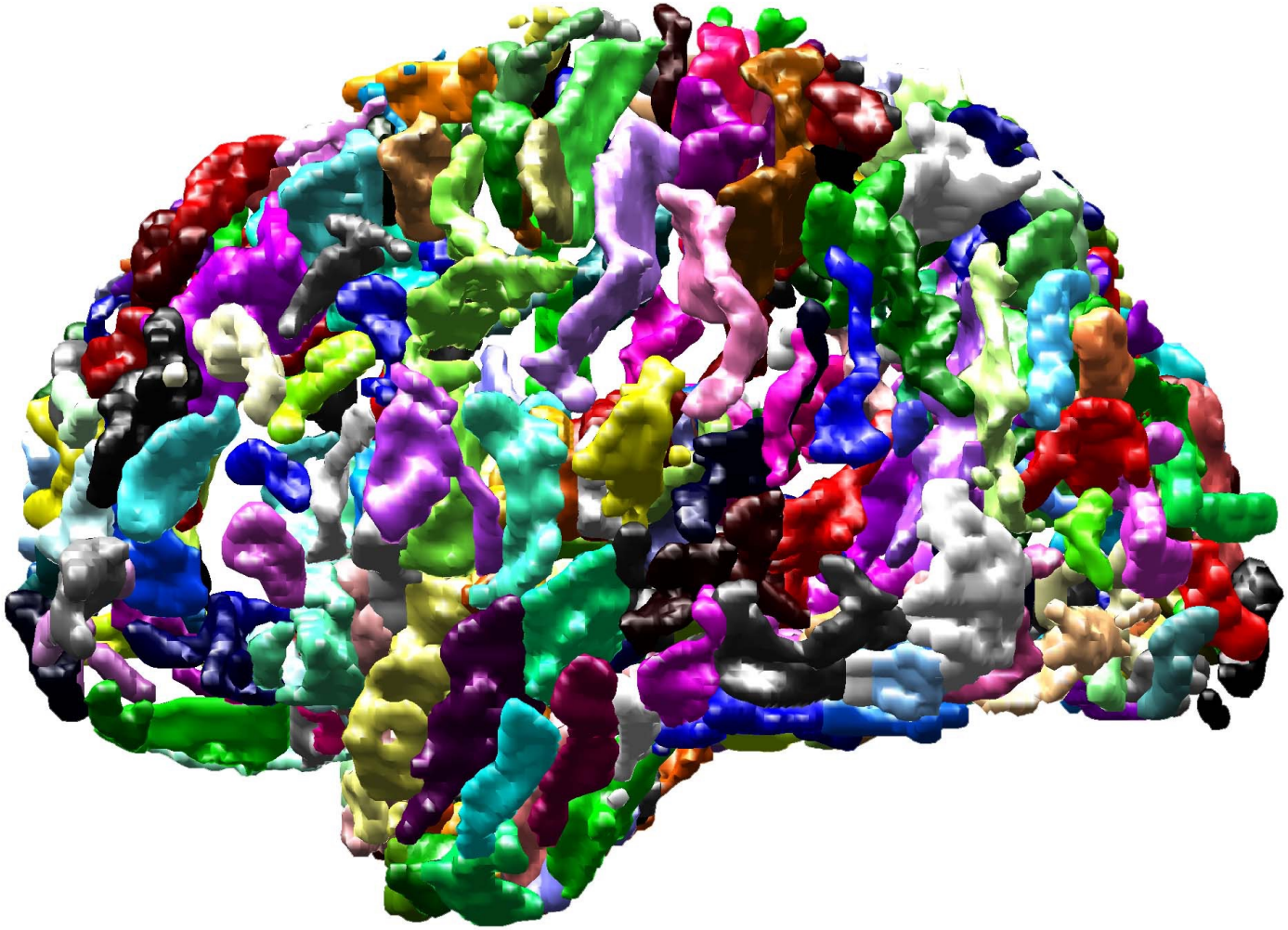
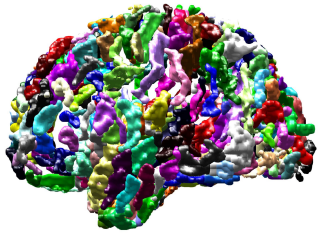
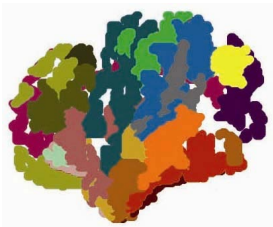


Mindboggle

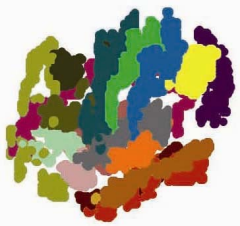
Extract pieces



Match pieces

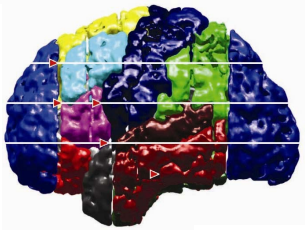


Transform boundaries



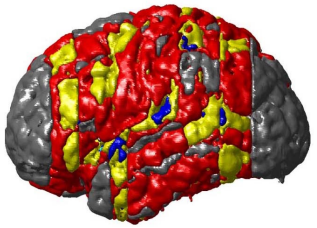
Warp labels

Evaluate



Use multiple atlases

Evaluate



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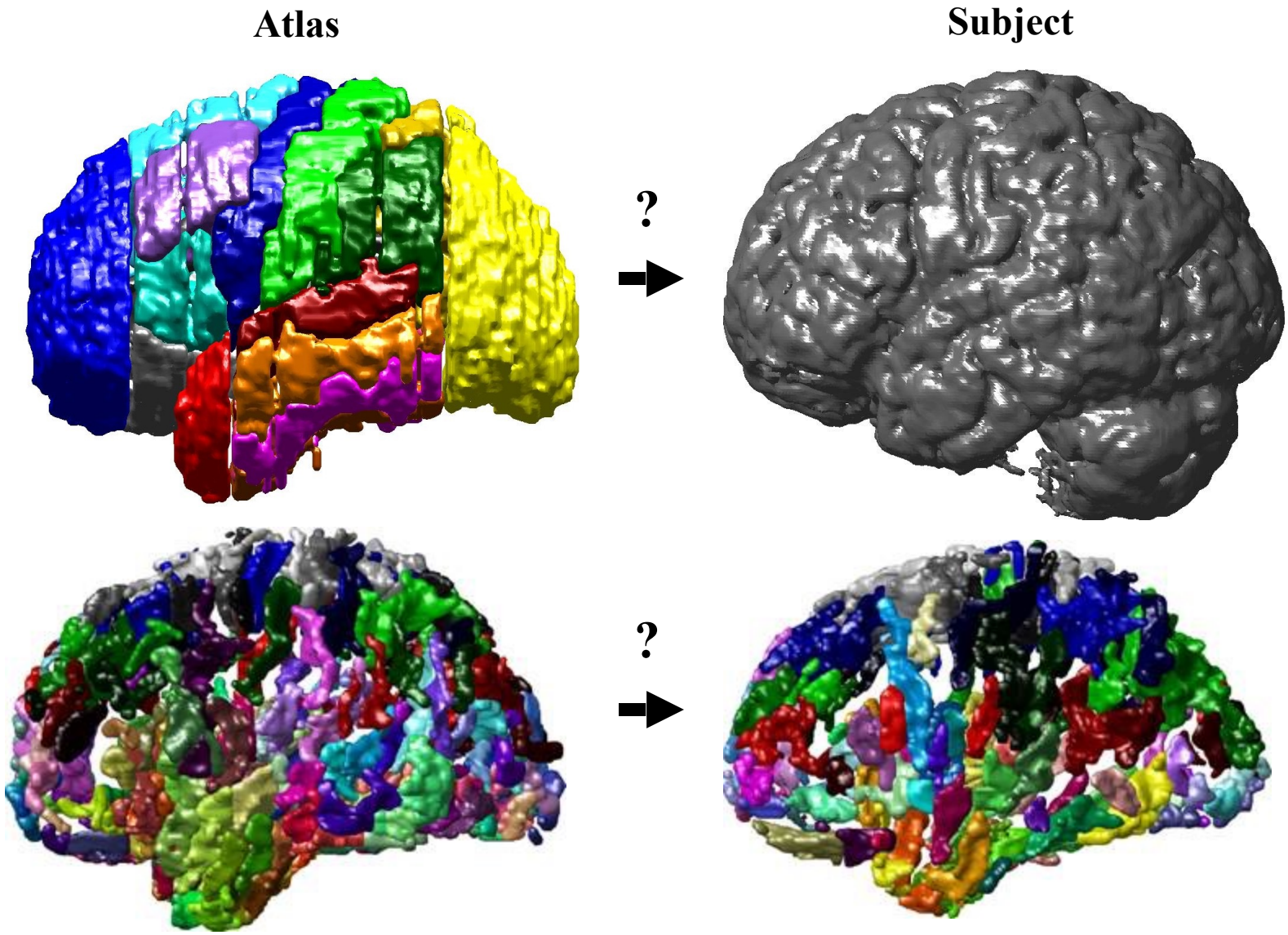
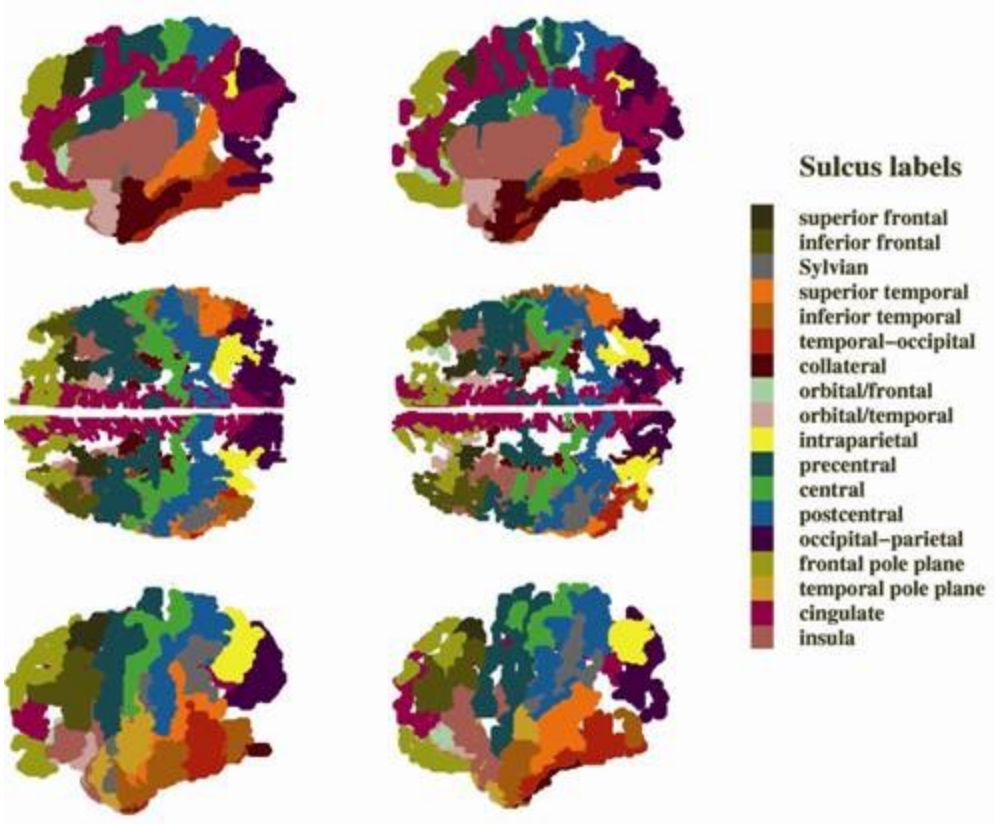


Match pieces

Atlas pieces
(grouped by sulci)

Subject pieces
(matches)

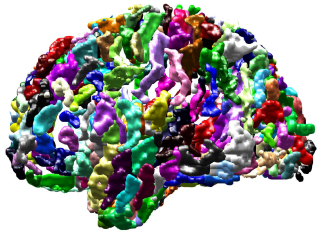


- Order matches by a **cost function**: $\mathbf{Cost = w_N N + w_V V + w_P P + w_O O}$

N = Δ # voxels **P** = Δ mean position
V = Δ # subvolumes **O** = non-overlap

Mindboggle

Extract pieces



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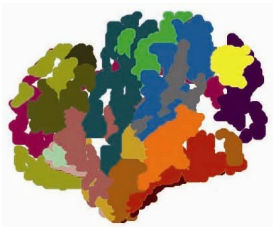
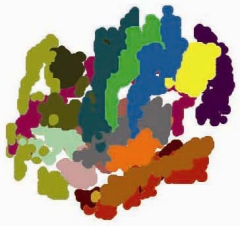
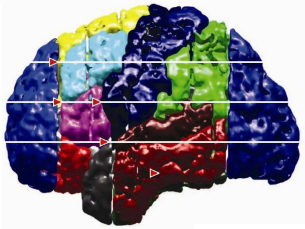


Transform boundaries



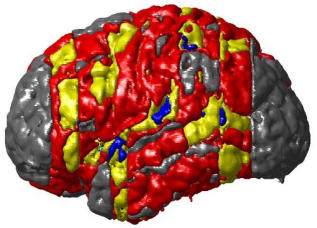
Warp labels

Evaluate



Use multiple atlases

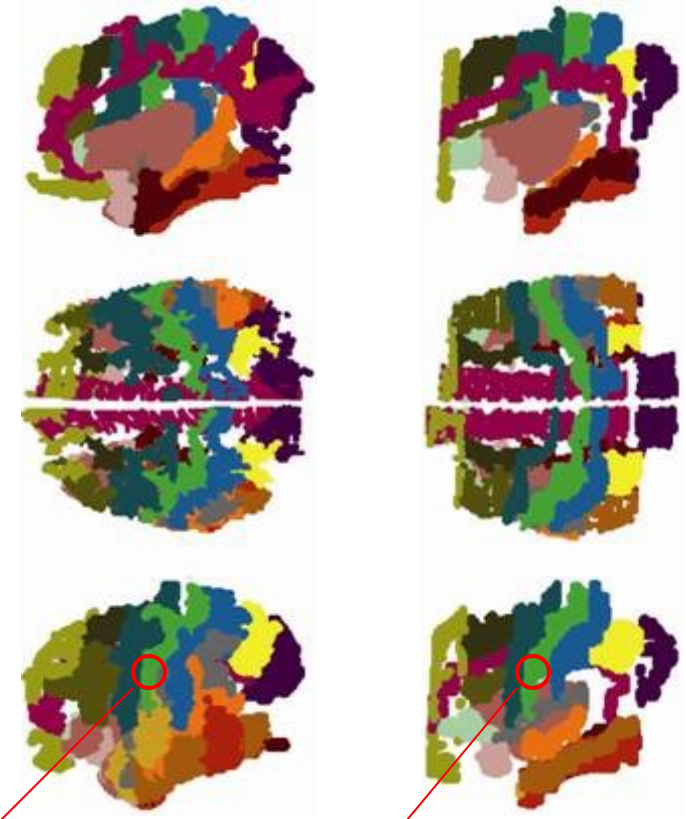
Evaluate

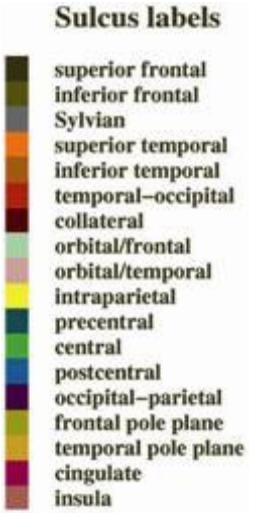


Transform boundaries

Atlas pieces
(grouped by sulci)

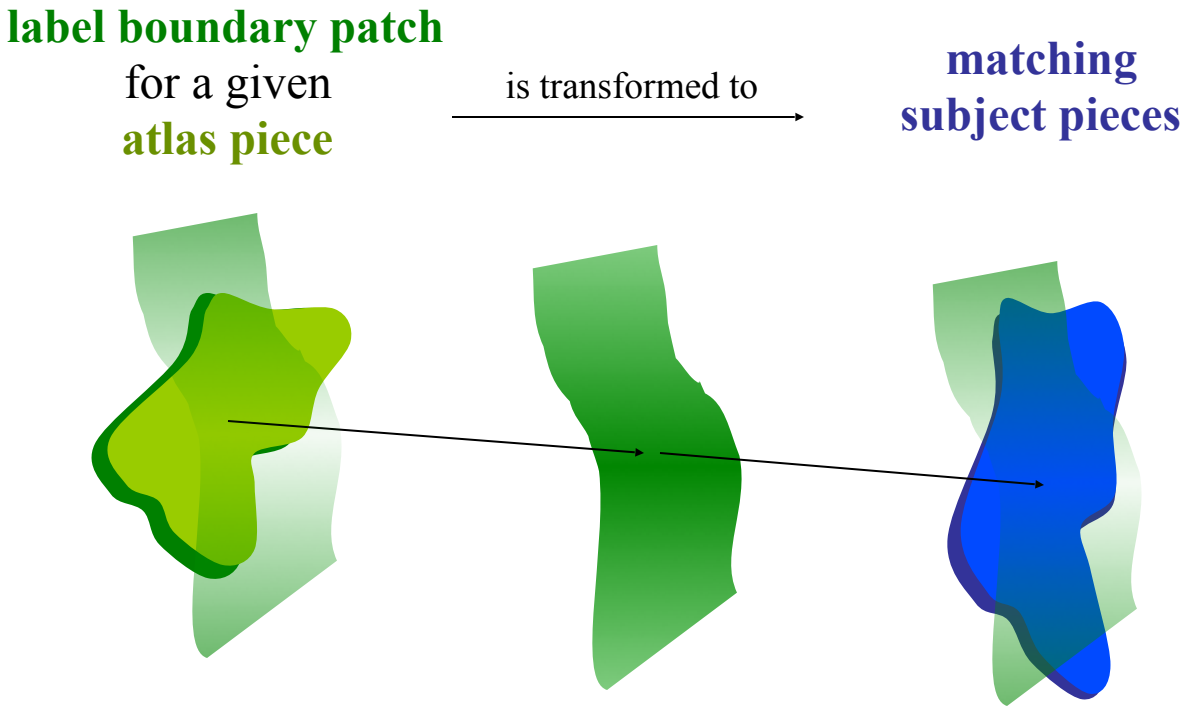
Label boundaries
(grouped by sulci)





- Each atlas piece is paired with a patch of nearest label boundary points.

Transform boundaries

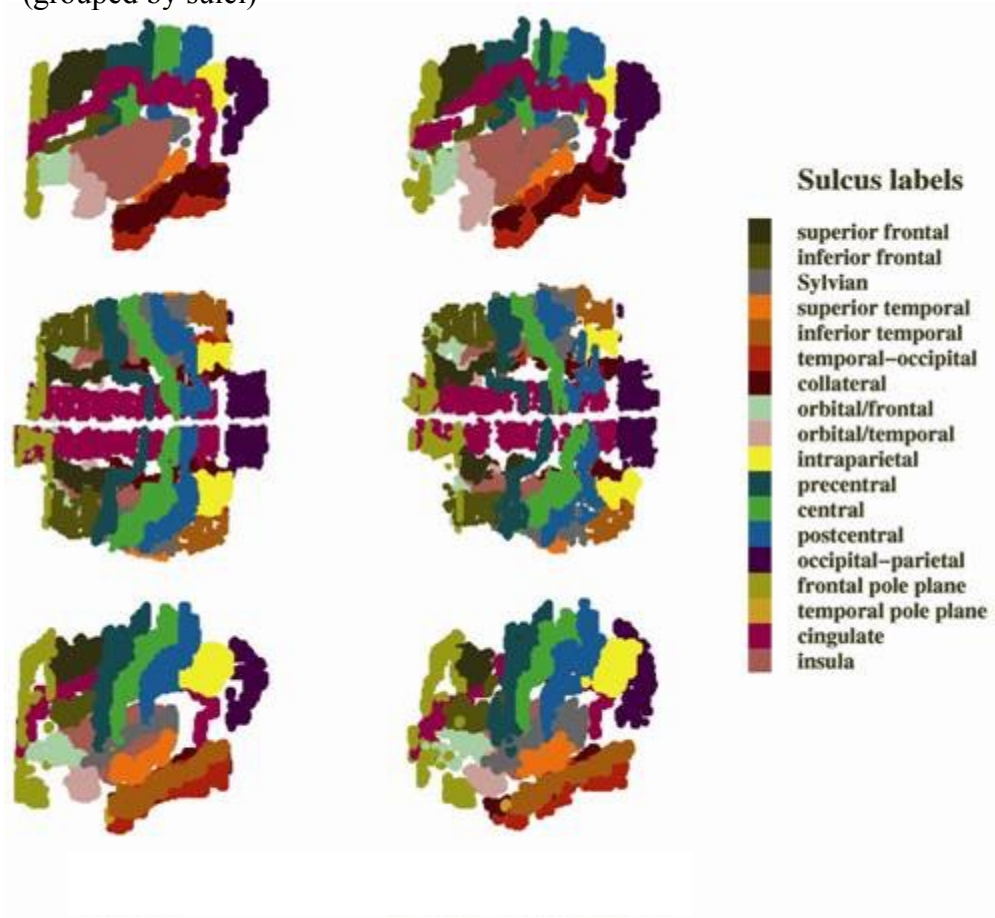


- Translate atlas label boundaries to the subject brain, patch by patch.
  Translation: mean (subject pieces) - mean (matching atlas piece).

Transform boundaries

Atlas boundaries → **Subject**

(grouped by sulci)



Mindboggle

Extract pieces

Match pieces

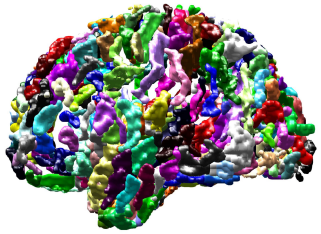
Transform boundaries

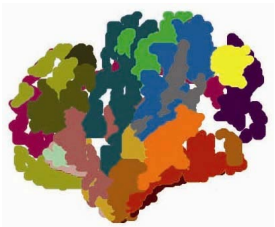
Warp labels

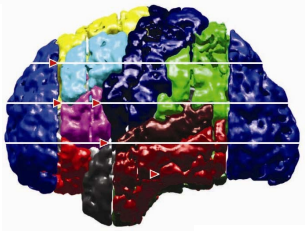
Evaluate

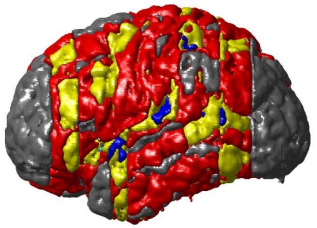
Use multiple atlases

Evaluate

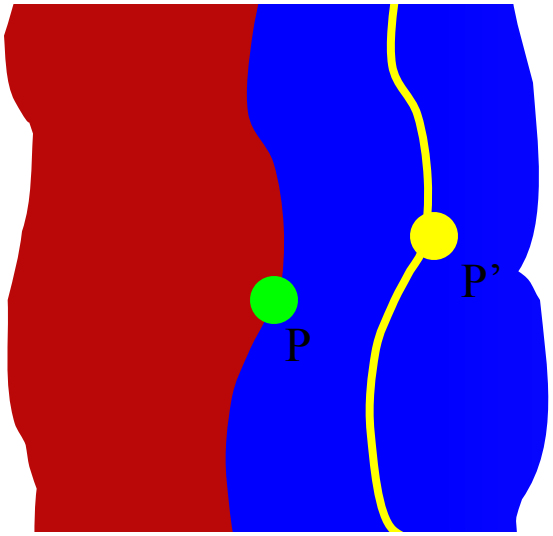






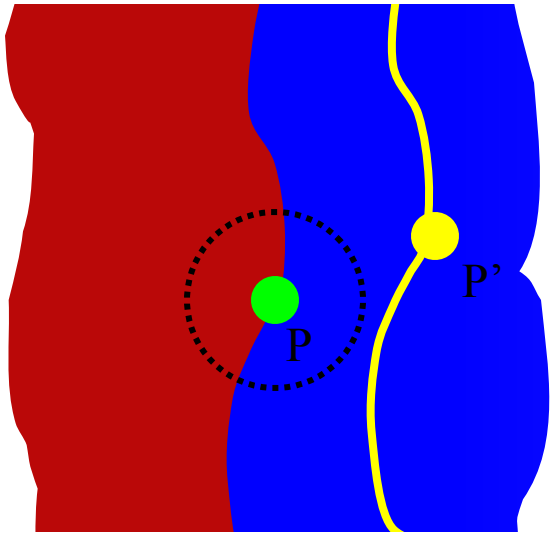


Warp labels



- **Select a pair of points** (P, P') in the original and transformed atlas patch.
- Find the nearest neighborhood of voxels to point P in the original atlas space.
- **Warp** the neighborhood of labels to coat transformed atlas boundaries (≈SOM).
- **Fill** the subject gray matter mask with new neighborhood majority atlas labels.

Warp labels



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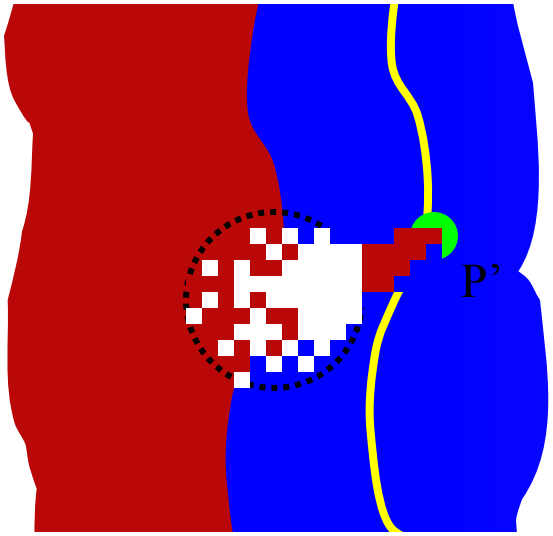
Warp labels



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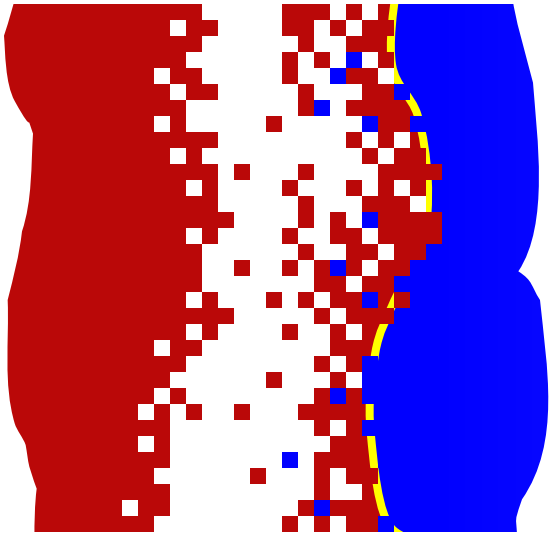
$$P_i(t) = P_i(t-1) + h(P,t)\,|P_i' - P_i(t-1)|$$

- **Fill** the subject gray matter mask with new neighborhood majority atlas labels.

Warp labels

precentral gyrus



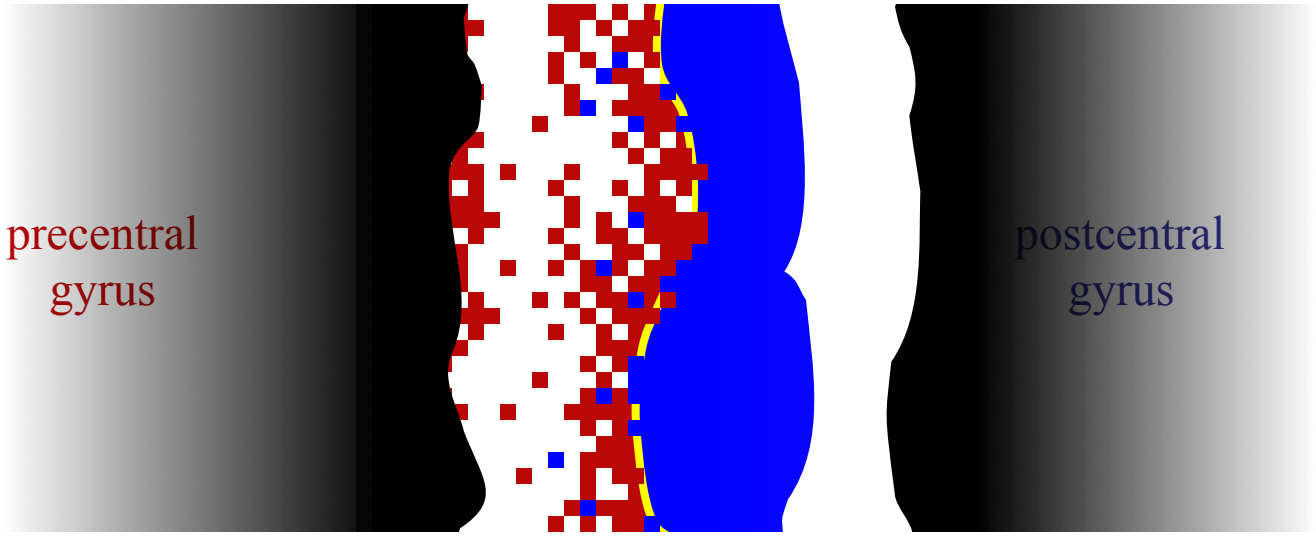
postcentral gyrus

- **Select a pair of points** (P, P') in the original and transformed atlas patch.
- Find the nearest neighborhood of voxels to point P in the original atlas space.
- **Warp** the neighborhood of labels to coat transformed atlas boundaries (≈SOM).

$$P_i(t) = P_i(t-1) + h(P,t)\,|P_i' - P_i(t-1)|$$

- **Fill** the subject gray matter mask with new neighborhood majority atlas labels.

Warp labels



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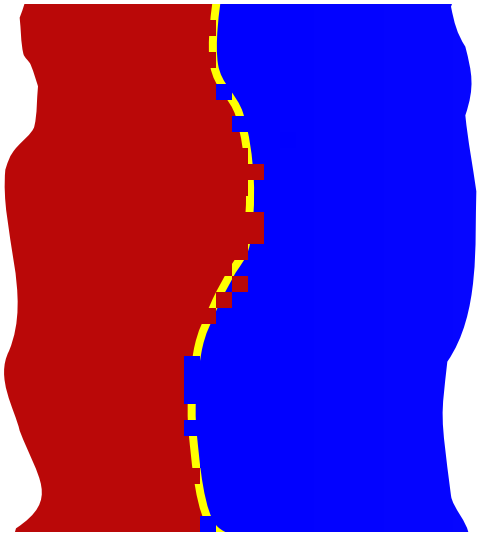
Warp labels

precentral gyrus



postcentral gyrus

- **Select a pair of points** (P, P') in the original and transformed atlas patch.
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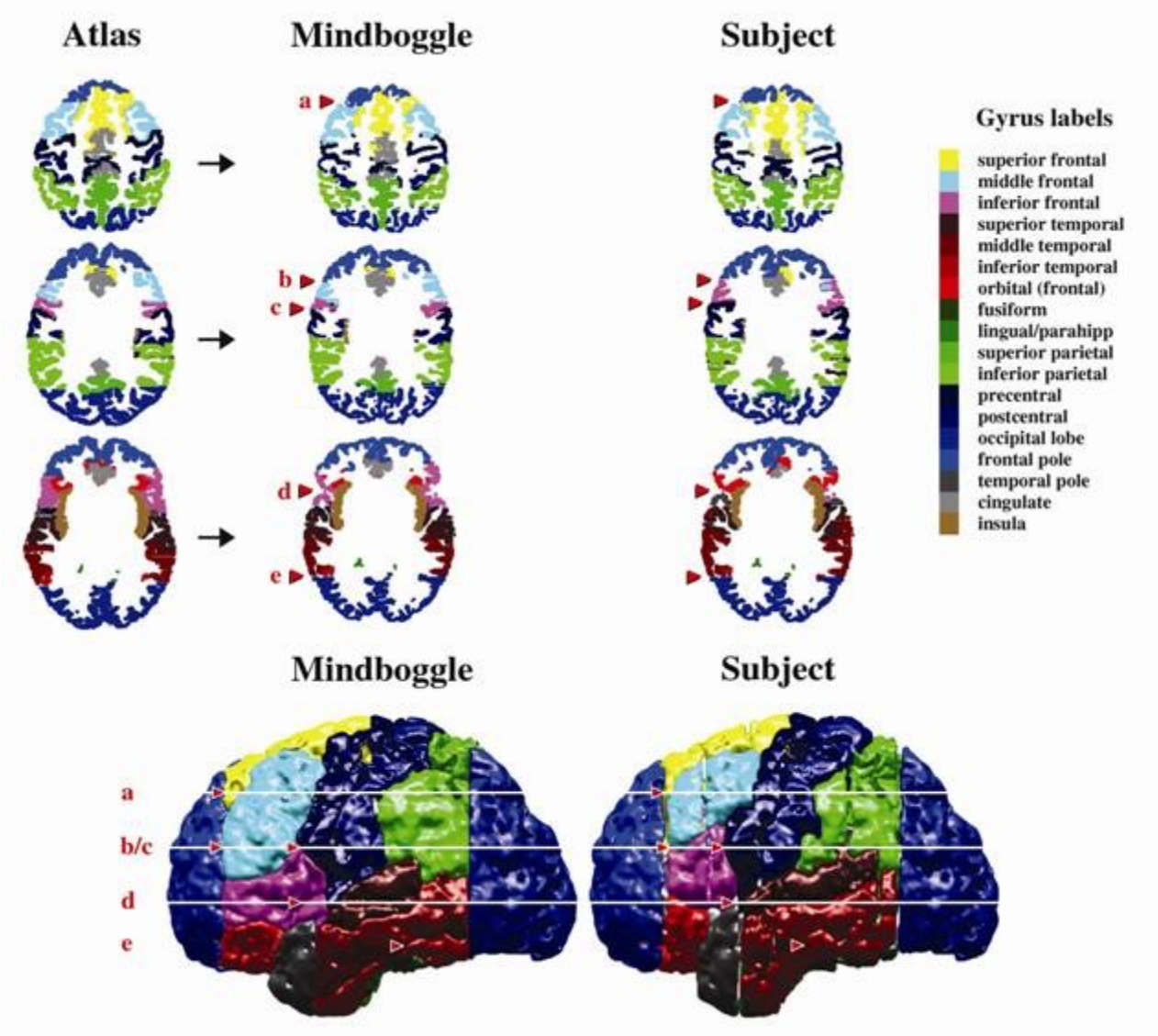
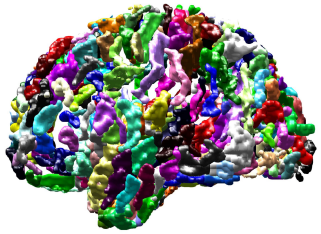
Warp labels

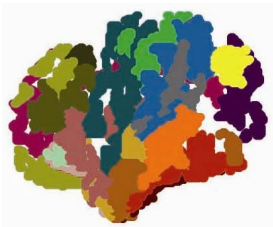

Atlas
Mindboggle
Subject
a
b
c
d
e
Gyrus labels
superior frontal
middle frontal
inferior frontal
superior temporal
middle temporal
inferior temporal
orbital (frontal)
fusiform
lingual/parahipp
superior parietal
inferior parietal
precentral
postcentral
occipital lobe
frontal pole
temporal pole
cingulate
insula
Mindboggle
Subject
a
b/c
d
e

Mindboggle

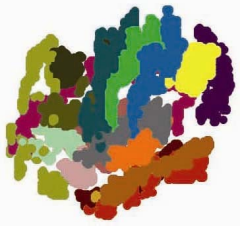
Extract pieces



Match pieces

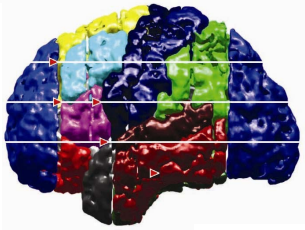


Transform boundaries



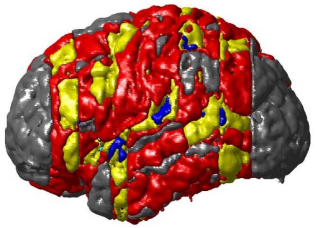
Warp labels

Evaluate

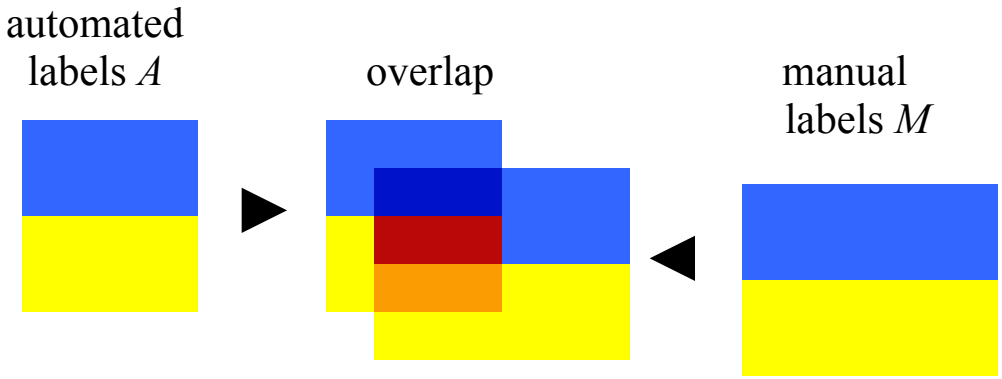


Use multiple atlases

Evaluate



Evaluation



Label agreement metrics:

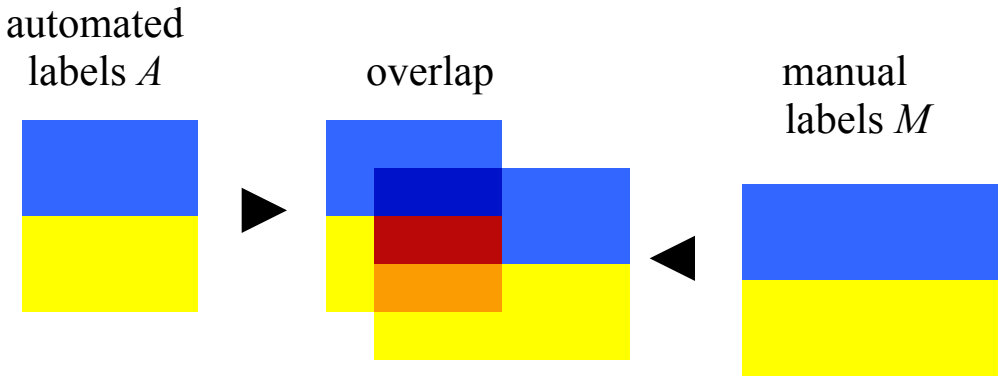
$$\frac{V_a = \text{intersection with the same label}}{V_c = \text{comparison volume}} = \frac{\text{intersection with the same label}}{?}$$

intersection $= V_a$ / intersection of atlas and subject = $\frac{\sum|A_i \cap M_i|}{\sum|A \cap M_i|}$

overlap $= V_a$ / union of atlas and subject = $\frac{\sum|A_i \cap M_j|}{\sum|A_i \cup M_i|}$

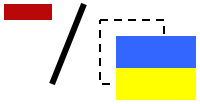
mask overlap, filled mask overlap $= V_a$ / subject = $\frac{\sum|A_i \cap M_i|}{\sum|M_i|}$

Evaluation



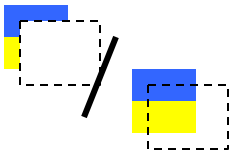
Error metrics:

Type I error (*A*,*M*) = $\sum[|A \cap M_i| - |A_i \cap M_i|] \Big/ \sum|M_i|$ =



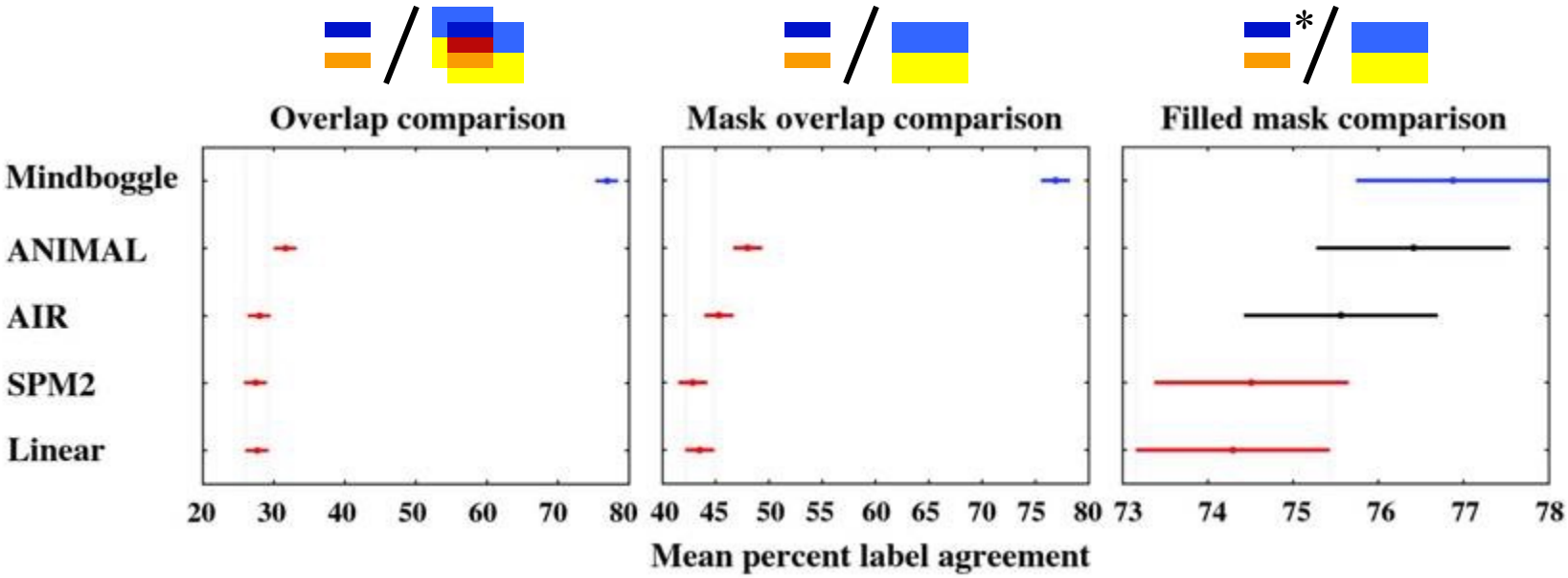
When incorrect labels are assigned to a region
(e.g. voxels in the superior frontal gyrus
are labeled as middle frontal gyrus).

Type II error (*A*,*M*) = $1 - \sum|A_i \cap M_i| \Big/ \sum|A_i|$ =



When a region's label is assigned to other regions
(e.g. voxels outside of superior frontal gyrus
are labeled as superior frontal gyrus).

Evaluation

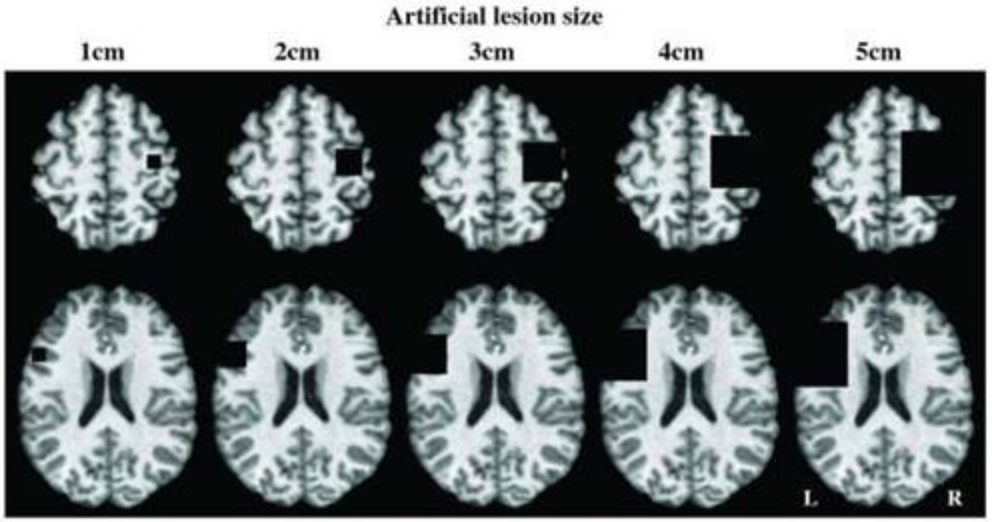


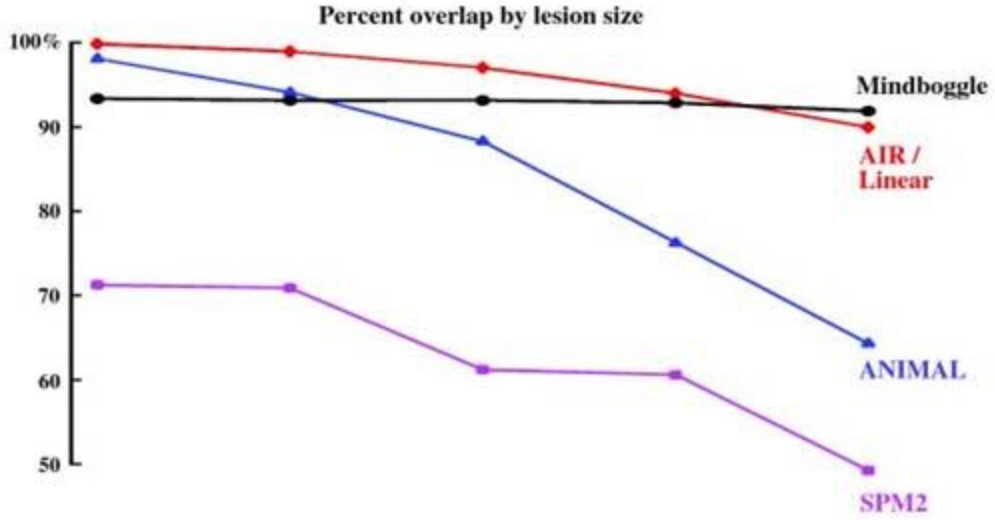
- A **one-way ANOVA** was performed to test if the means are the same for the label agreements obtained by each of the methods.

- A **multiple comparison test** was then performed to determine which pair of means are significantly different (95% confidence interval around the mean, based on the Studentized range distribution).

- Mindboggle obtained a significantly higher mean filled mask label agreement than did linear registration or SPM2 ($p < 0.05$).

Evaluation

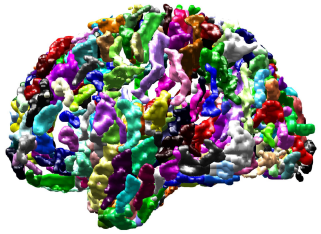




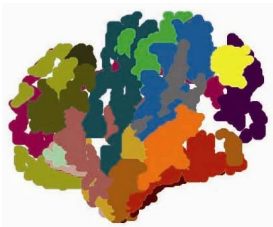
- The atlas was used to label an artificially lesioned version of itself.

Mindboggle

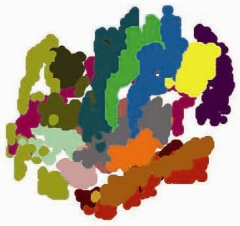
Extract pieces



Match pieces

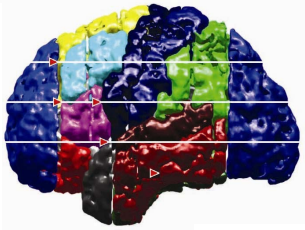


Transform boundaries



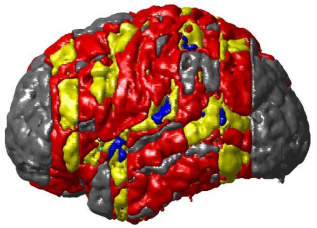
Warp labels

Evaluate



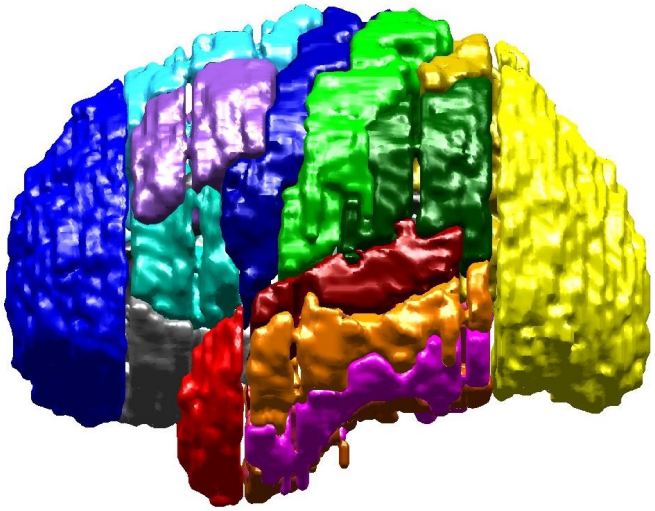
Use multiple atlases

Evaluate



A single atlas

Atlas

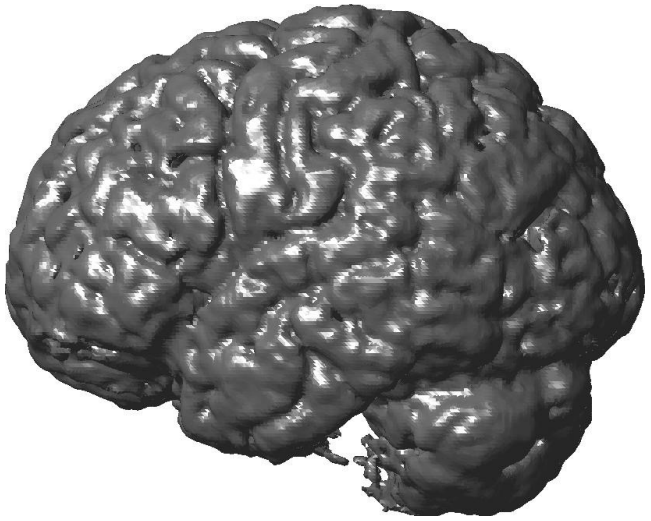


Labels

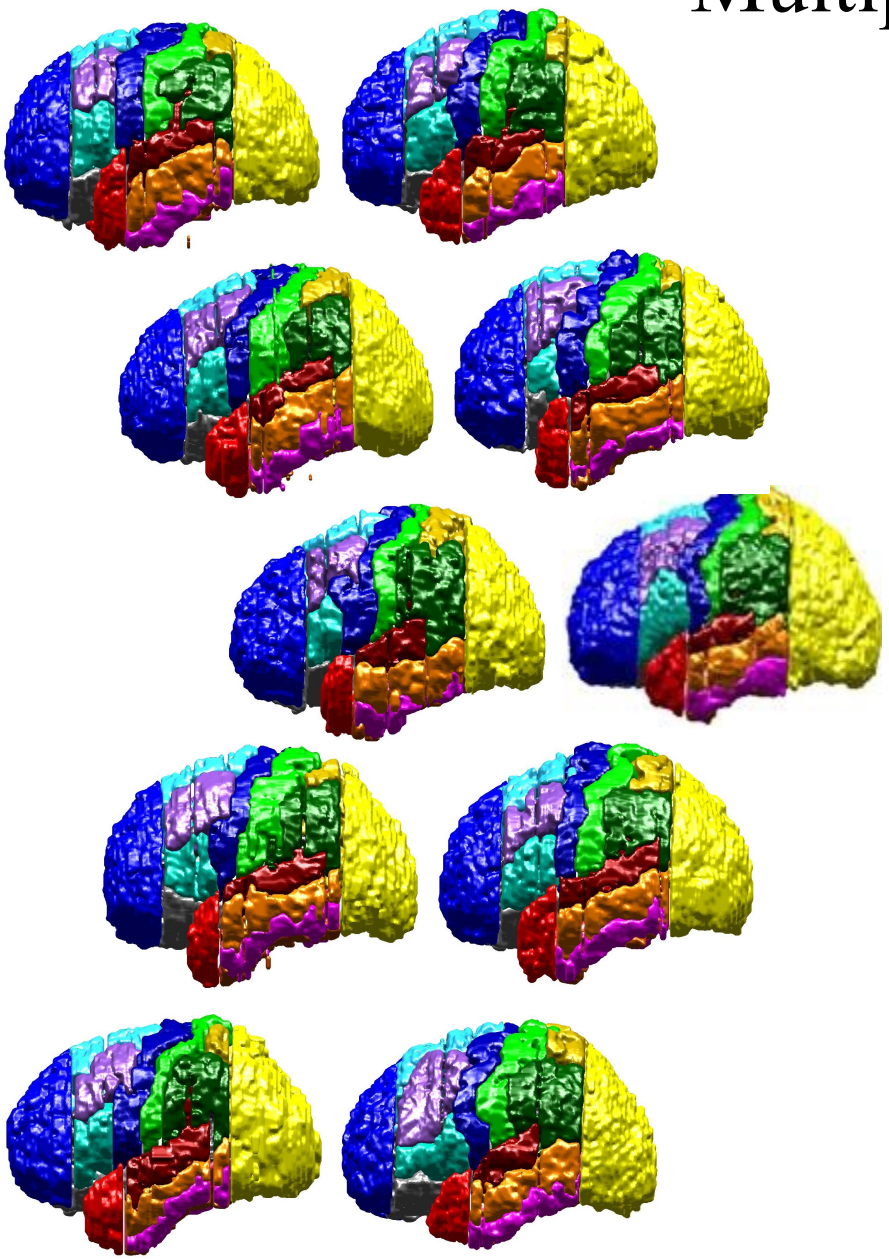
- frontal pole
- superior frontal
- middle frontal
- inferior frontal
- orbital (frontal)
- precentral
- postcentral
- superior parietal
- inferior parietal
- temporal pole
- superior temporal
- middle temporal
- inferior temporal
- fusiform
- lingual/parahippocampal
- occipital lobe
- cingulate
- insula

?

Subject

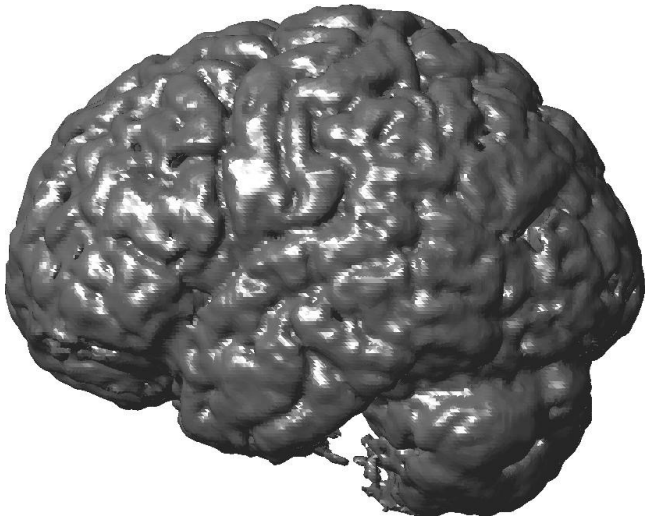


Multiple atlases



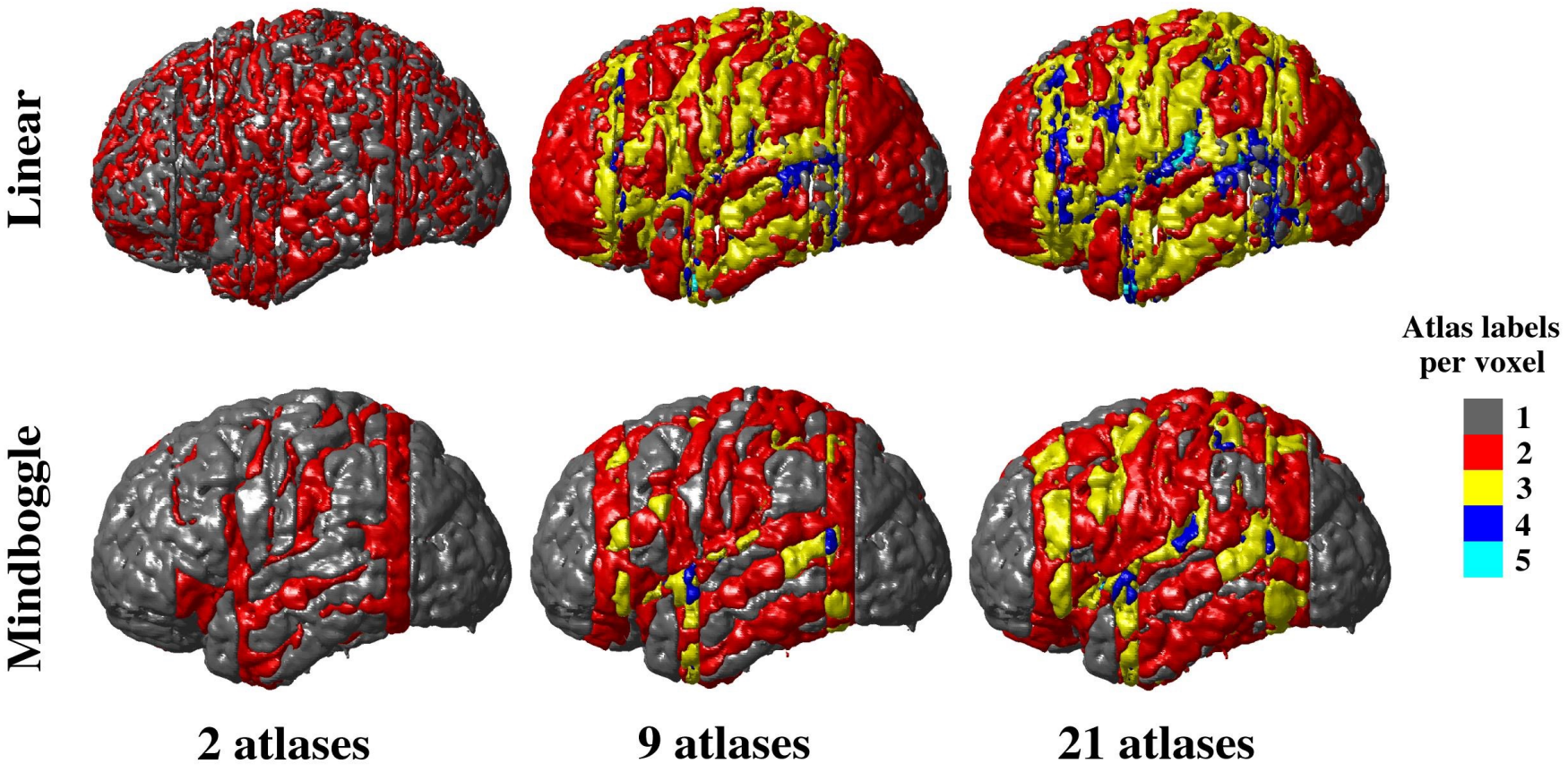
?

Subject



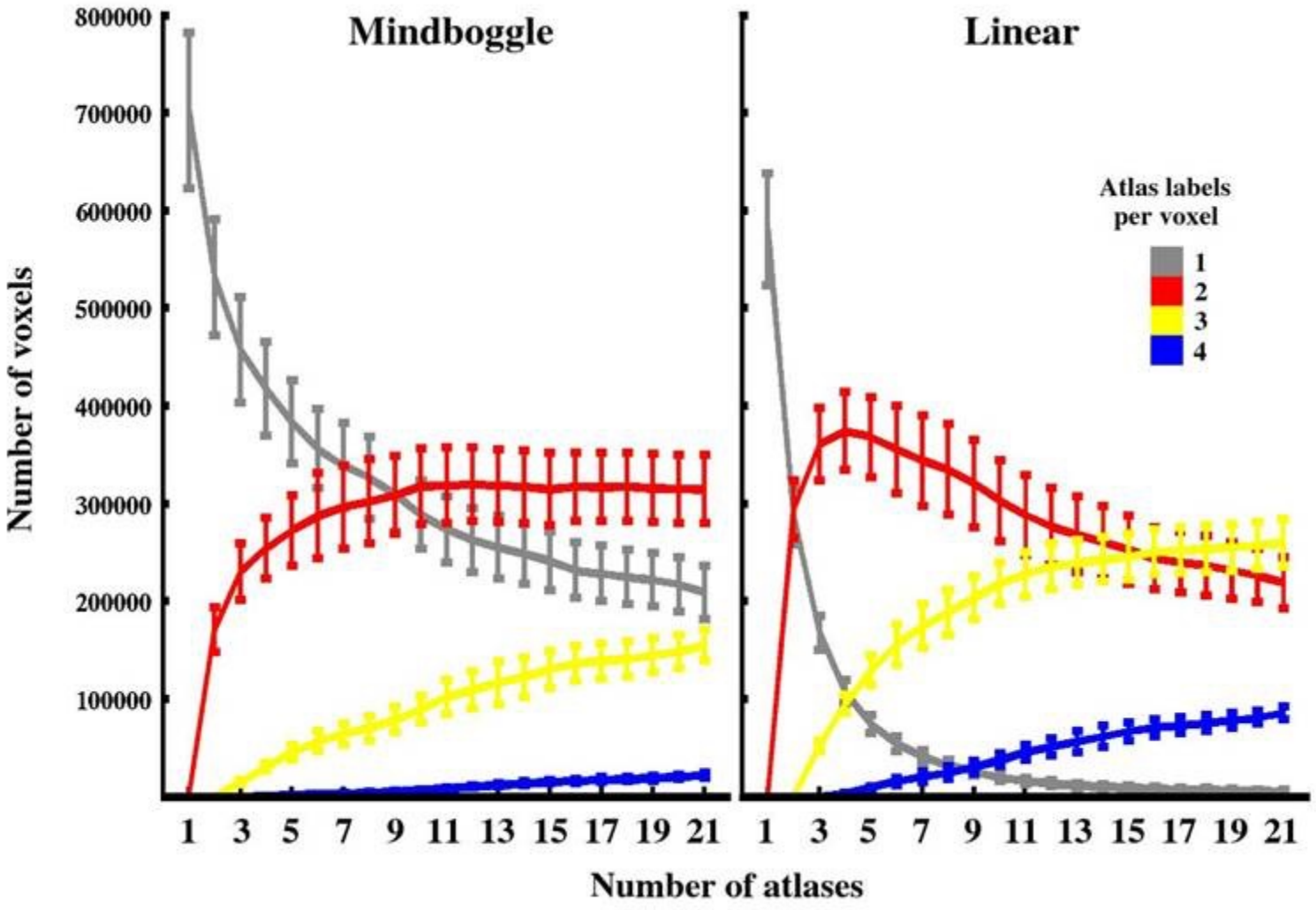
Multiple atlases

Number of labels per voxel



Multiple atlases

Number of labels per voxel: voxel counts



Mindboggle

Extract pieces

Match pieces

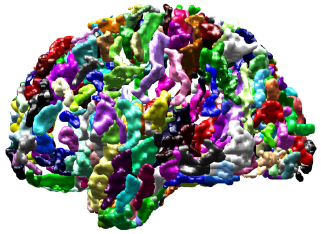
Transform boundaries

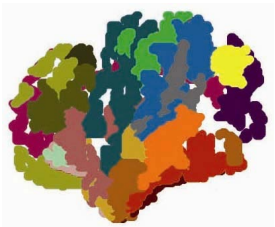
Warp labels

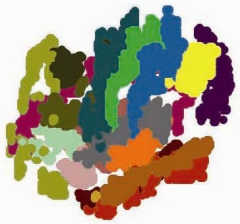
Evaluate

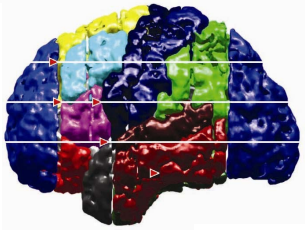
Use multiple atlases

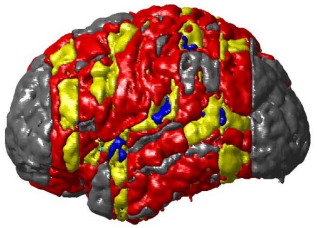
Evaluate





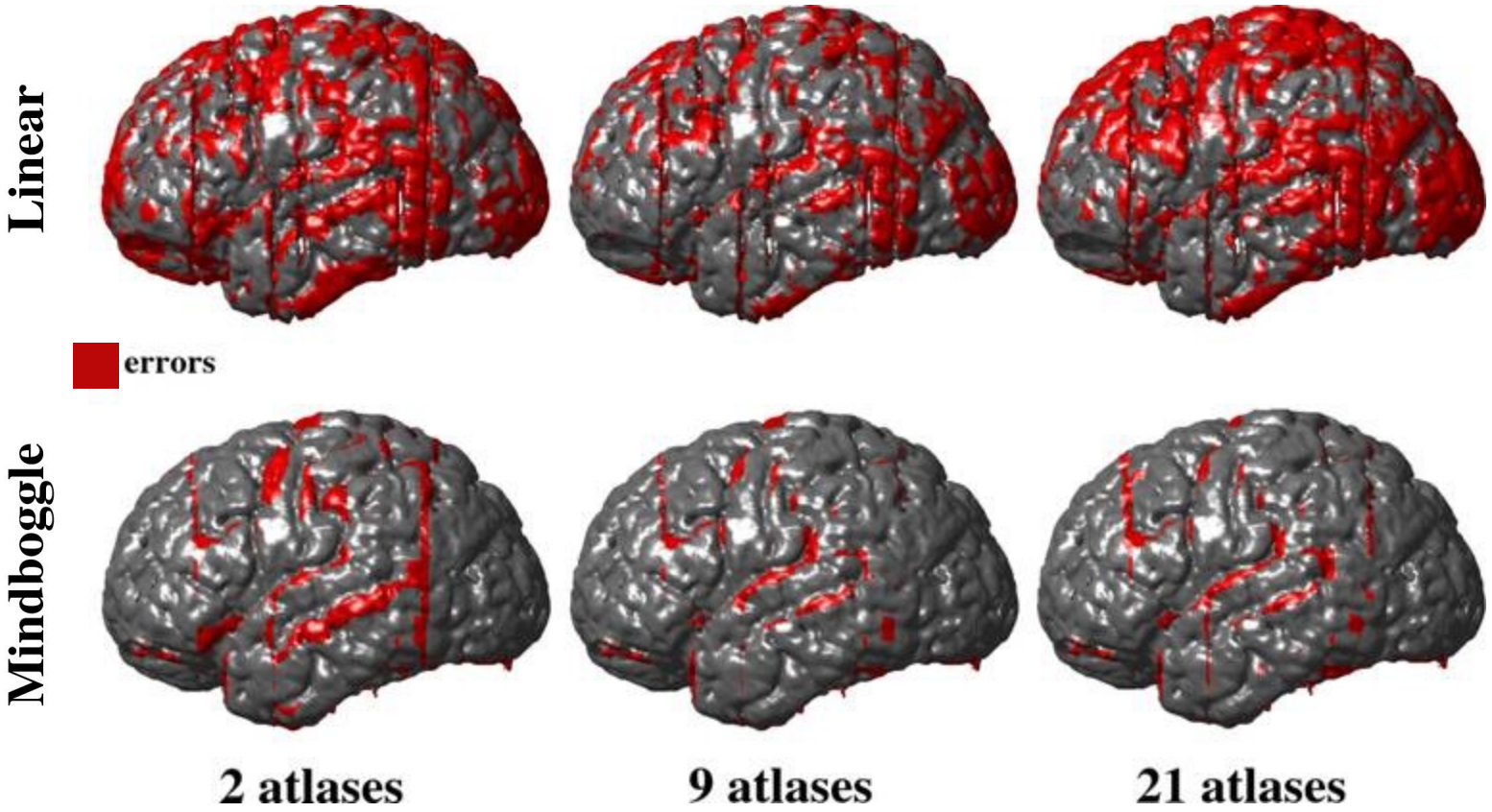






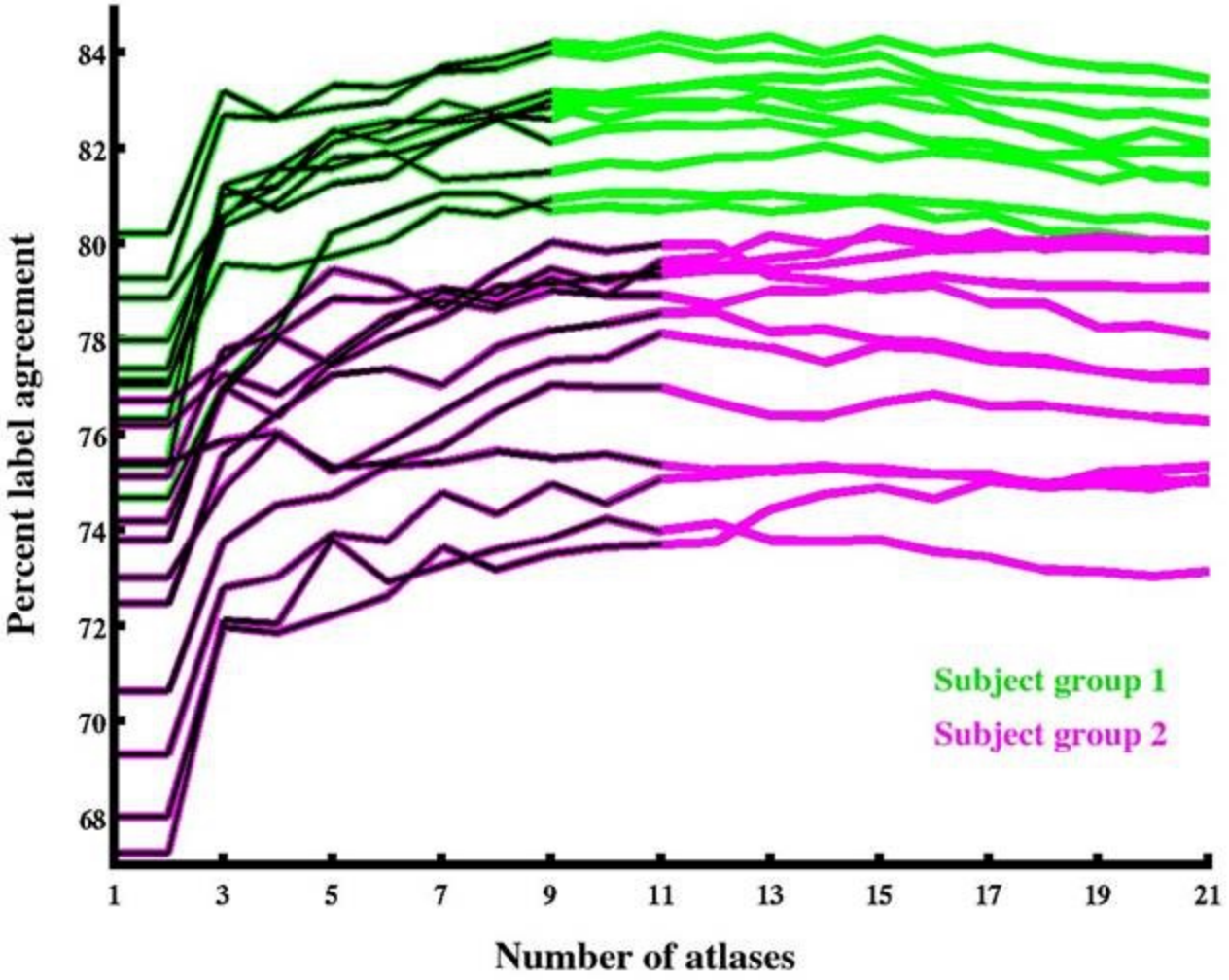
Evaluation

Errors: automated labels ≠ manual labels



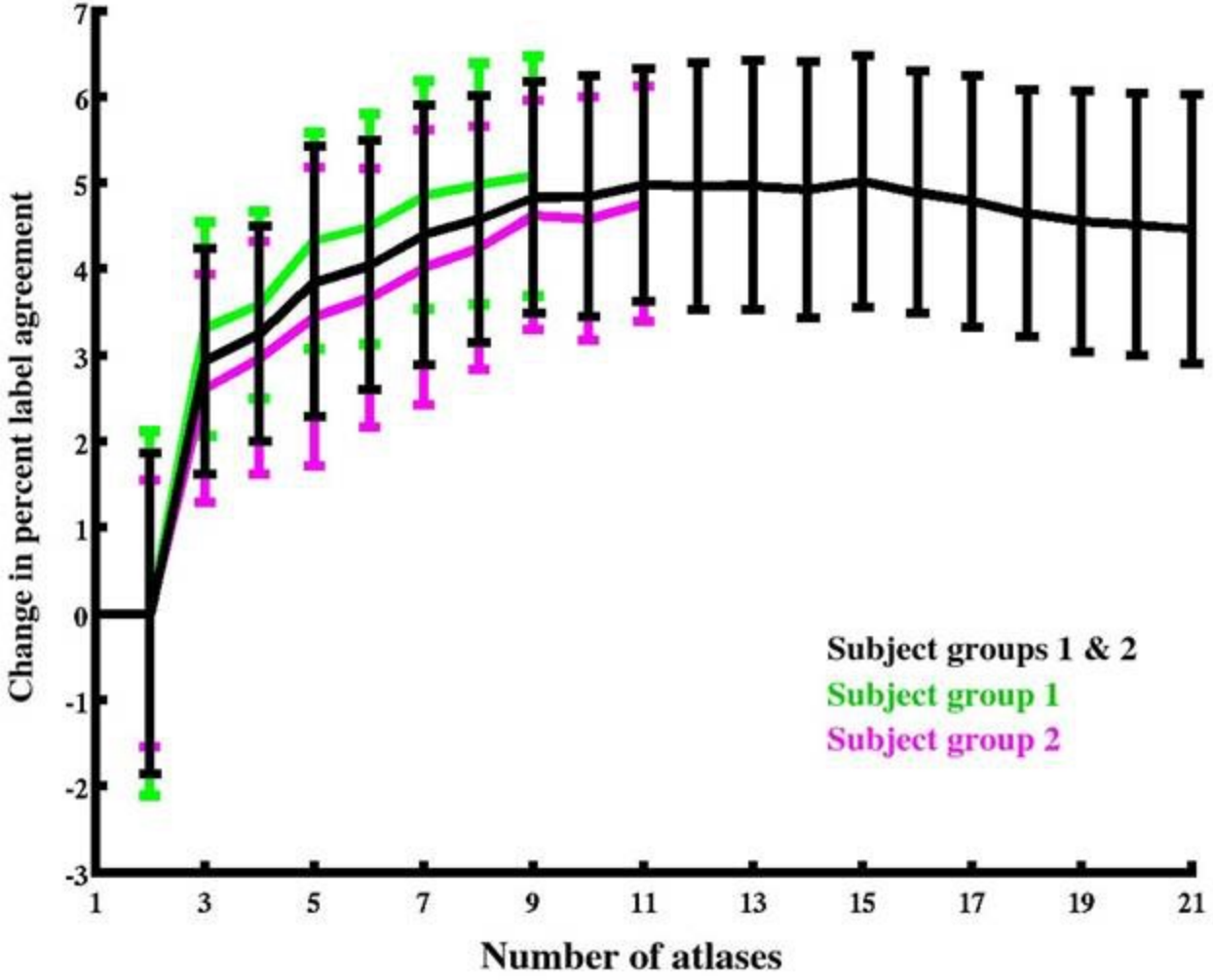
Evaluation

Percent label agreement
by subject, number of atlases



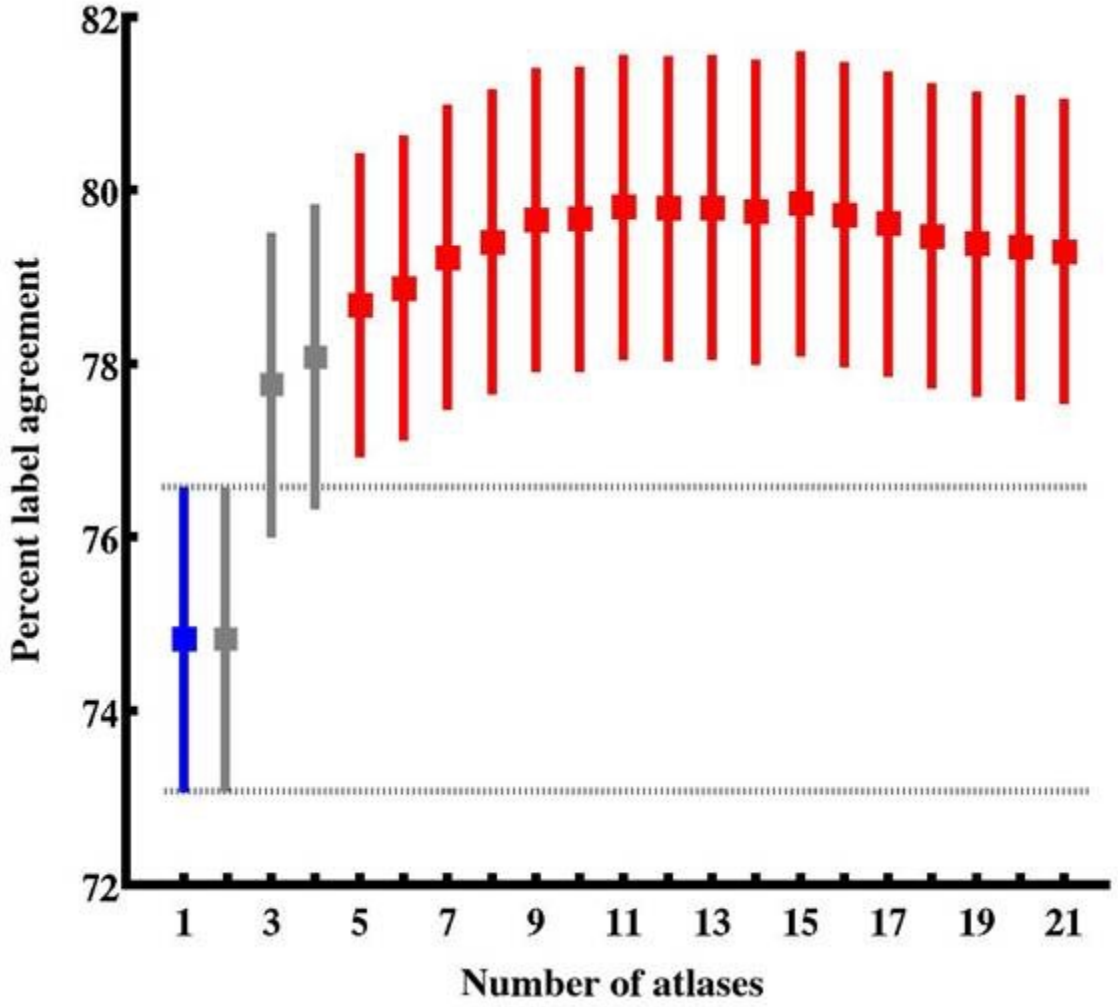
Evaluation

Change in percent label agreement by subject group, number of atlases



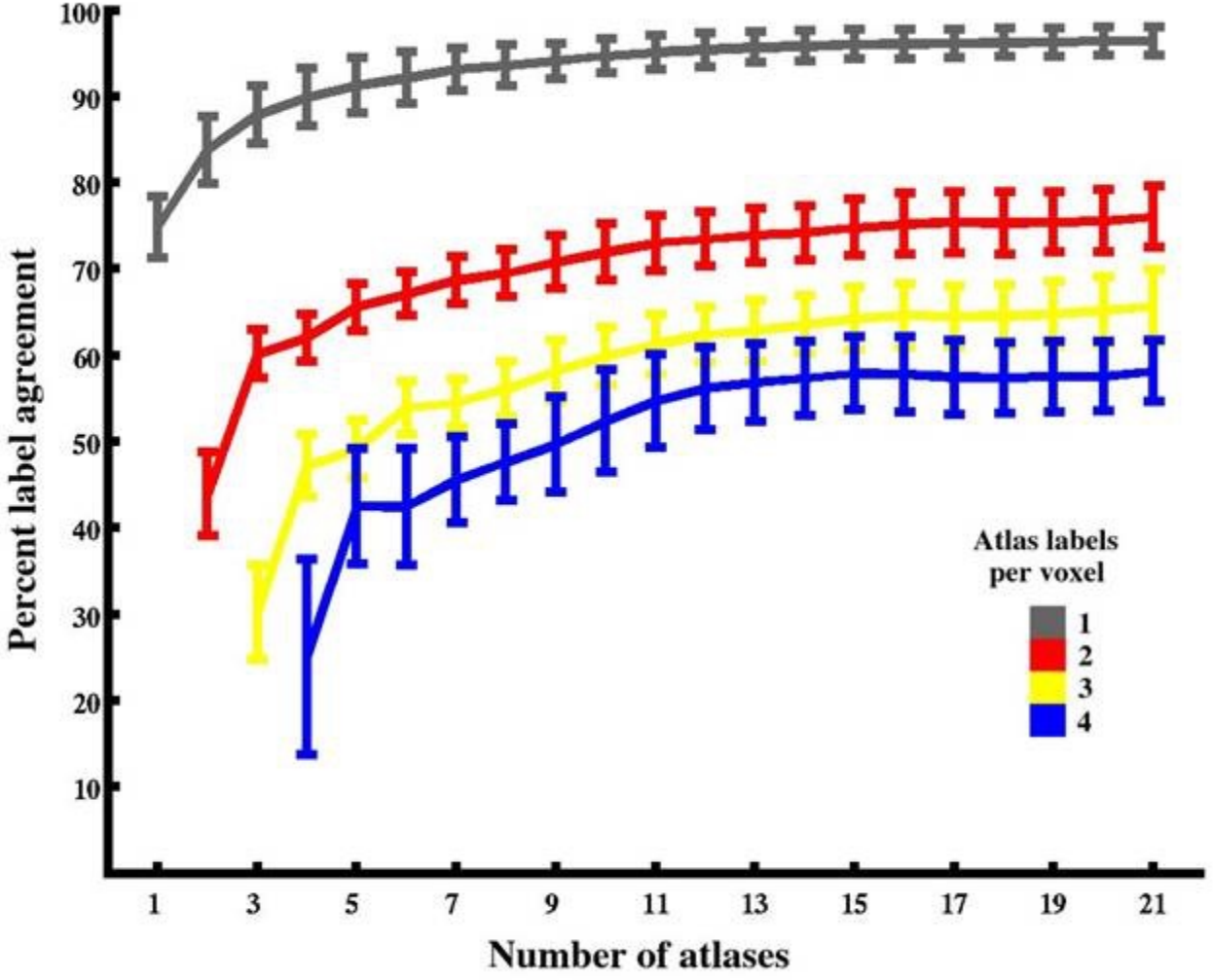
Evaluation

ANOVA, multiple comparison



Evaluation

Percent label agreement
by number of labels per voxel, number of atlases



Conclusions

Mindboggle:

- Fully automated
- Feature-based (vs. intensity-based registration)
- Does not assume that different brains preserve topography
- Robust to reduced and nonuniform image quality
- Competitive with standard techniques
- Performs just as well when parts of brain are removed
- Labels may be transferred to any regions of interest (e.g. structures or activity data)
- Multiple atlases provide independent label sets, confidence measures, higher accuracy

Future directions

More information may be found on the website:

http://www.arnoklein.net/mindboggle.html

and in two publications:

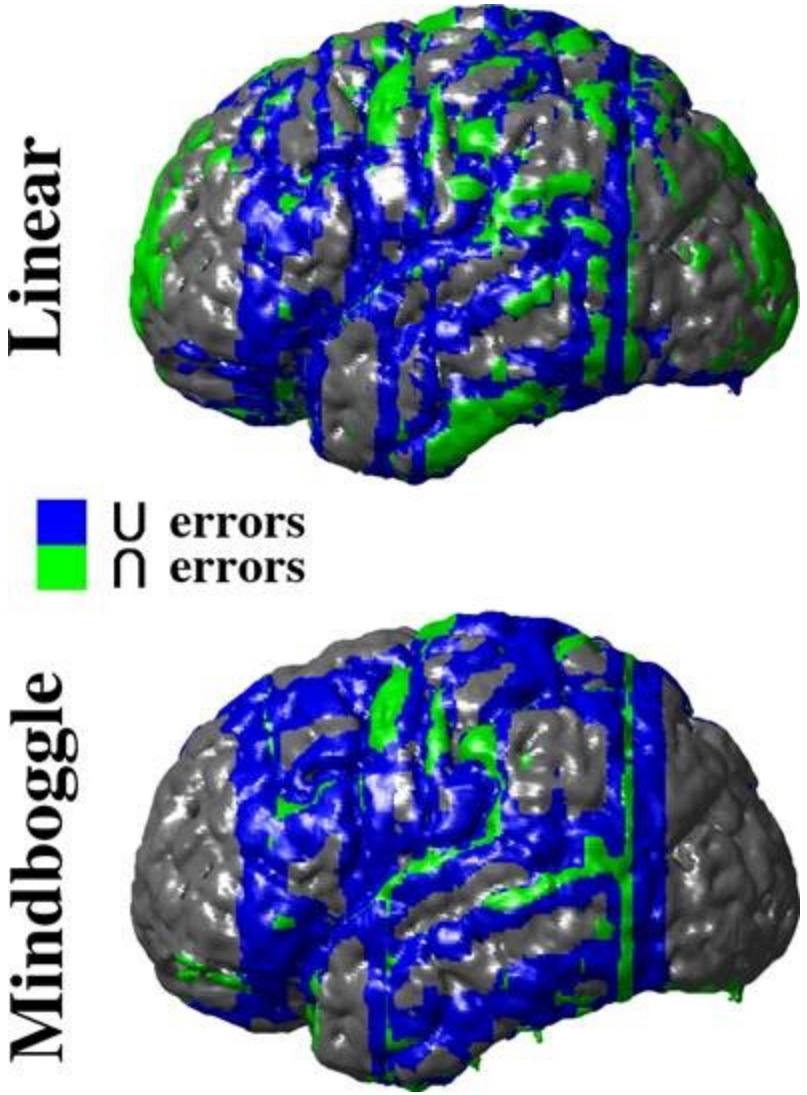
(1) under review, outlining and evaluation Mindboggle (NeuroImage)
(2) submitted, concerning multiple atlases (BioMed Central Medicine www.biomedcentral.com)

The software will undergo beta-testing in the Hirsch lab for a few months before being released.

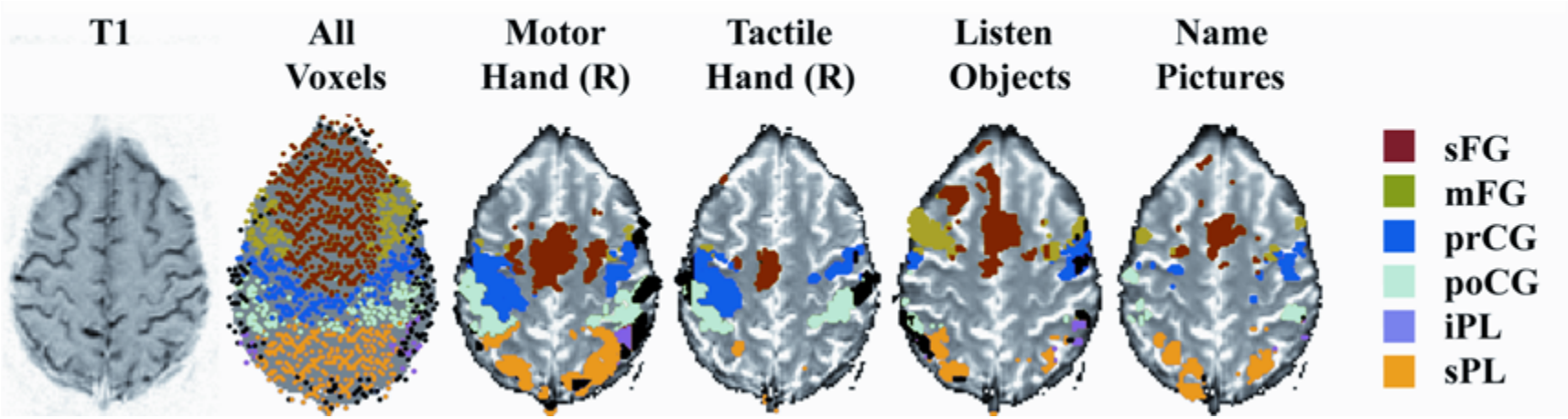
Acknowledgments

Joy Hirsch	fMRI Research Center Columbia University
Brett Mensh	New York State Psychiatric Institute Columbia University
Satrajit Ghosh, Jason Tourville:	Cognitive and Neural Systems Boston University Frank Guenther, PI; supported by NIH grant R01 DC02852
Jack Grinband	Columbia University

Single atlas variance



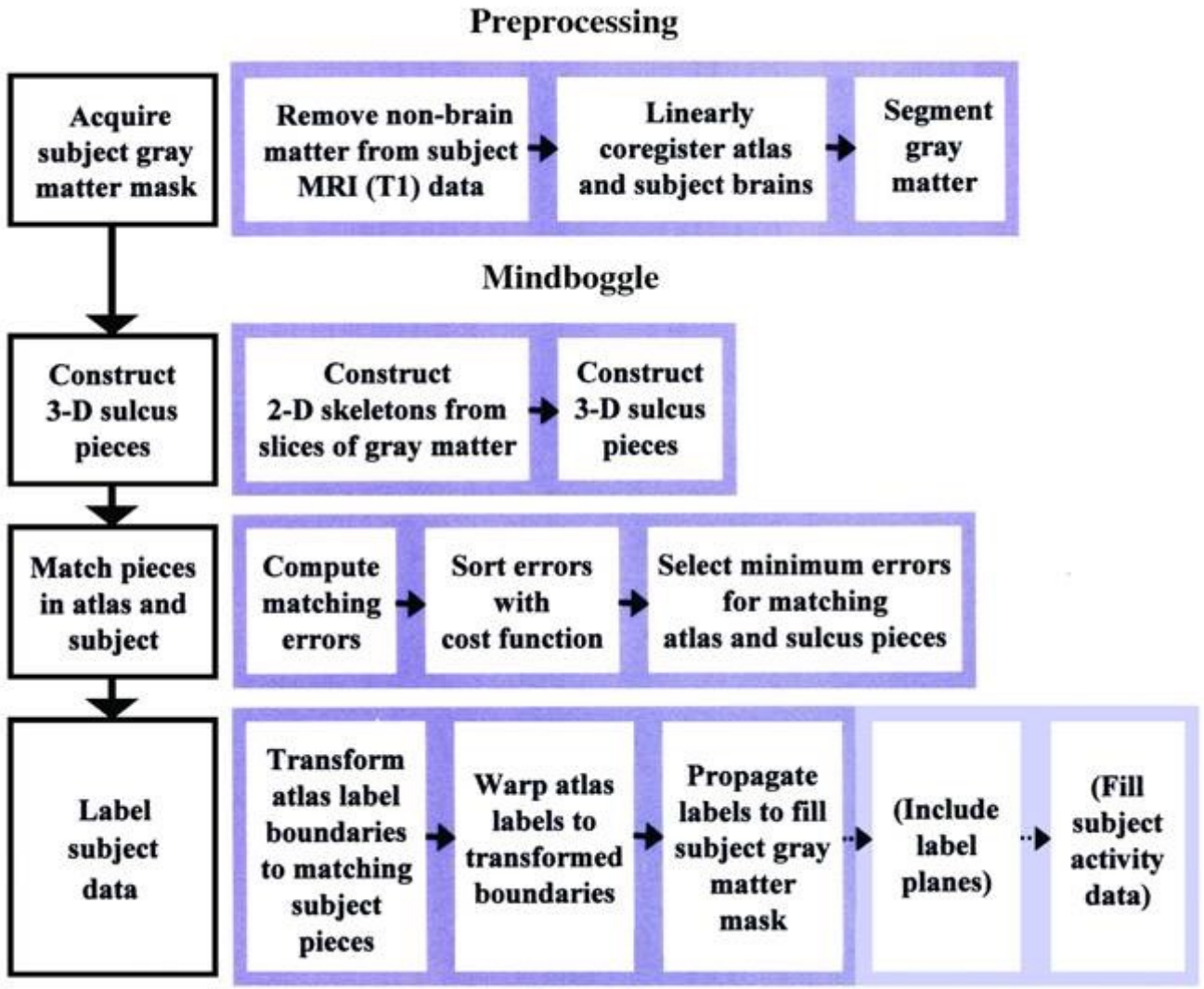
Functional mapping tests



The resulting labels may be transferred to a coregistered volume of activity data.

Mindboggle labeled activity from 5 subjects undergoing 4 standard tasks that are known to elicit activity in specific regions (Hirsch, 2000). We determined whether Mindboggle's labels included those regions. According to Mindboggle, of the 45 gyrii expected to be activated (9 gyrii distributed across 4 tasks performed by 5 subjects), 44 were activated, well within expected variance of the subject pool.

Flowchart


Preprocessing
Acquire subject gray matter mask
Remove non-brain matter from subject MRI (T1) data
Linearly coregister atlas and subject brains
Segment gray matter
Mindboggle
Construct 3-D sulcus pieces
Construct 2-D skeletons from slices of gray matter
Construct 3-D sulcus pieces
Match pieces in atlas and subject
Compute matching errors
Sort errors with cost function
Select minimum errors for matching atlas and sulcus pieces
Label subject data
Transform atlas label boundaries to matching subject pieces
Warp atlas labels to transformed boundaries
Propagate labels to fill subject gray matter mask
(Include label planes)
(Fill subject activity data)