



# **Morphometrics with SPM12**

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# What kind of differences are we looking for?

- Usually, we try to localise regions of difference.
  - **Univariate models.**
  - Typically involves fitting a GLM
  - Typically localising volumetric differences
- Some anatomical differences can not be localised.
  - Need **multivariate models.**
  - Differences in terms of proportions among measurements.
  - Where would the difference between male and female faces be localised?
- Need to select the best model of difference to use, before trying to fill in the details.

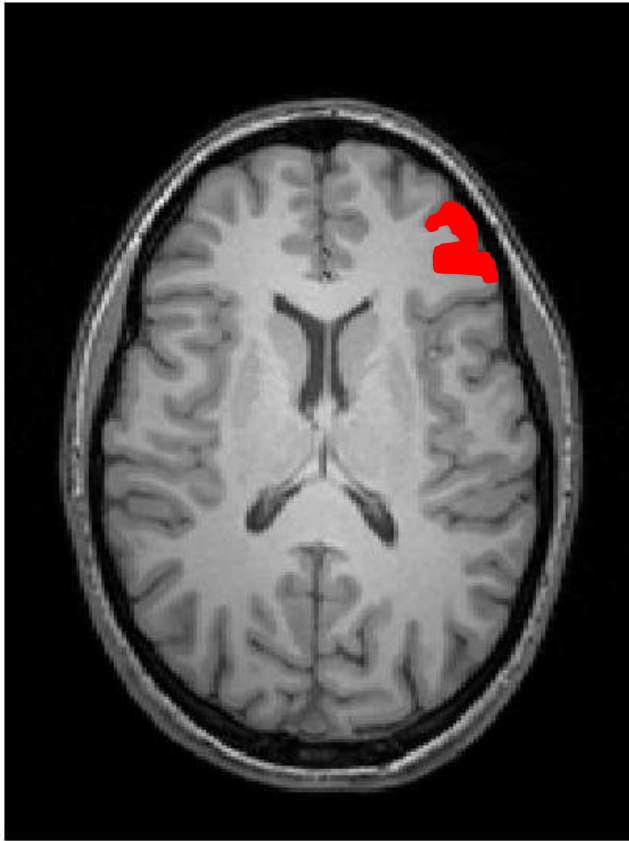
# Overview

- **Voxel-Based Morphometry**
- Diffeomorphic Registration
- Tensor-Based Morphometry
- Longitudinal Registration

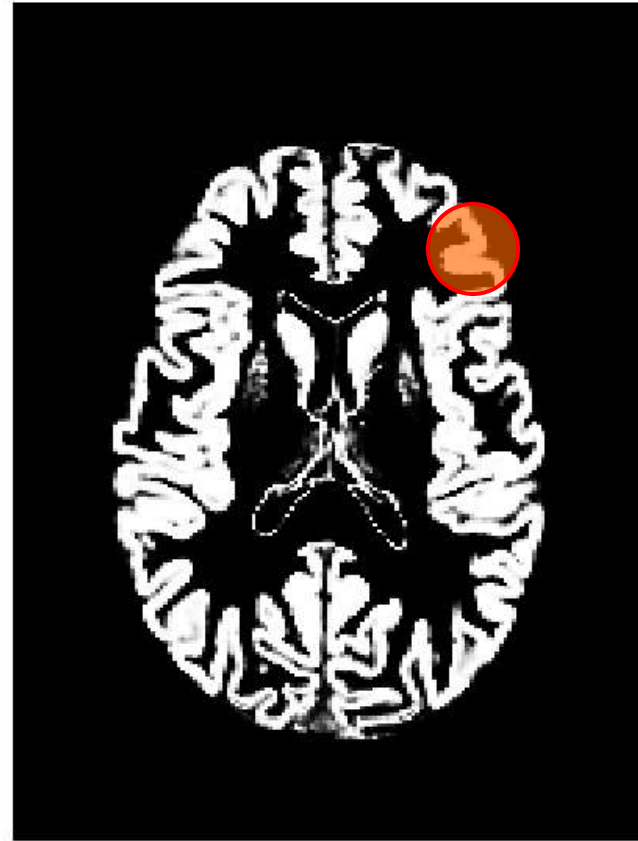
# Voxel-Based Morphometry

- Produce a map of statistically significant differences among populations of subjects.
  - e.g. compare a patient group with a control group.
  - or identify correlations with age, test-score etc.
- The data are pre-processed to sensitise the tests to regional tissue volumes.
  - Usually grey or white matter.

# Volumetry

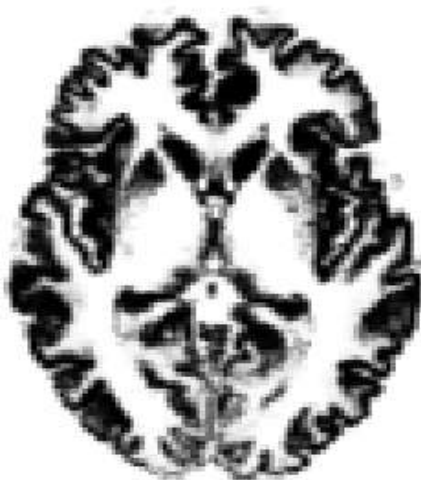


T1-Weighted MRI



Grey Matter

Original



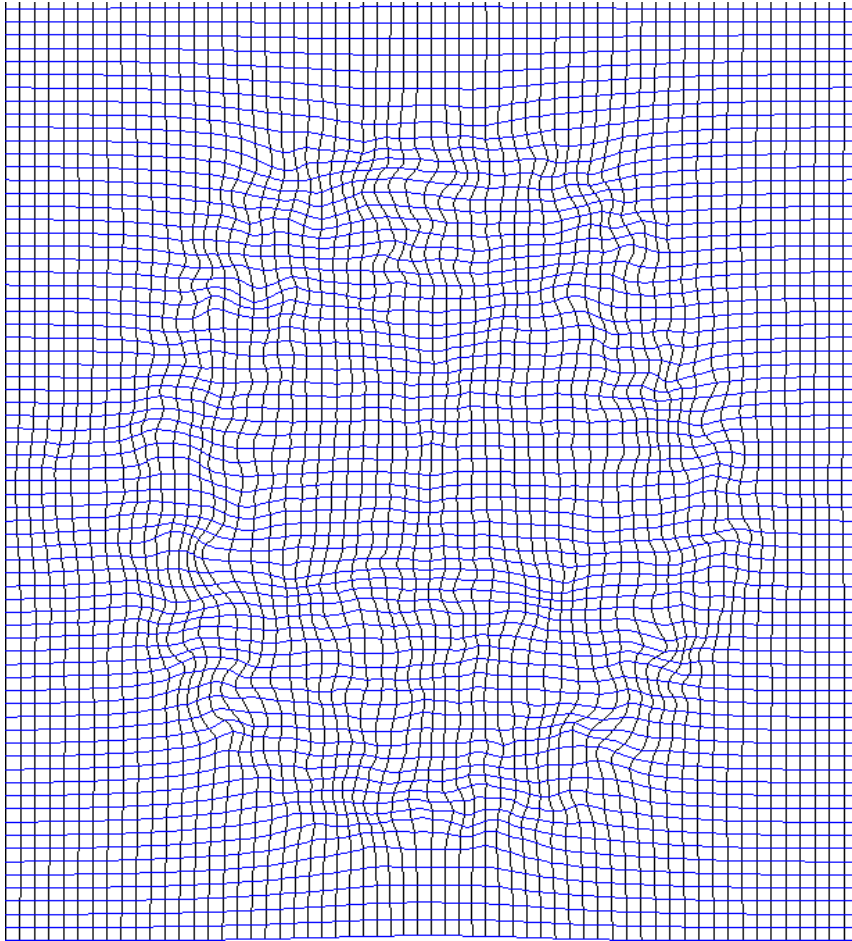
Warped



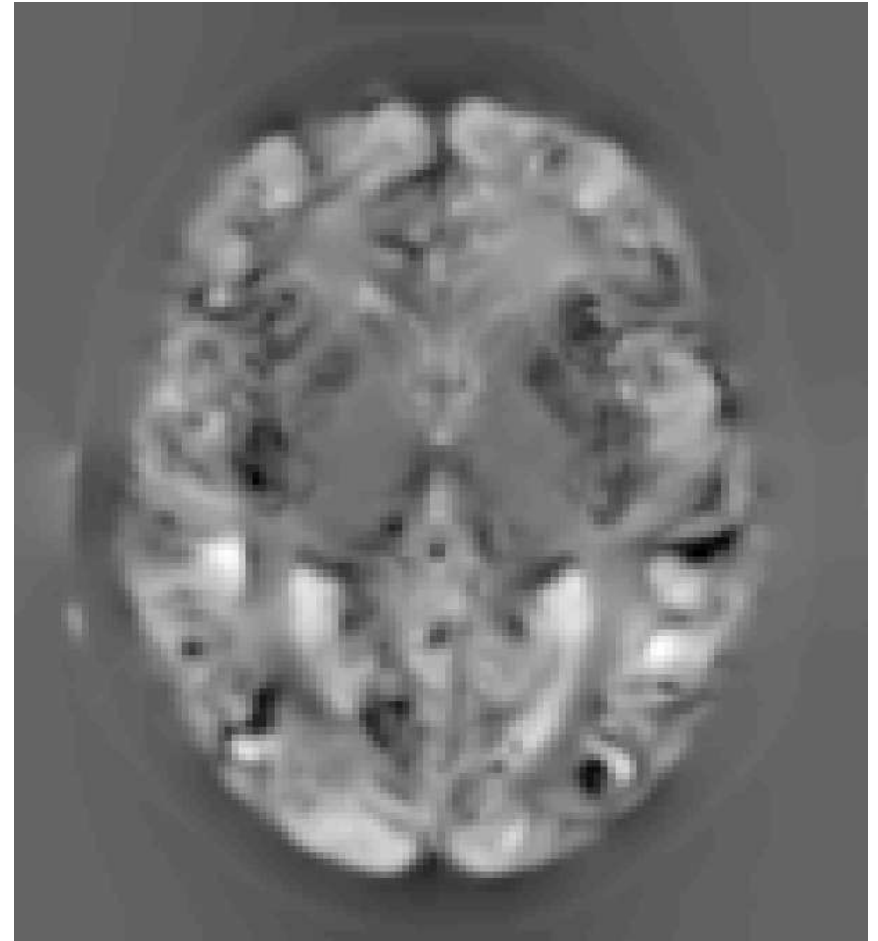
Template



“Modulation” – change of variables.



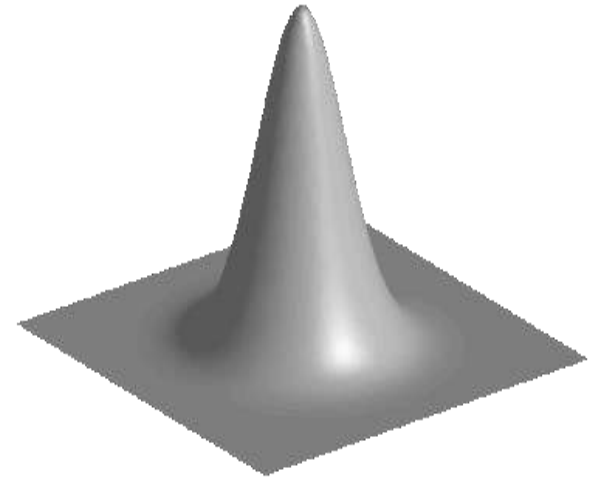
Deformation Field



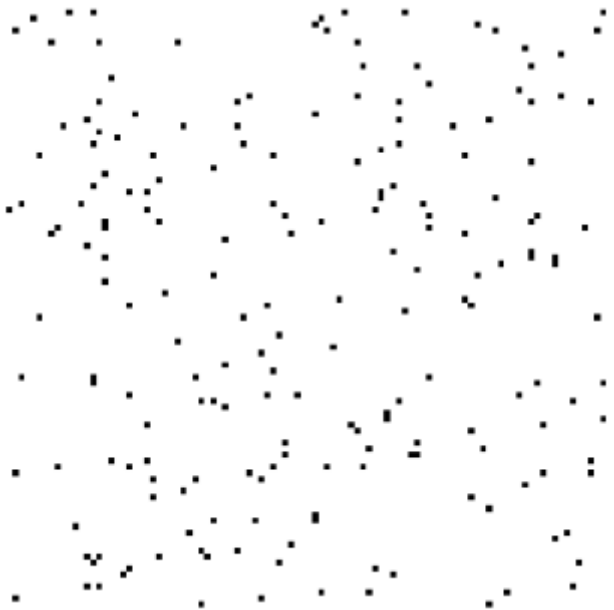
Jacobians determinants  
Encode relative volumes.

# Smoothing

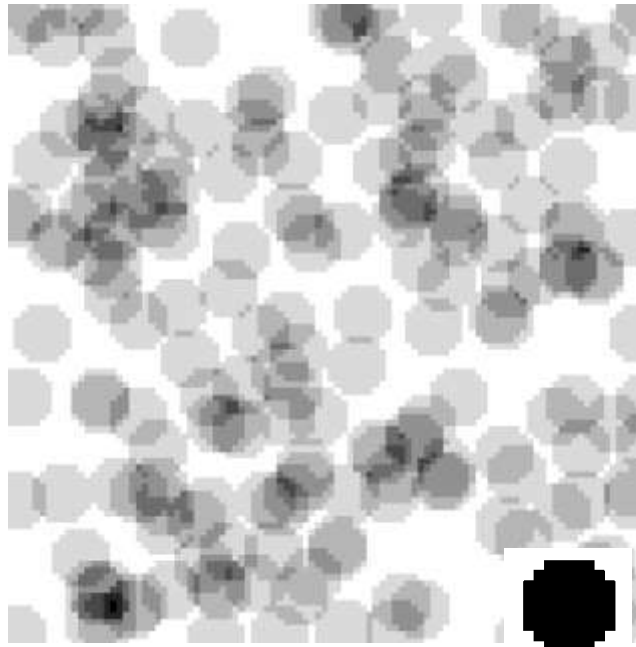
Each voxel after smoothing effectively becomes the result of applying a weighted region of interest (ROI).



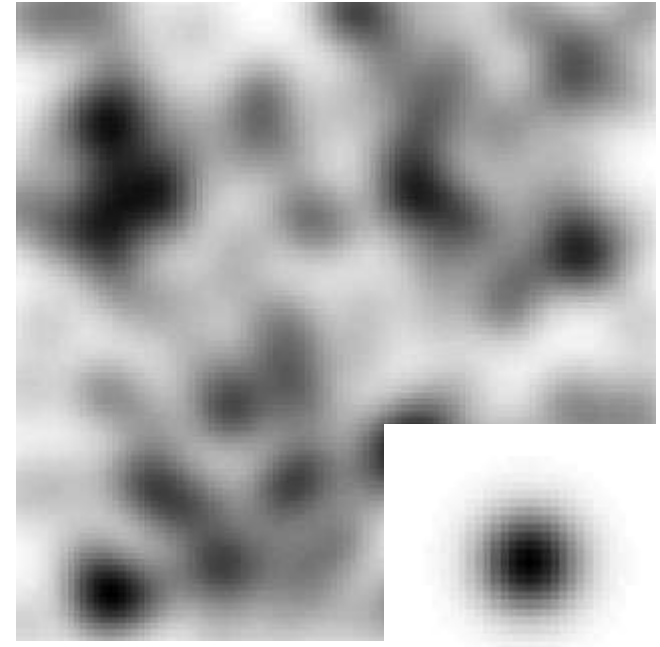
Before convolution



Convolved with a circle



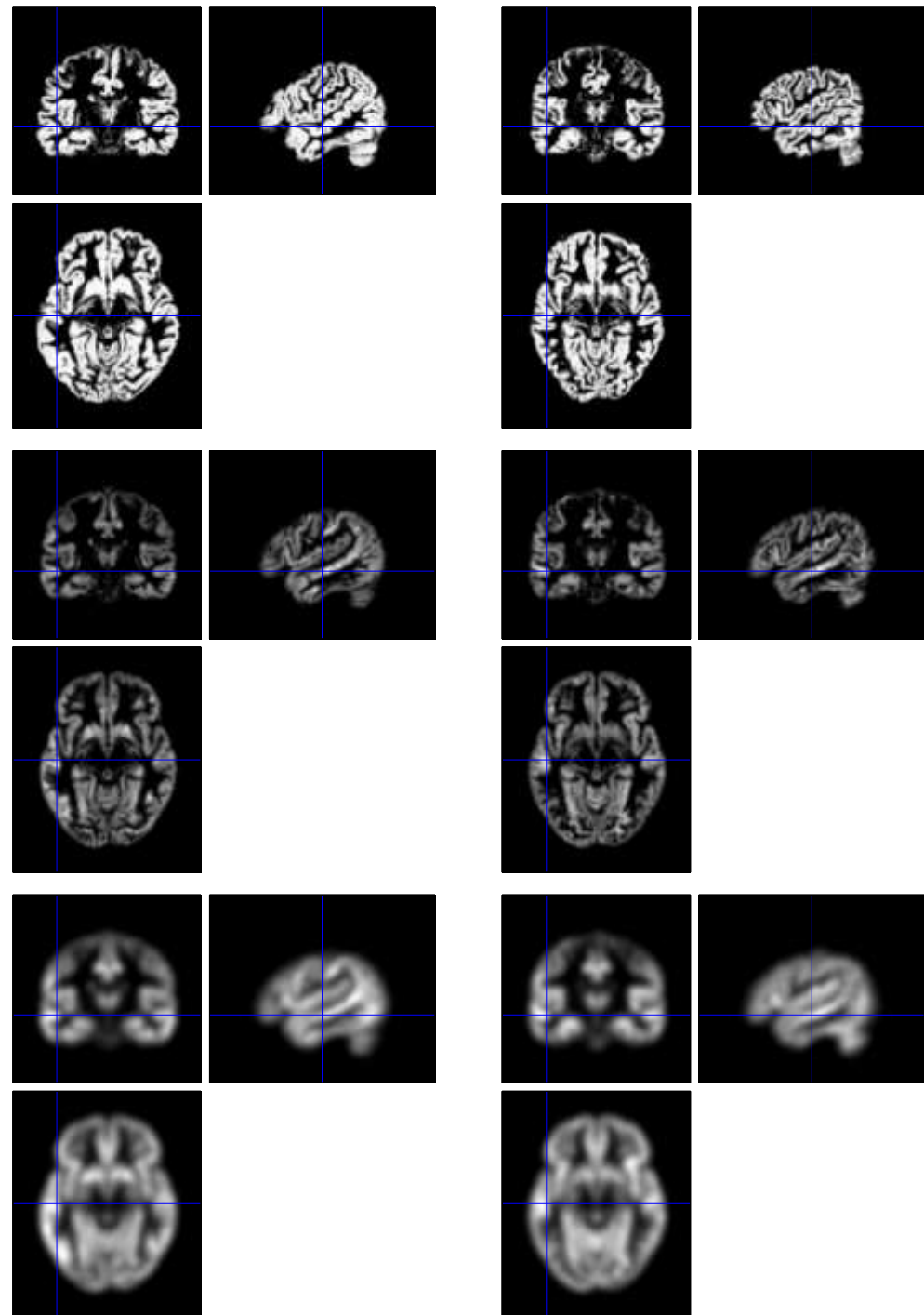
Convolved with a Gaussian



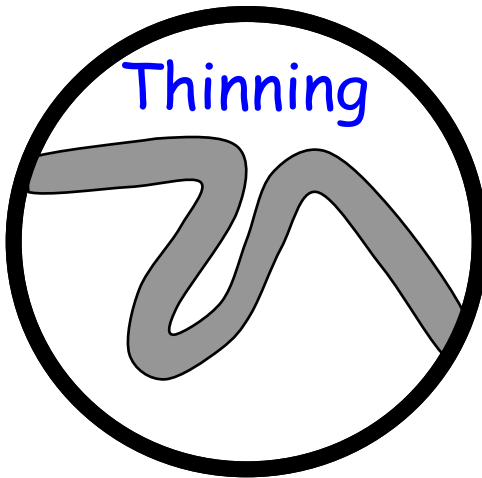
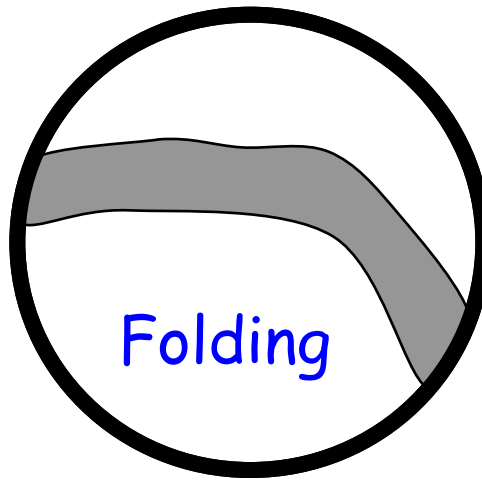
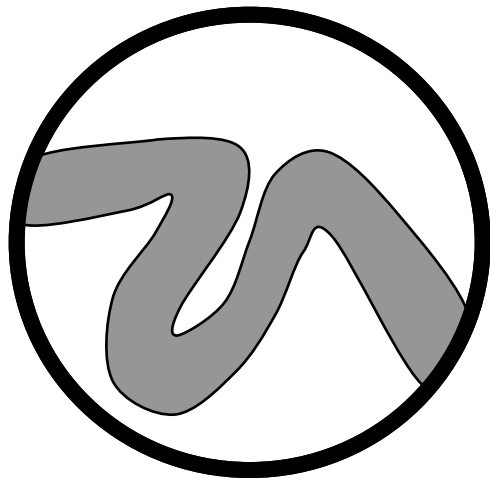


# VBM Pre-processing in SPM12

- Use Segment for characterising intensity distributions of tissue classes, and writing out “imported” images that *Dartel* can use.
- Run *Dartel* to estimate all the deformations.
- *Dartel* warping to generate smoothed, “modulated”, warped grey matter.
- Statistics.



# Some Explanations of the Differences



# Some References

- Ashburner & Friston. “*Unified Segmentation*”. NeuroImage **26**:839-851, 2005.
- Ashburner. “*A Fast Diffeomorphic Image Registration Algorithm*”. NeuroImage 38:95-113 (2007).
- Ashburner & Friston. “*Computing Average Shaped Tissue Probability Templates*”. NeuroImage **45**:333-341, 2009.
- Ashburner. “*Computational Anatomy with the SPM software*”. Magnetic Resonance Imaging **27**(8):1163-1174, 2009.

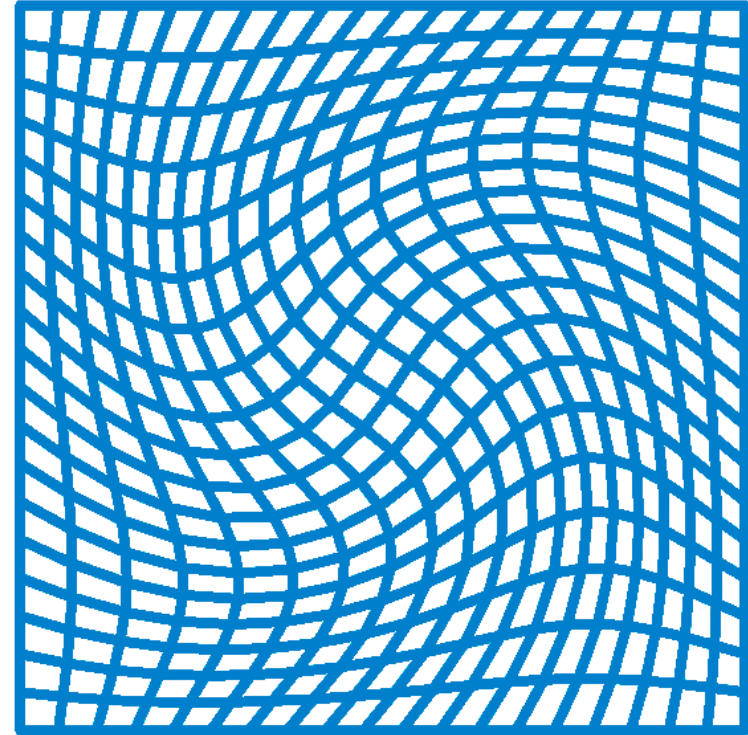
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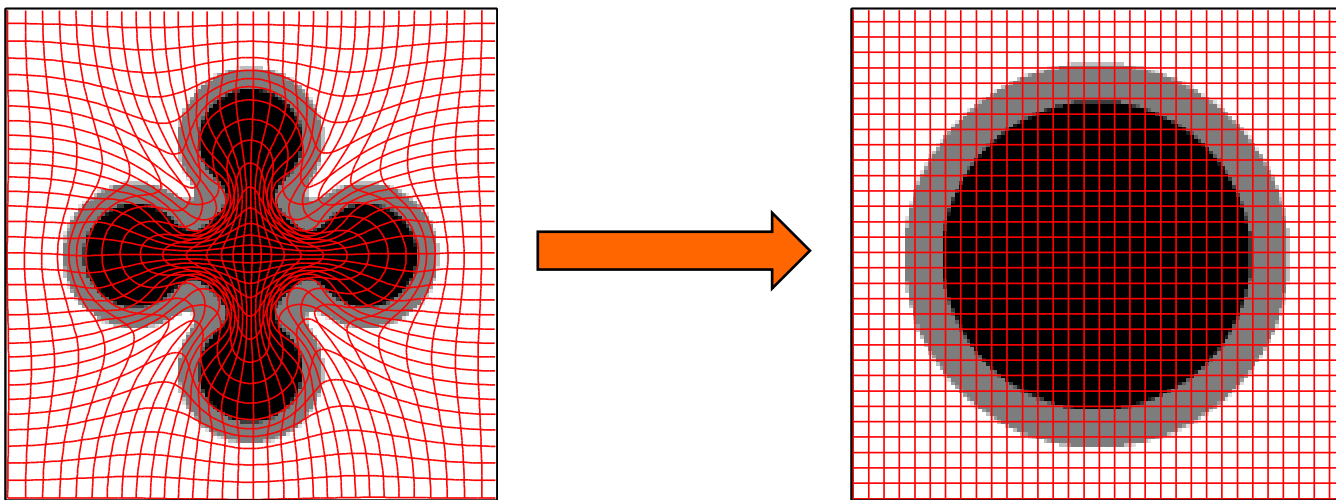
# Diffeomorphism

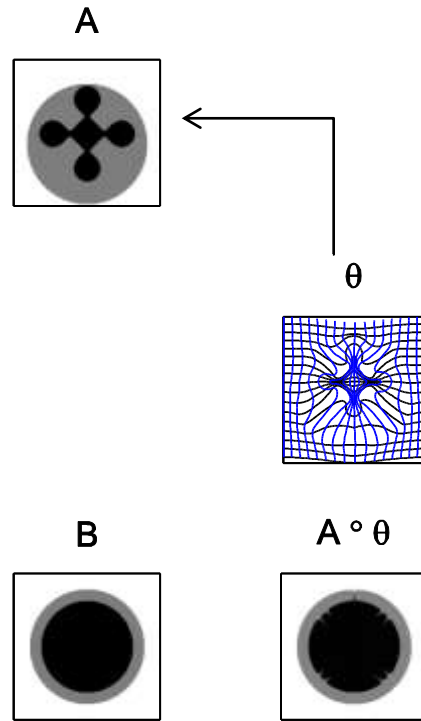
In mathematics, a diffeomorphism is an isomorphism in the category of smooth manifolds. It is an invertible function that maps one differentiable manifold to another, such that both the function and its inverse are smooth.

Wikipedia



# Deformations





# Composition

# Small Deformation Approximation

The composition:

$$\vartheta \circ \phi$$

Would be approximated with:

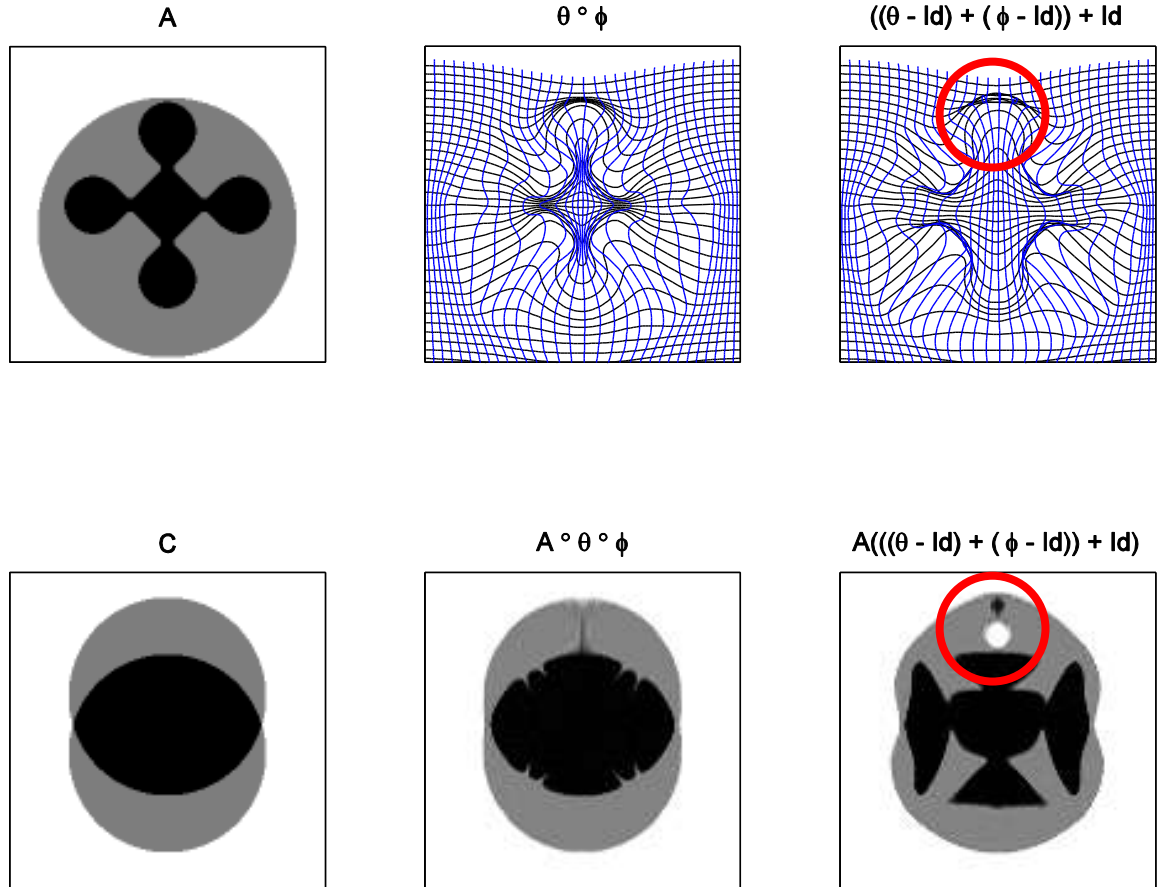
$$\text{Id} + ((\vartheta - \text{Id}) + (\phi - \text{Id}))$$

The inversion:

$$\phi^{-1}$$

Would be approximated with:

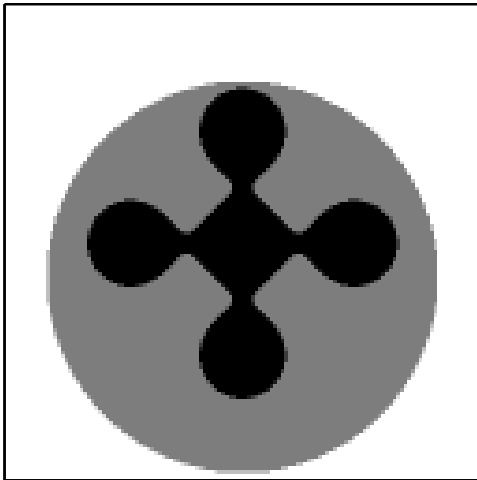
$$\text{Id} - (\phi - \text{Id})$$



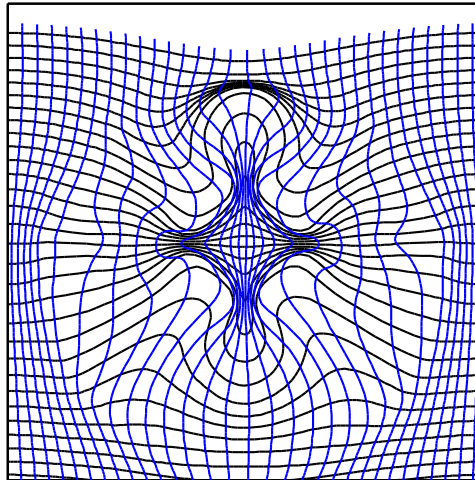
Not good approximations for large deformations.



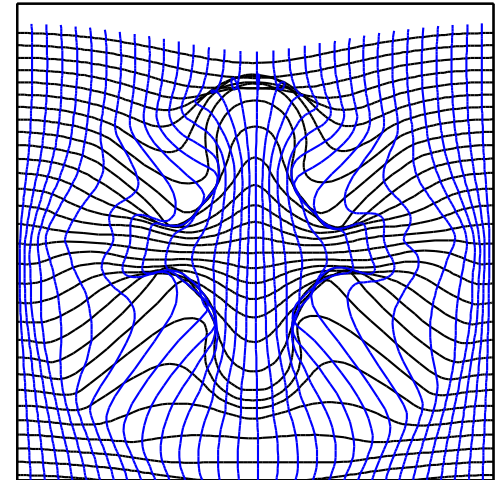
A



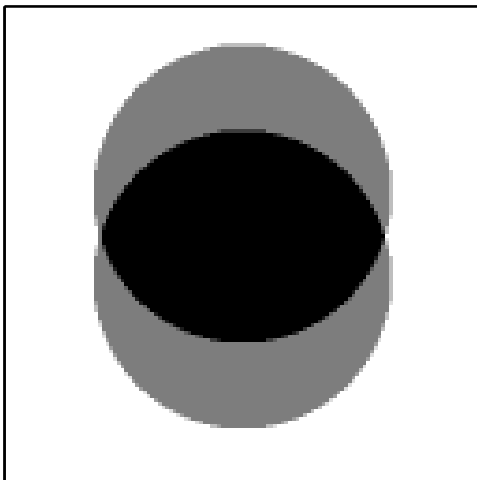
$\theta \circ \phi$



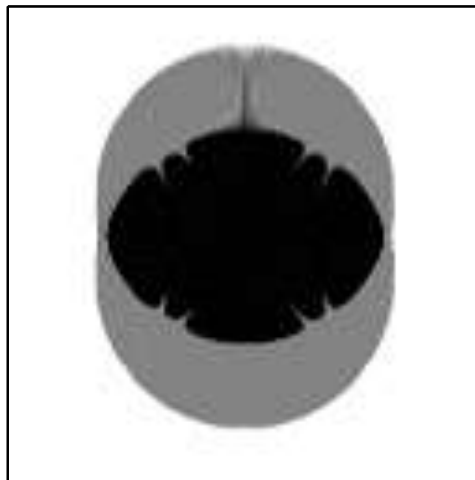
$((\theta - \text{Id}) + (\phi - \text{Id})) + \text{Id}$



C



$A \circ \theta \circ \phi$



$A(((\theta - \text{Id}) + (\phi - \text{Id})) + \text{Id})$



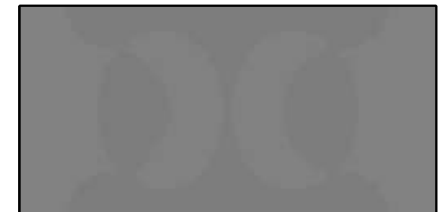
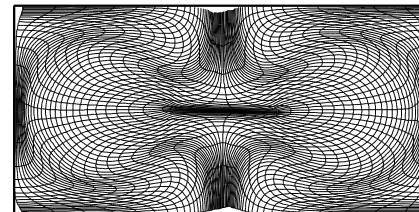
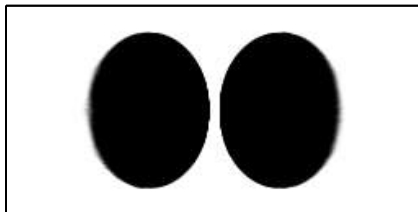
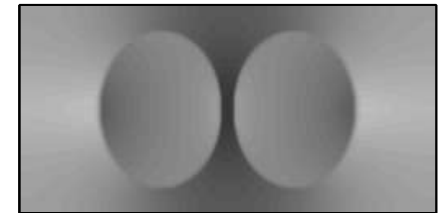
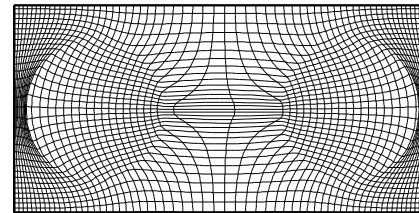
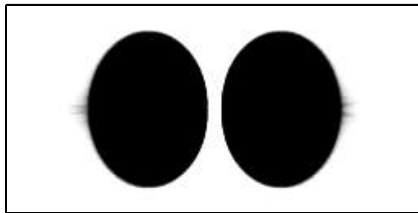
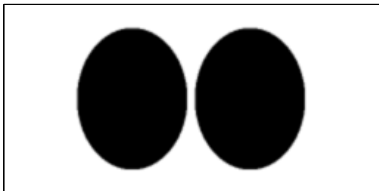
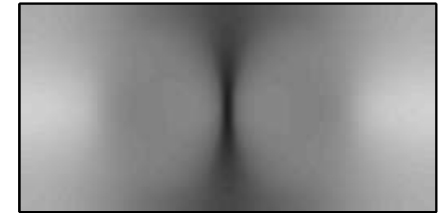
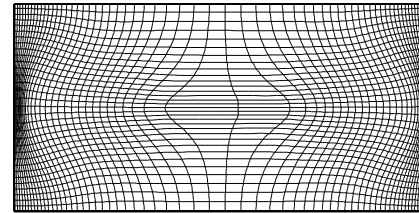
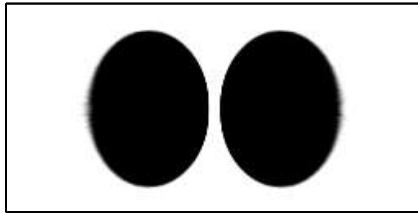
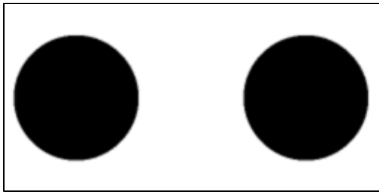
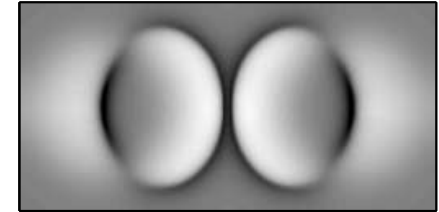
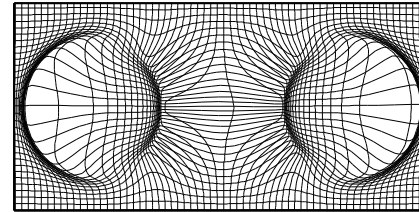
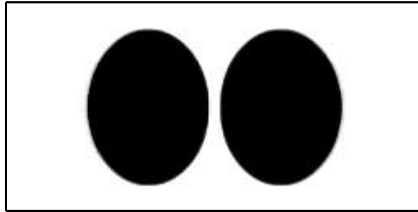
# Diffeomorphic Image Registration

- Minimises two terms:
  1. A measure of distance between images
  2. A measure of the amount of distortion.

Because we can not simply add displacement fields, large deformations are generated by composing many small deformations.

The amount of distortion is computed by summing up the distortion measures from the small displacements.

# Effect of Different Distortion Measures



# Two diffeomorphic approaches in SPM

## **Dartel.**

- Uses the same small deformation composed multiple times.
- Faster than Geodesic Shooting.
- Gives similar deformations to Geodesic Shooting.
- Currently more additional utilities.

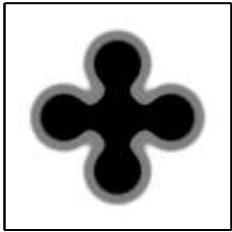
## **Geodesic Shooting**

- Uses the optimal series of small deformations, which are composed together.
- More mathematically correct than Dartel.
- Gives nicer maps of volume change than Dartel.
- Likely to replace Dartel in future.

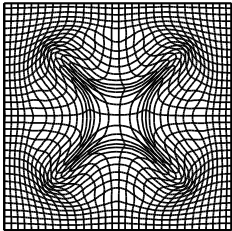
# Dartel & GS Compared

## Dartel

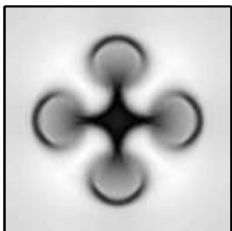
$$\mu \circ \chi$$



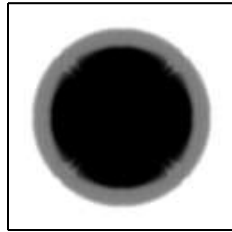
$$\chi$$



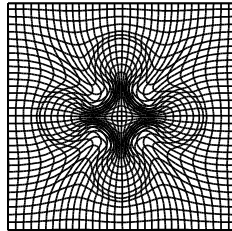
$$|J\chi|$$



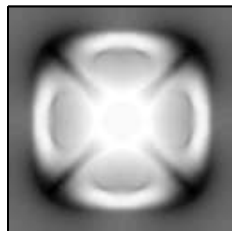
$$f \circ \chi^{-1}$$



$$\chi^{-1}$$

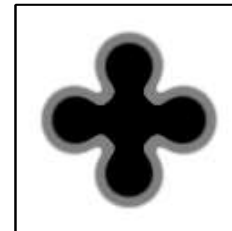


$$|J\chi^{-1}|$$

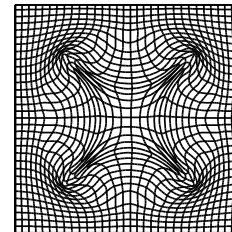


## Geodesic Shooting

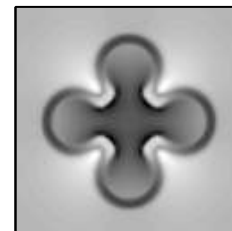
$$\mu \circ \theta$$



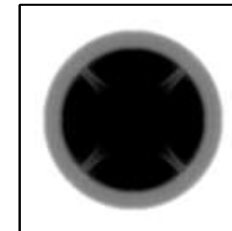
$$\theta$$



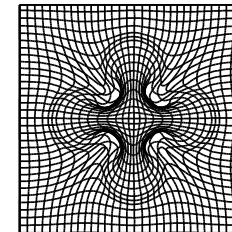
$$|J\theta|$$



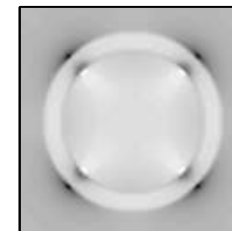
$$f \circ \phi$$



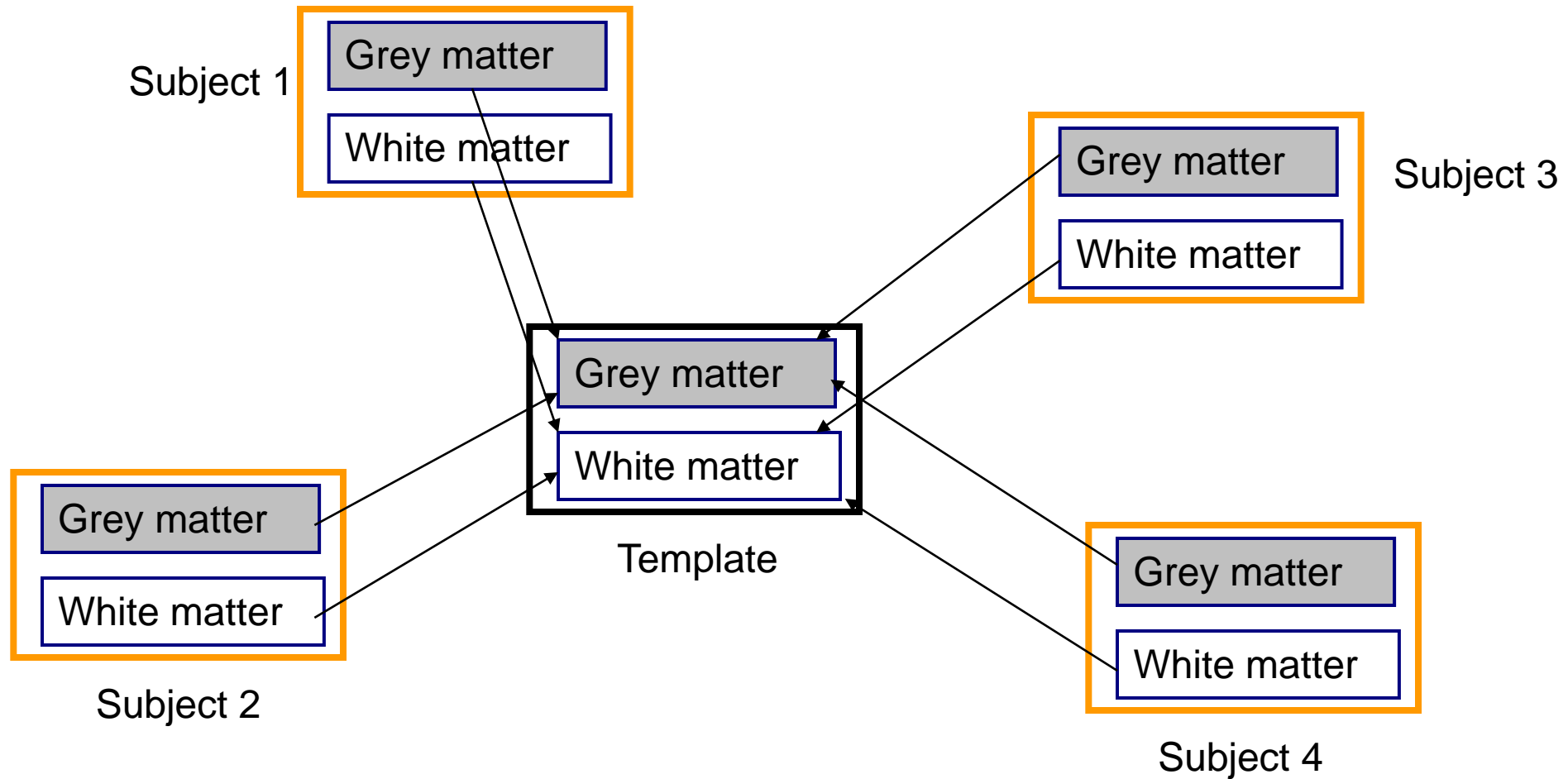
$$\phi$$



$$|J\phi|$$



# Simultaneous registration of GM to GM and WM to WM



# Template

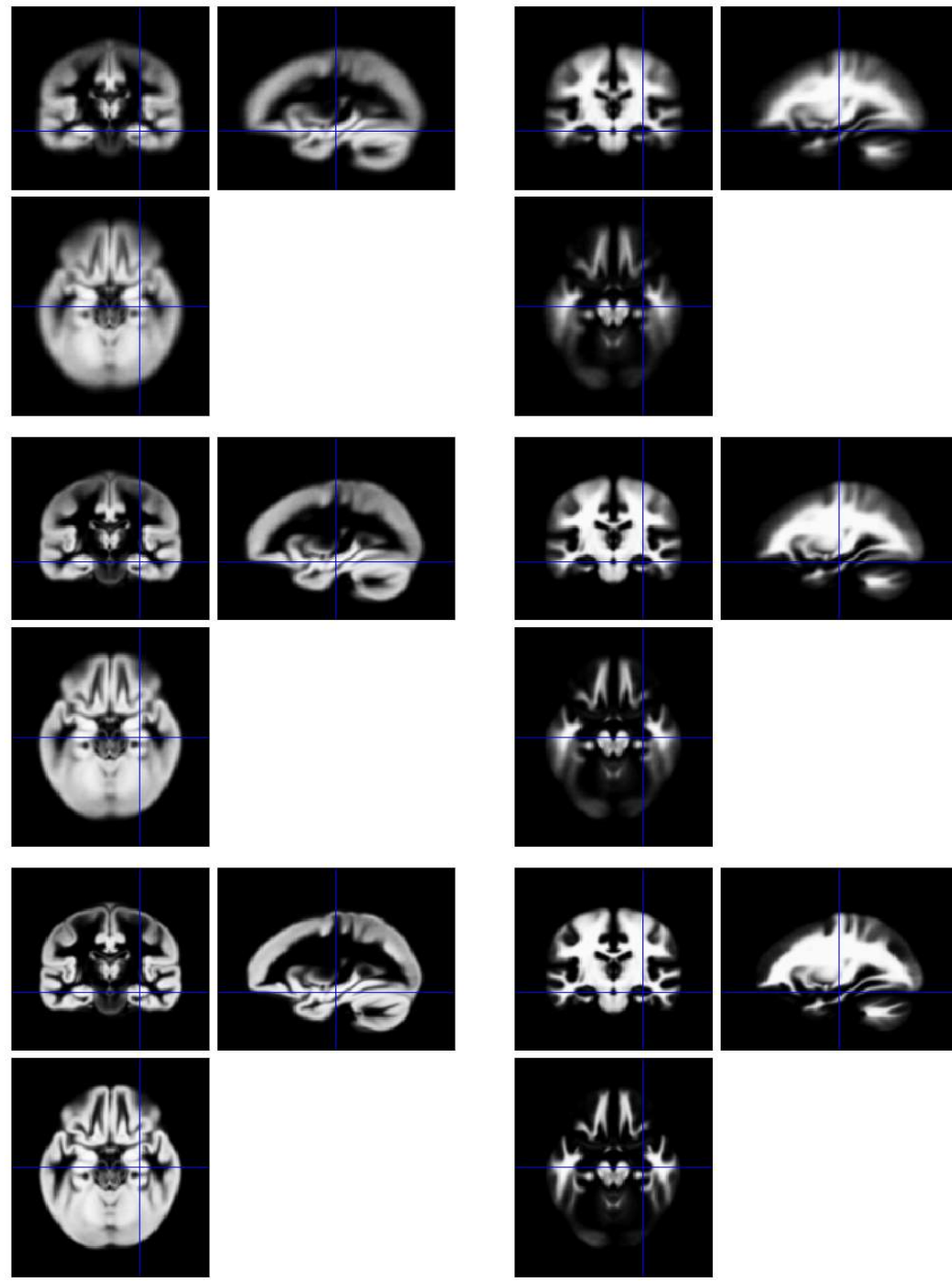
Iteratively generated  
from all subjects in  
study

Begin with rigidly  
aligned tissue  
probability maps

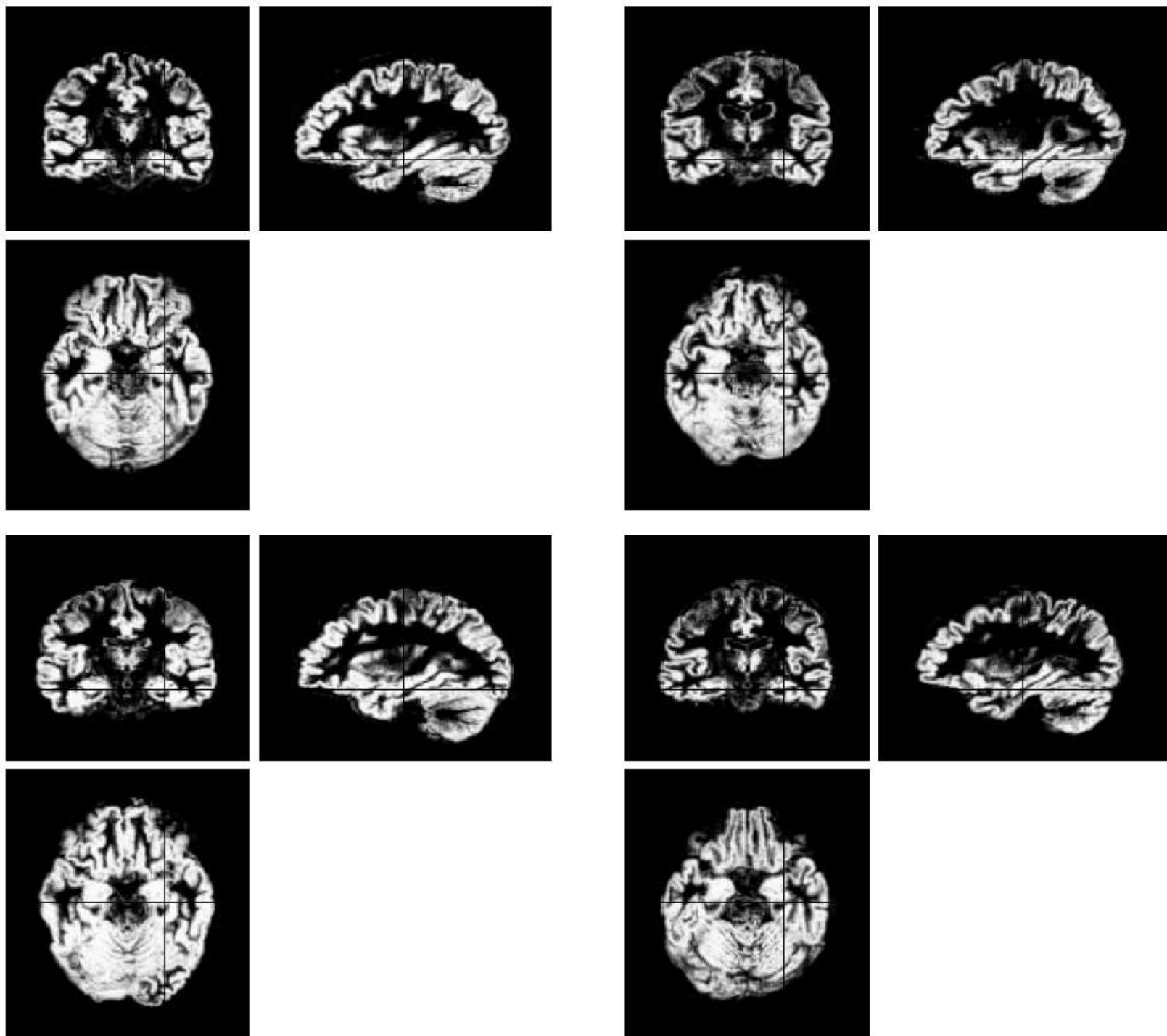
Initial  
Average

After a few  
iterations

Final  
template

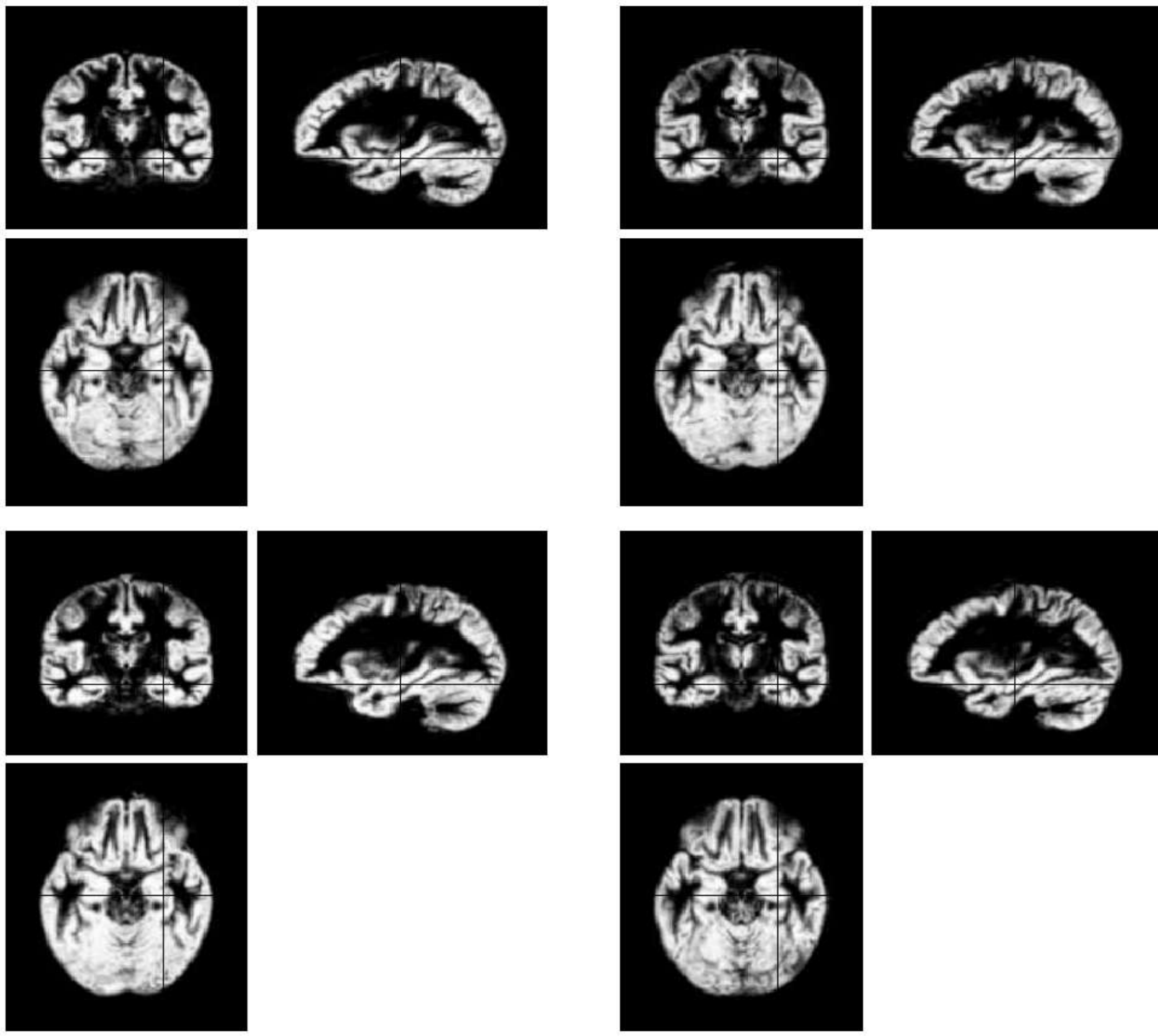


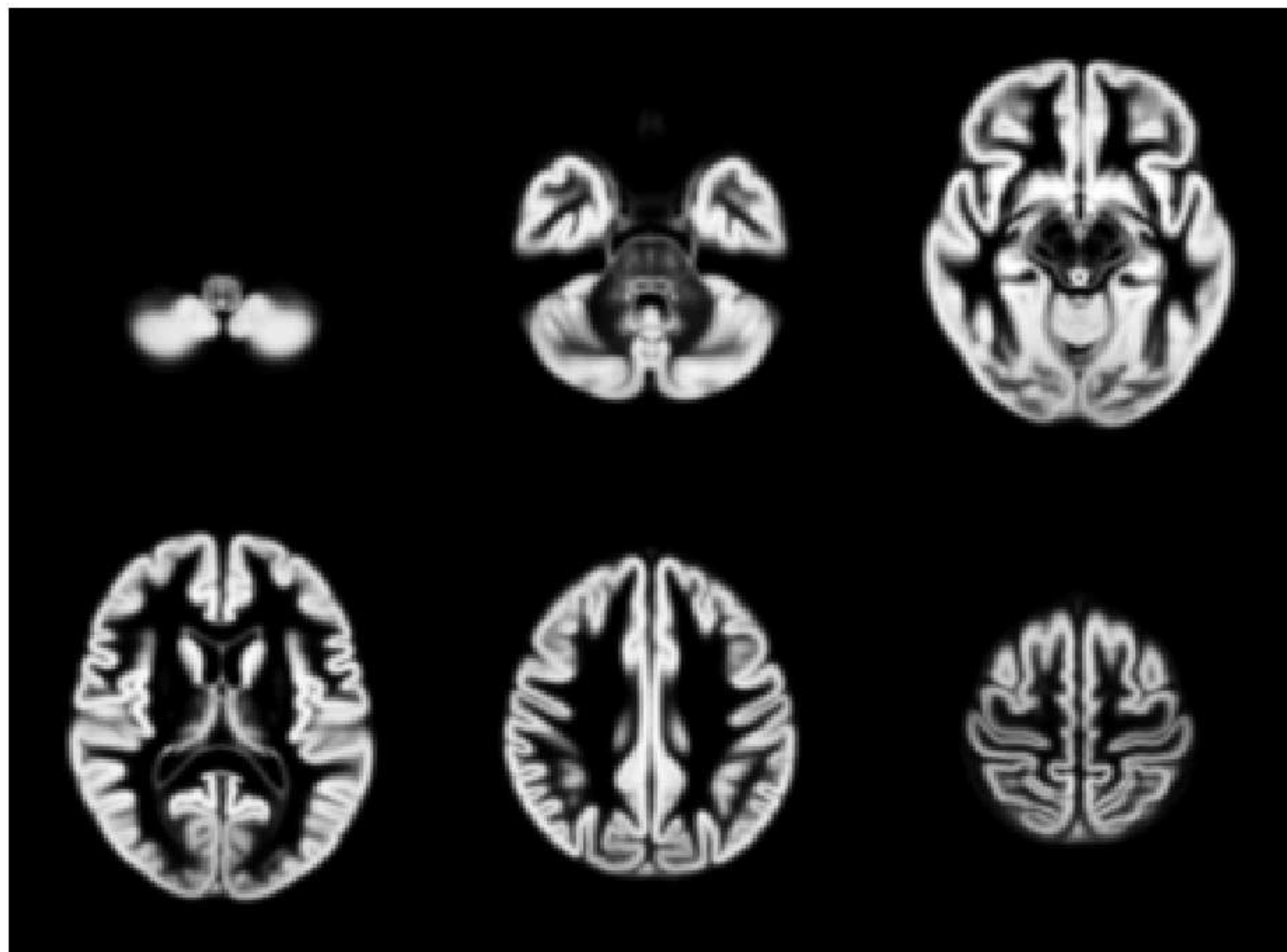
Initial  
GM images

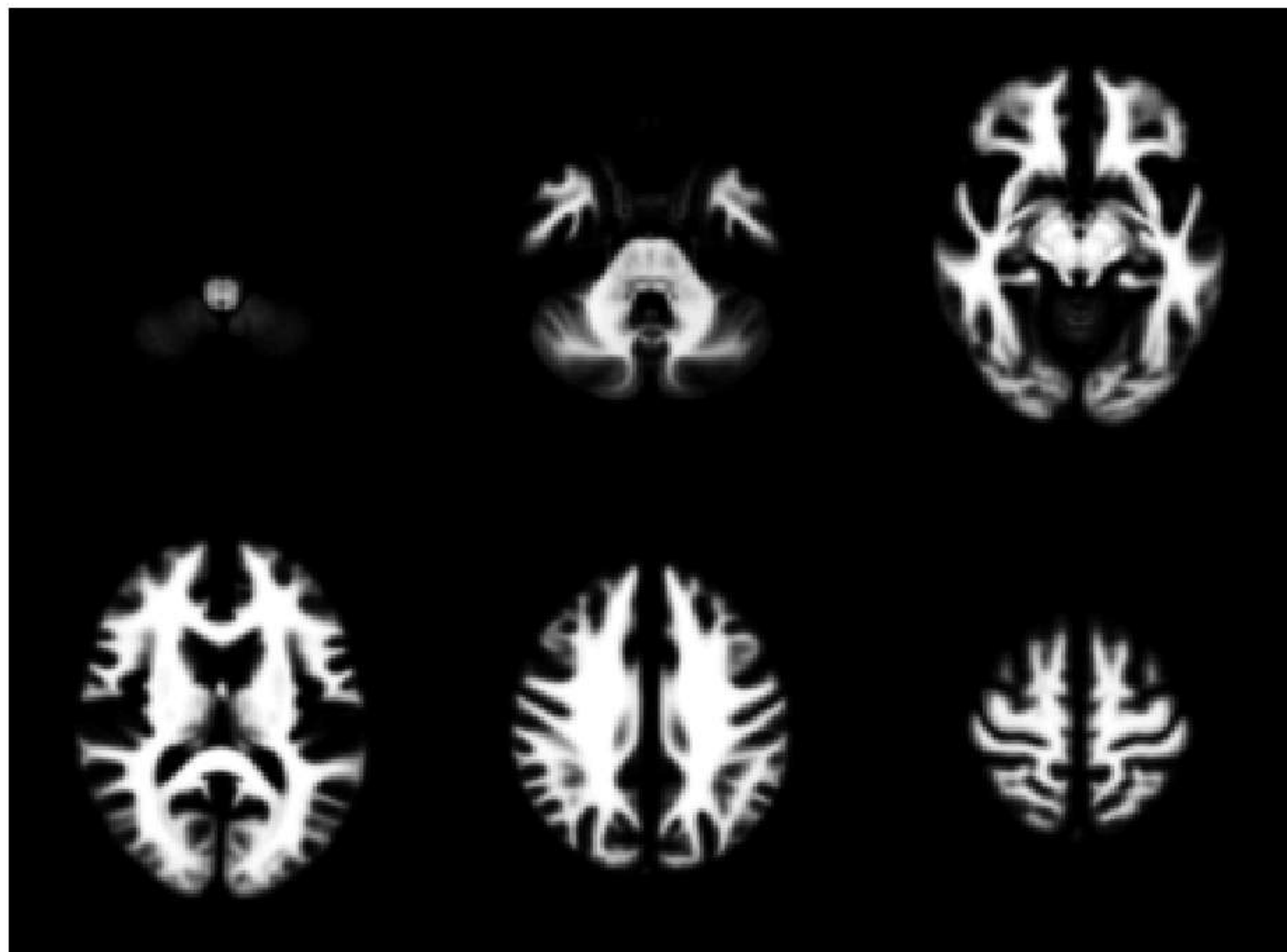


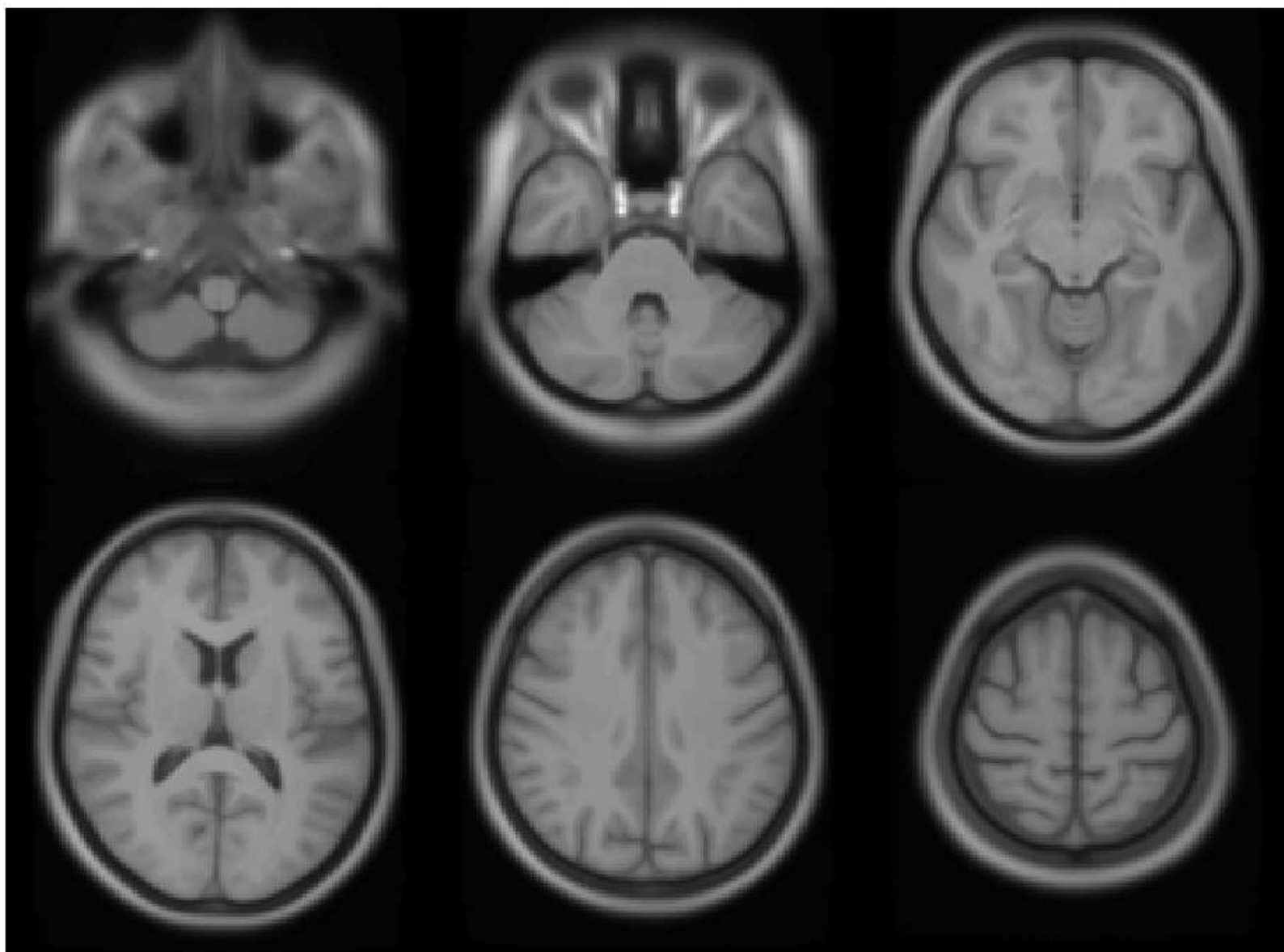


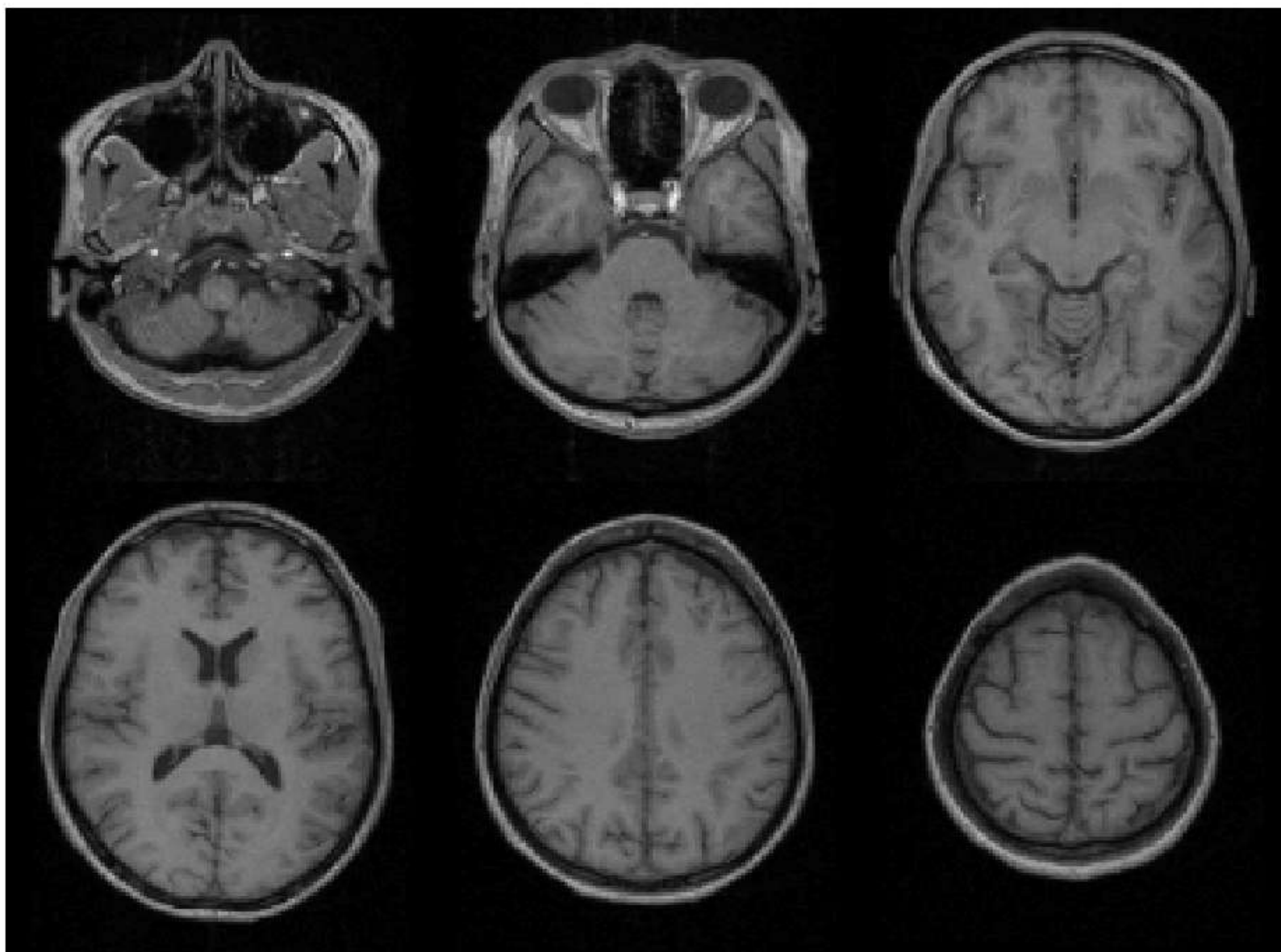
Warped  
GM images

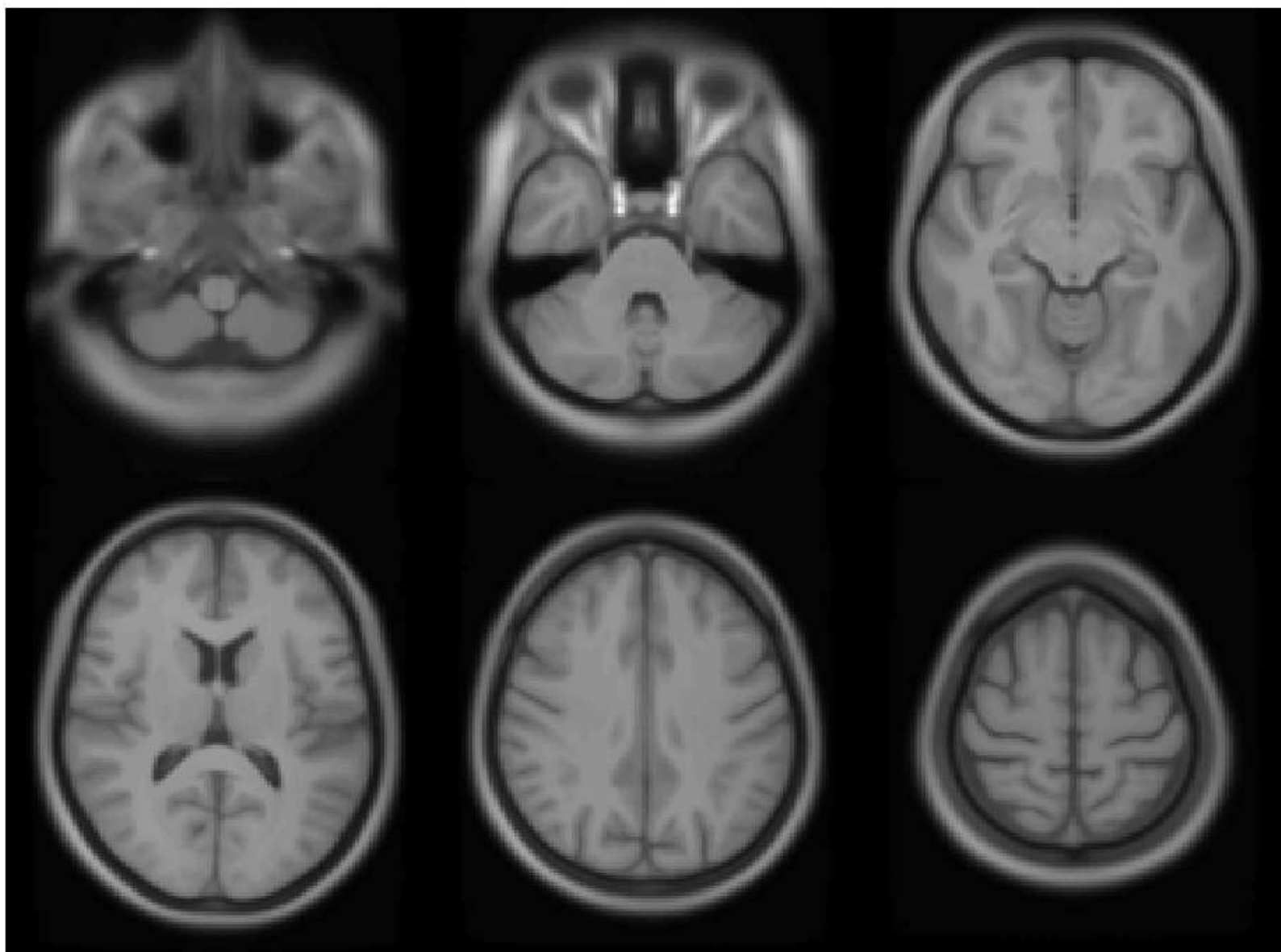


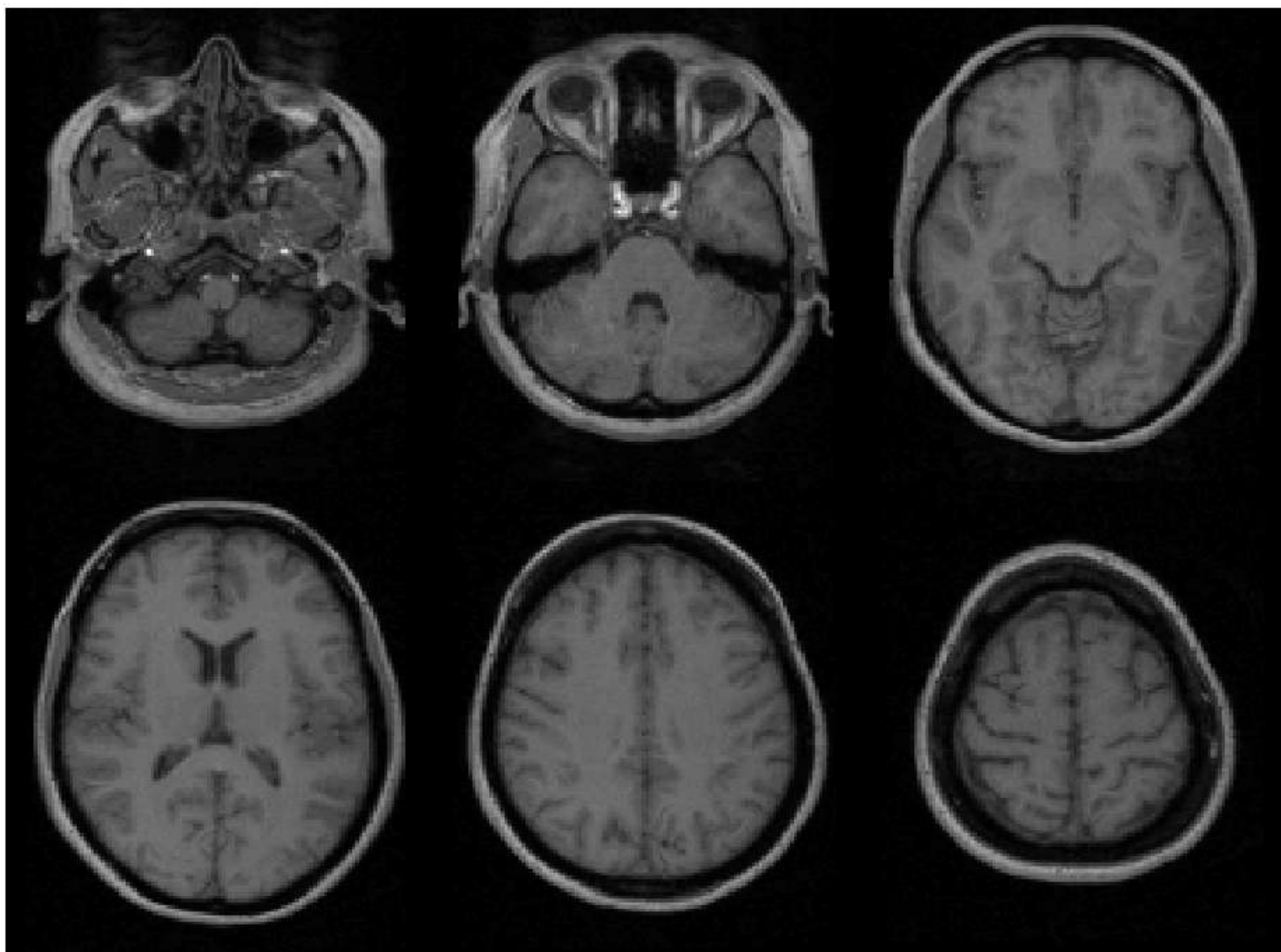


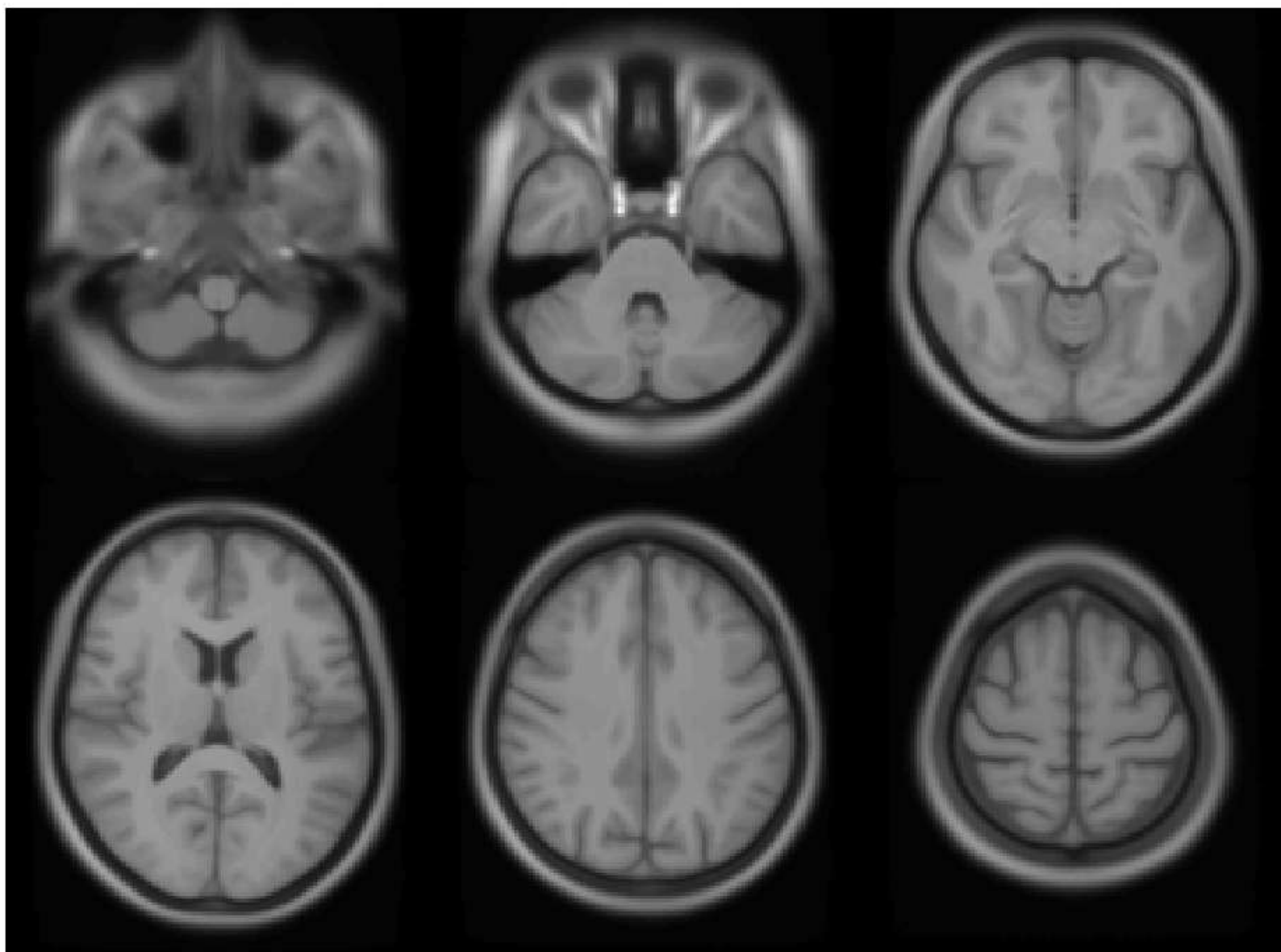




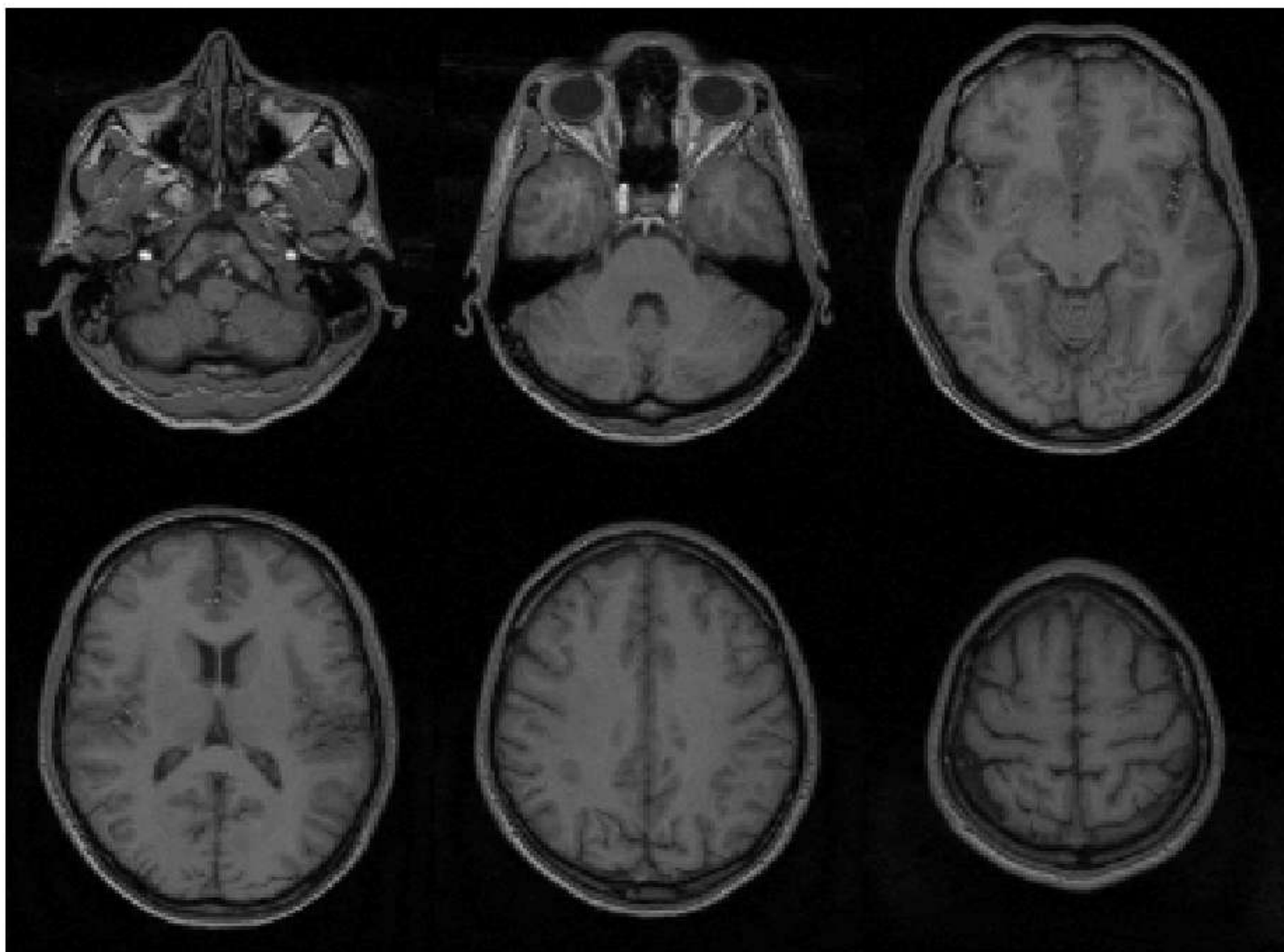


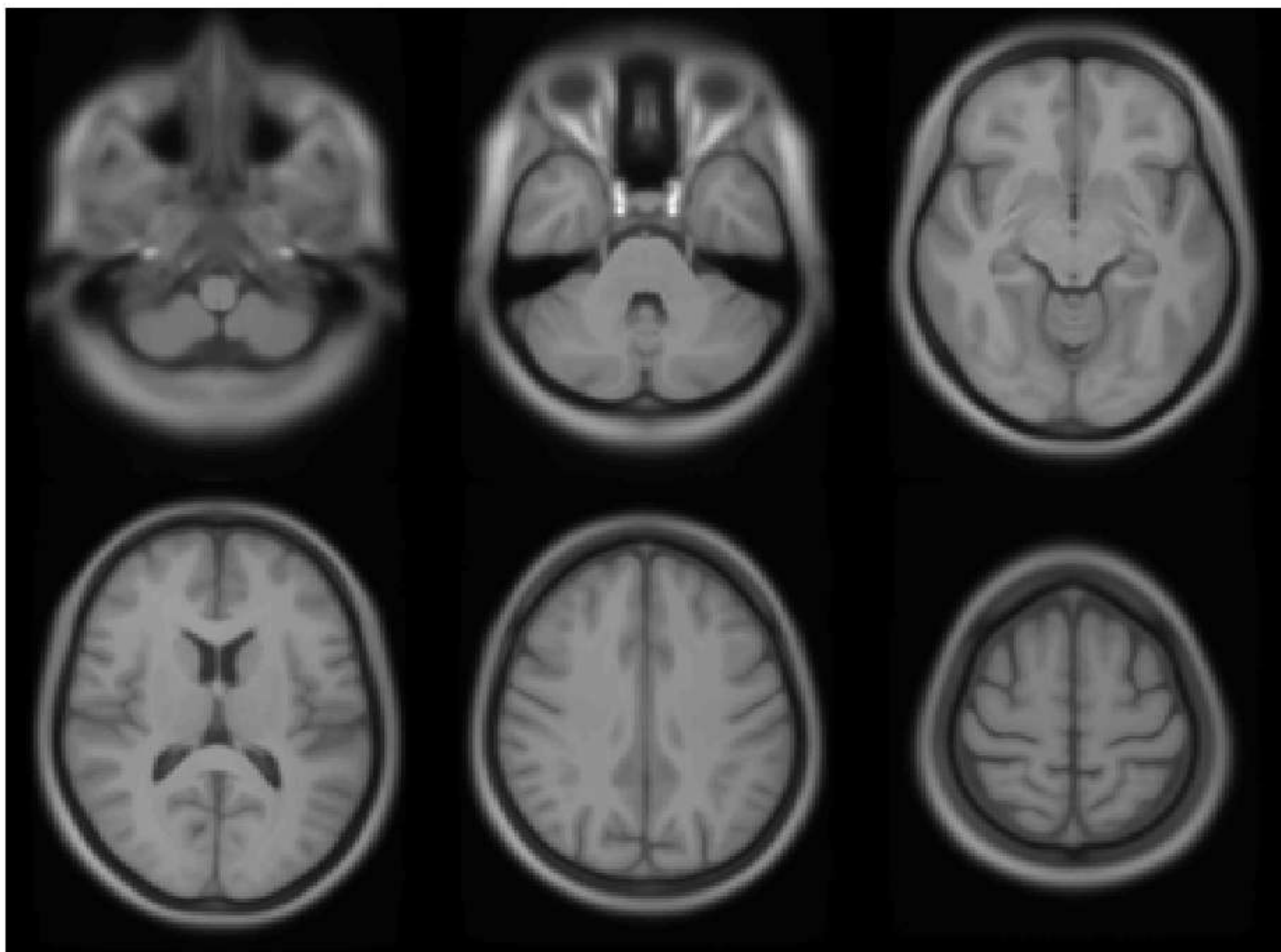








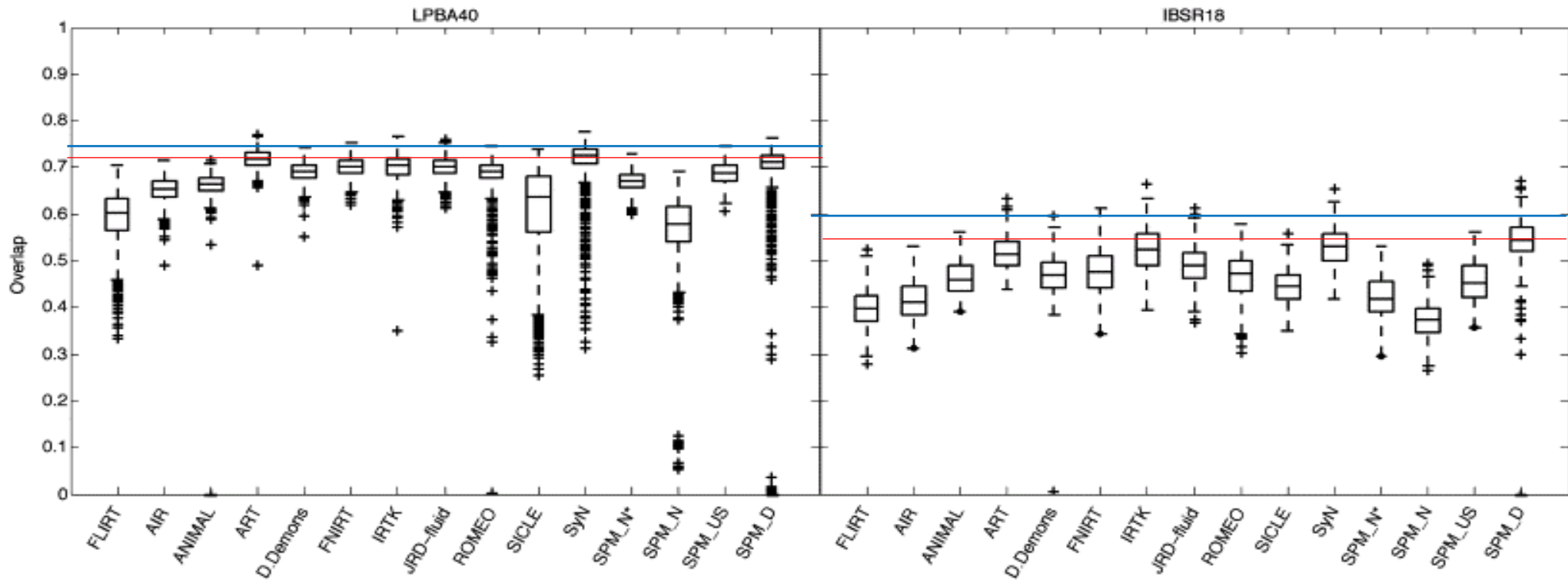




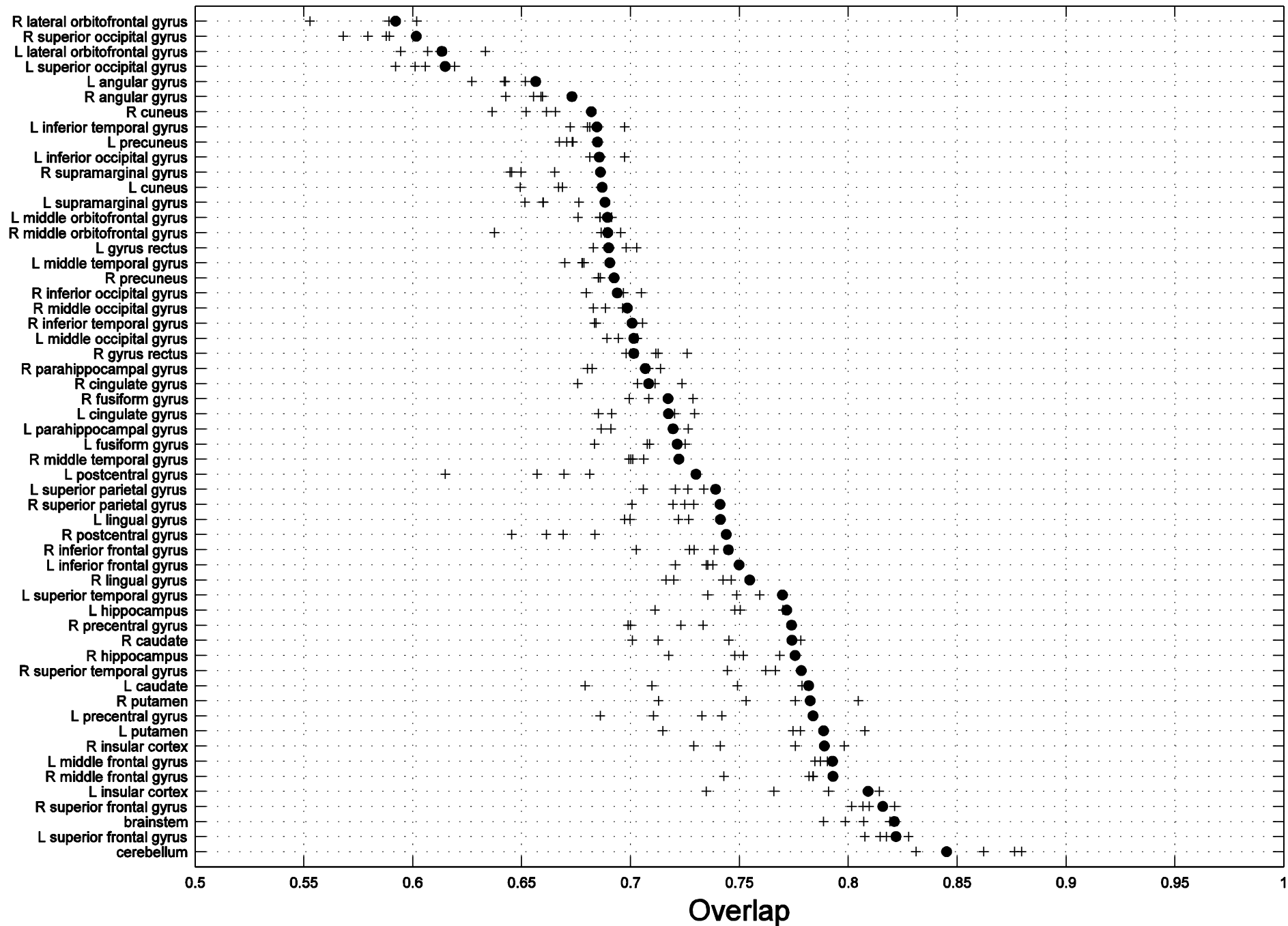
LPBA40

IBSR18

# Evaluations of nonlinear registration algorithms



# LPBA40



# Why use diffeomorphic registration?

$$2 \times 2 \neq 3$$

This is what you get from approximating a multiplication using additions.

$$((2-1)+(2-1))+1 = 3$$

It almost works for values close to 1.

$$1.01 \times 1.01 = 1.0201$$

$$((1.01-1)+(1.01-1))+1 = 1.02$$

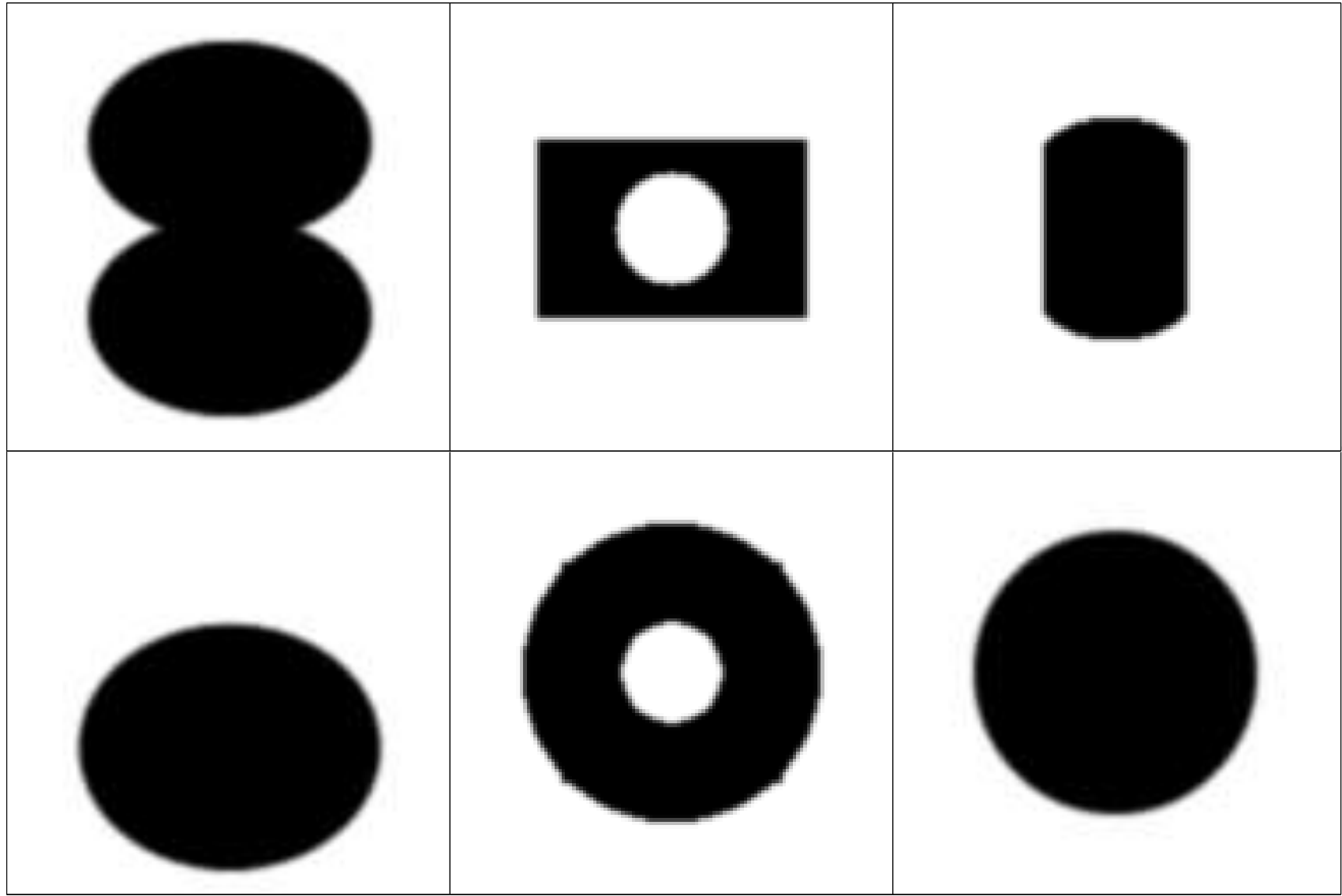
# Some References

- Ashburner. “*A Fast Diffeomorphic Image Registration Algorithm*”. NeuroImage 38:95-113, 2007.
- Ashburner & Friston. “*Computing Average Shaped Tissue Probability Templates*”. NeuroImage **45**:333-341, 2009.
- Ashburner & Friston. “*Diffeomorphic registration using geodesic shooting and Gauss–Newton optimisation*”. NeuroImage 55(3):954-967, 2011.
- Klein, Andersson, Ardekani, Ashburner, Avants, Chiang, Christensen, Collins, Gee, Hellier, Song, Jenkinson, Lepage, Rueckert, Thompson, Vercauteren, Woods, Mann & Parsey. “*Evaluation of 14 nonlinear deformation algorithms applied to human brain MRI registration*”. NeuroImage 46:786-802, 2009.

# Overview

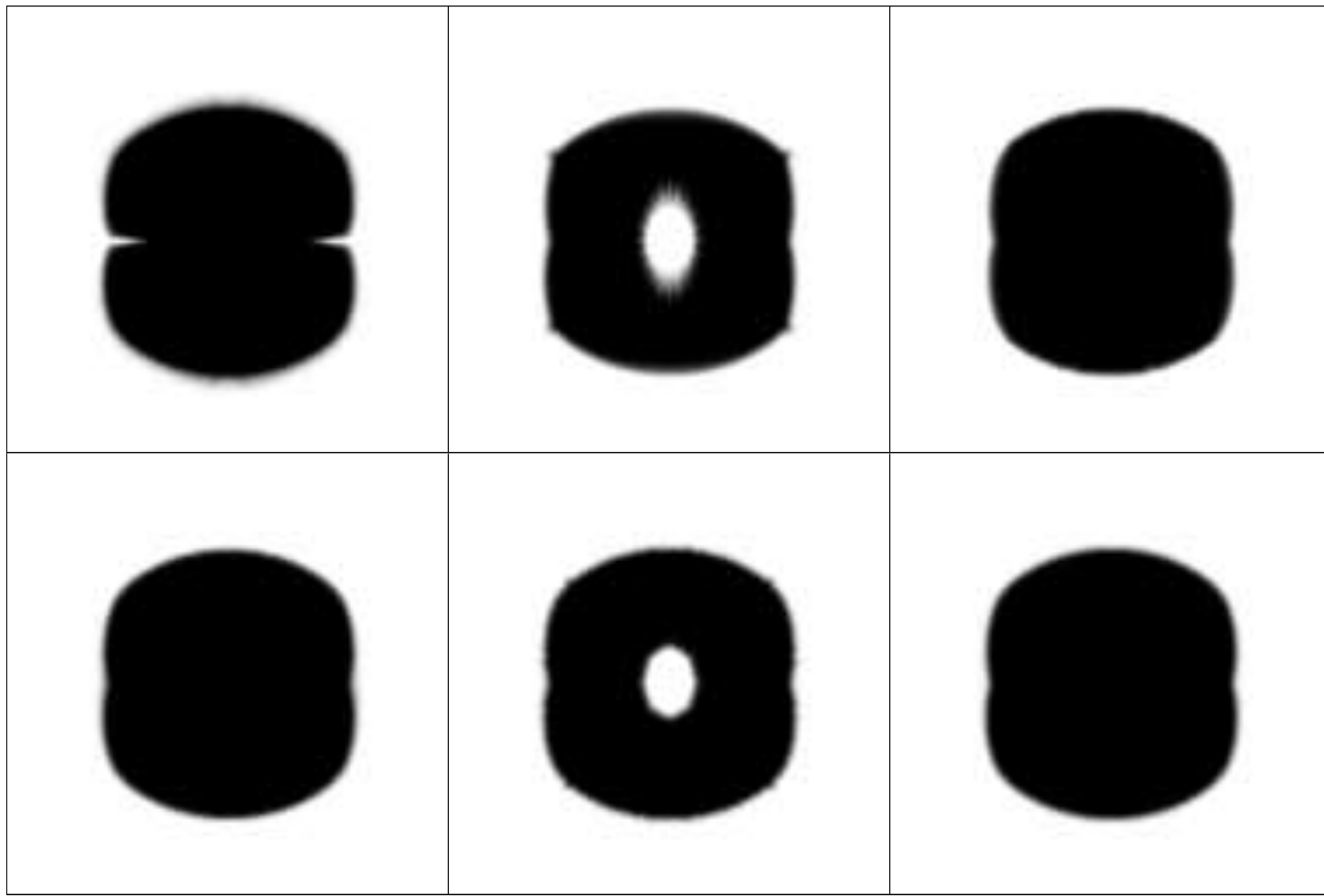
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- Diffeomorphic Registration
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# Some 2D Shapes

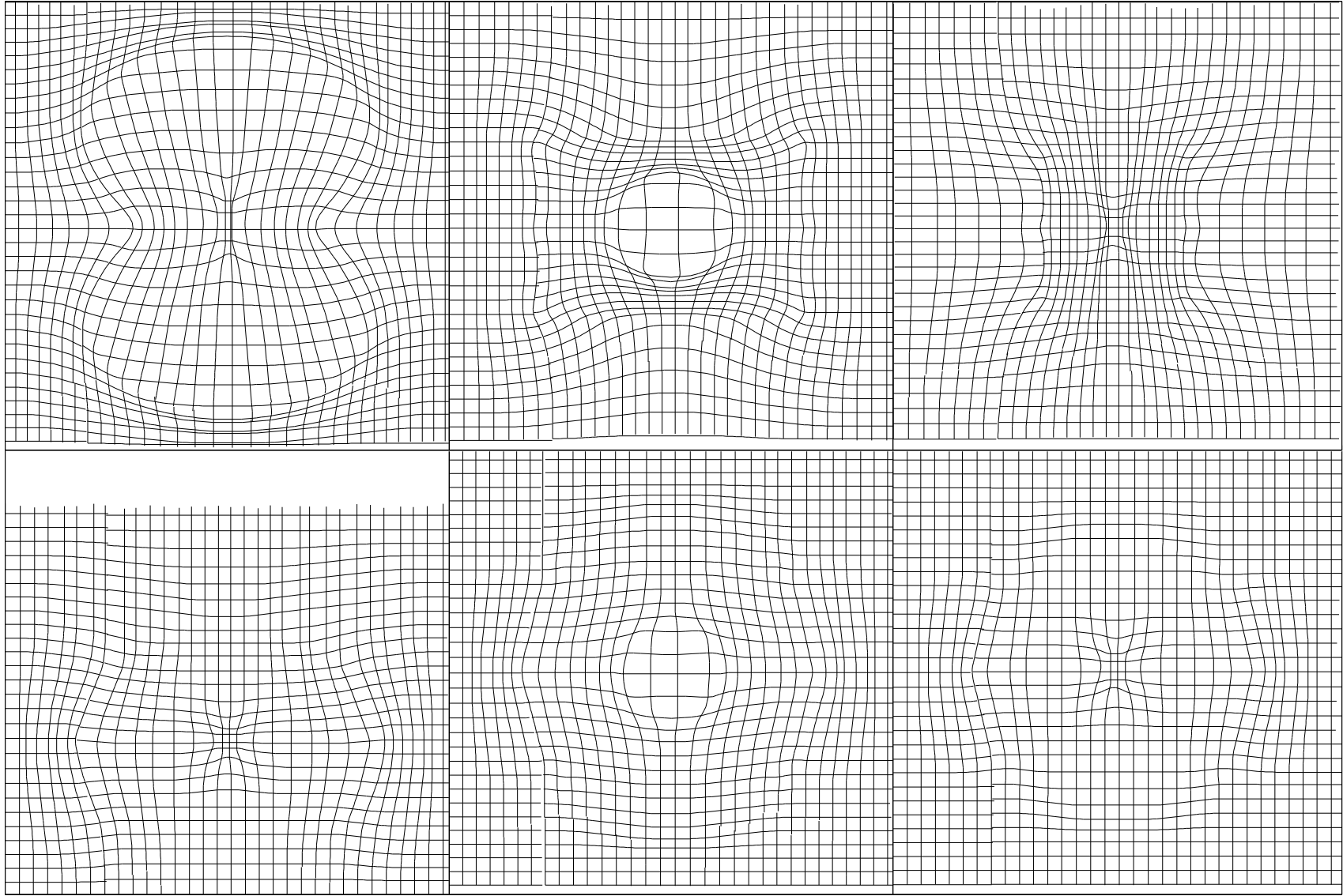




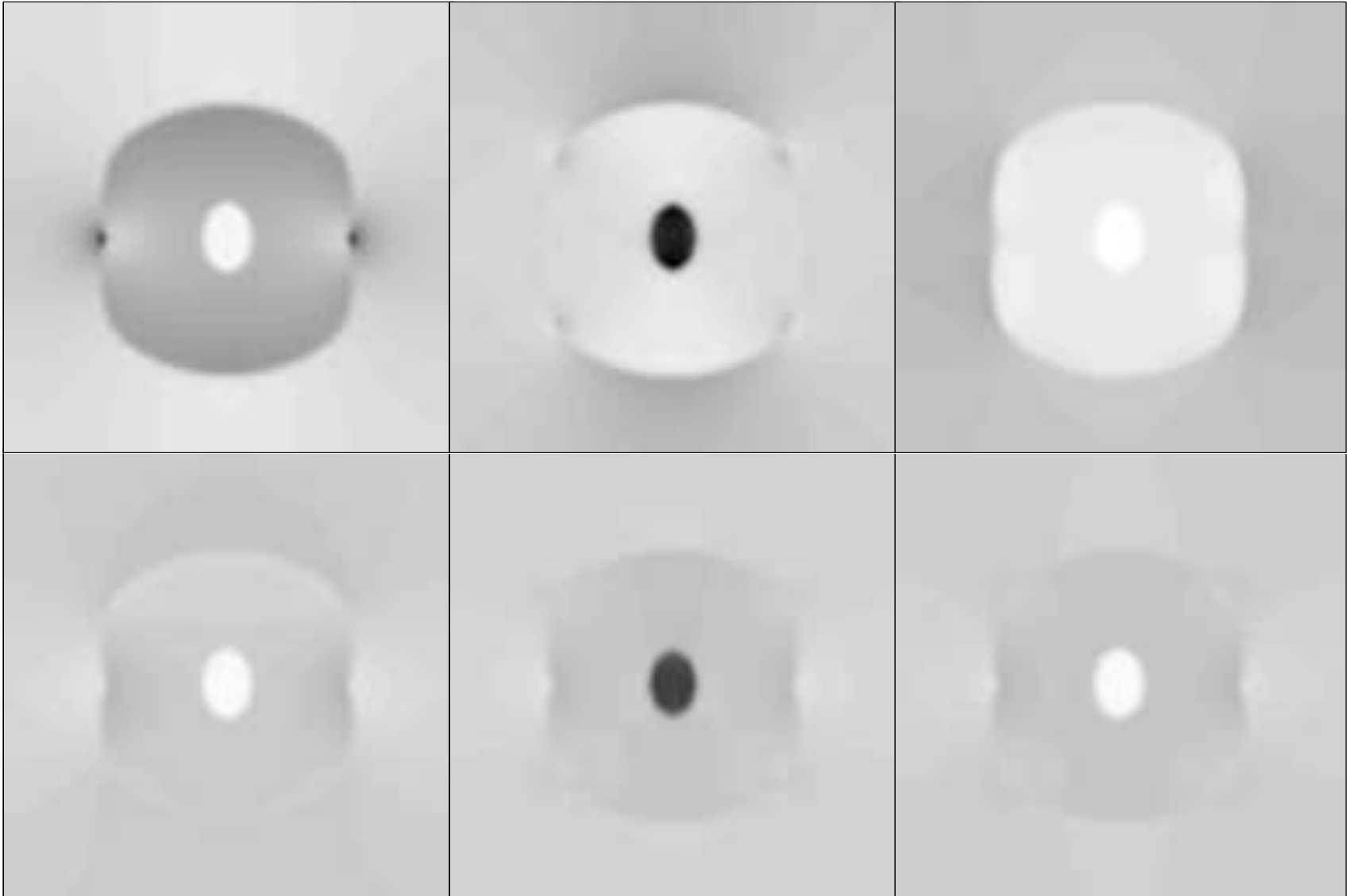
# Shapes aligned to their average



These were the deformations for that



and these are the Jacobian determinants



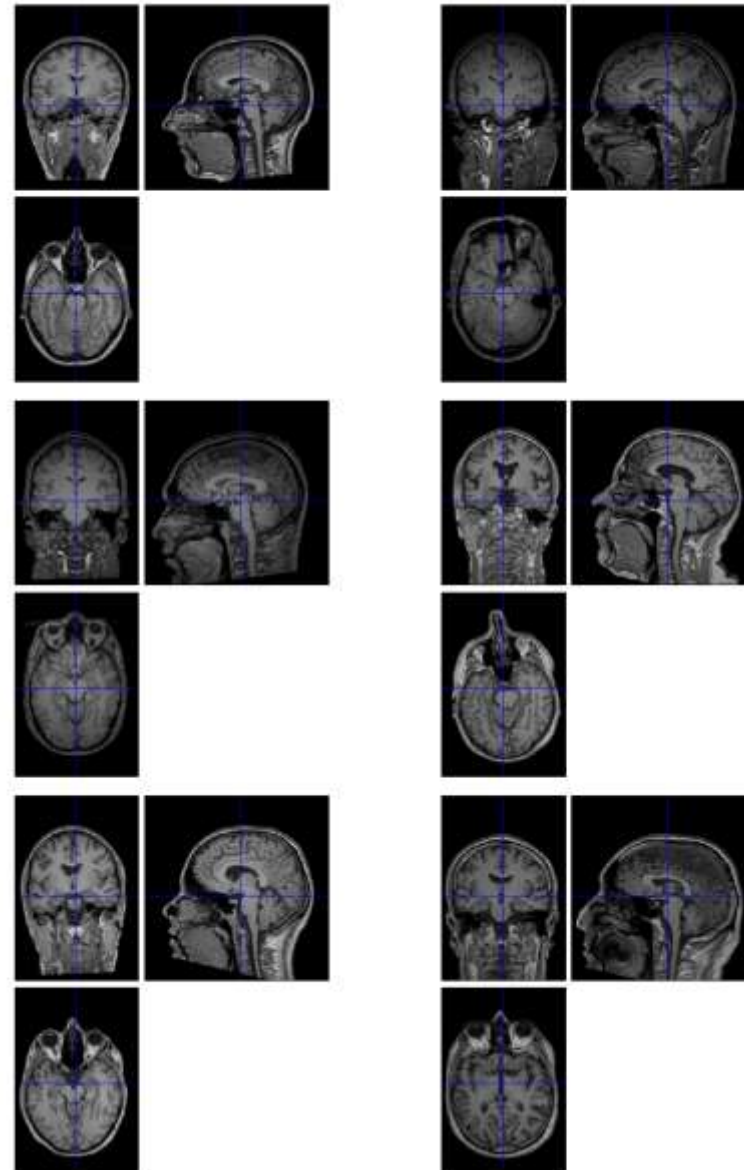
# Cross-Sectional Data

Used 550 T1w brain MRI from IXI (Information eXtraction from Images) dataset.

- <http://www.brain-development.org/>

Data from three different hospitals in London:

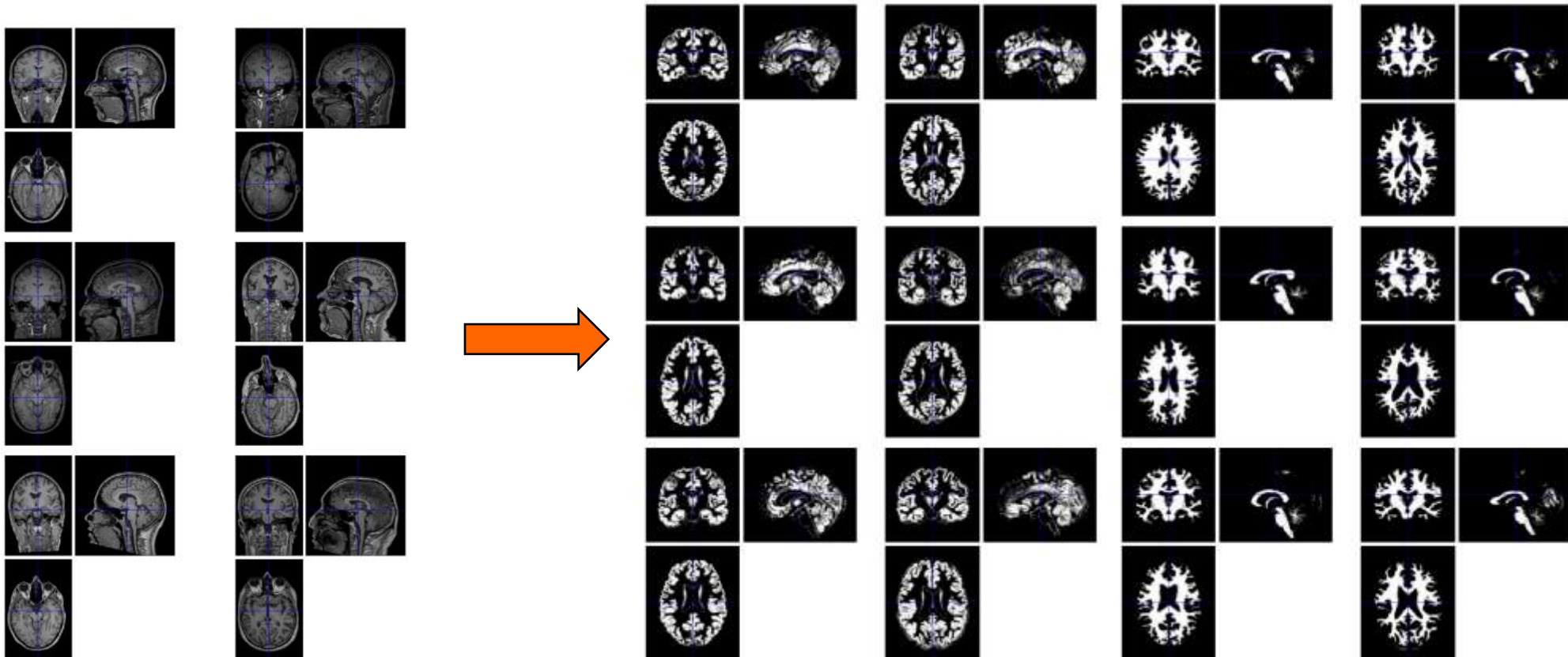
- Hammersmith Hospital using a Philips 3T system
- Guy's Hospital using a Philips 1.5T system
- Institute of Psychiatry using a GE 1.5T system



# Segmentation

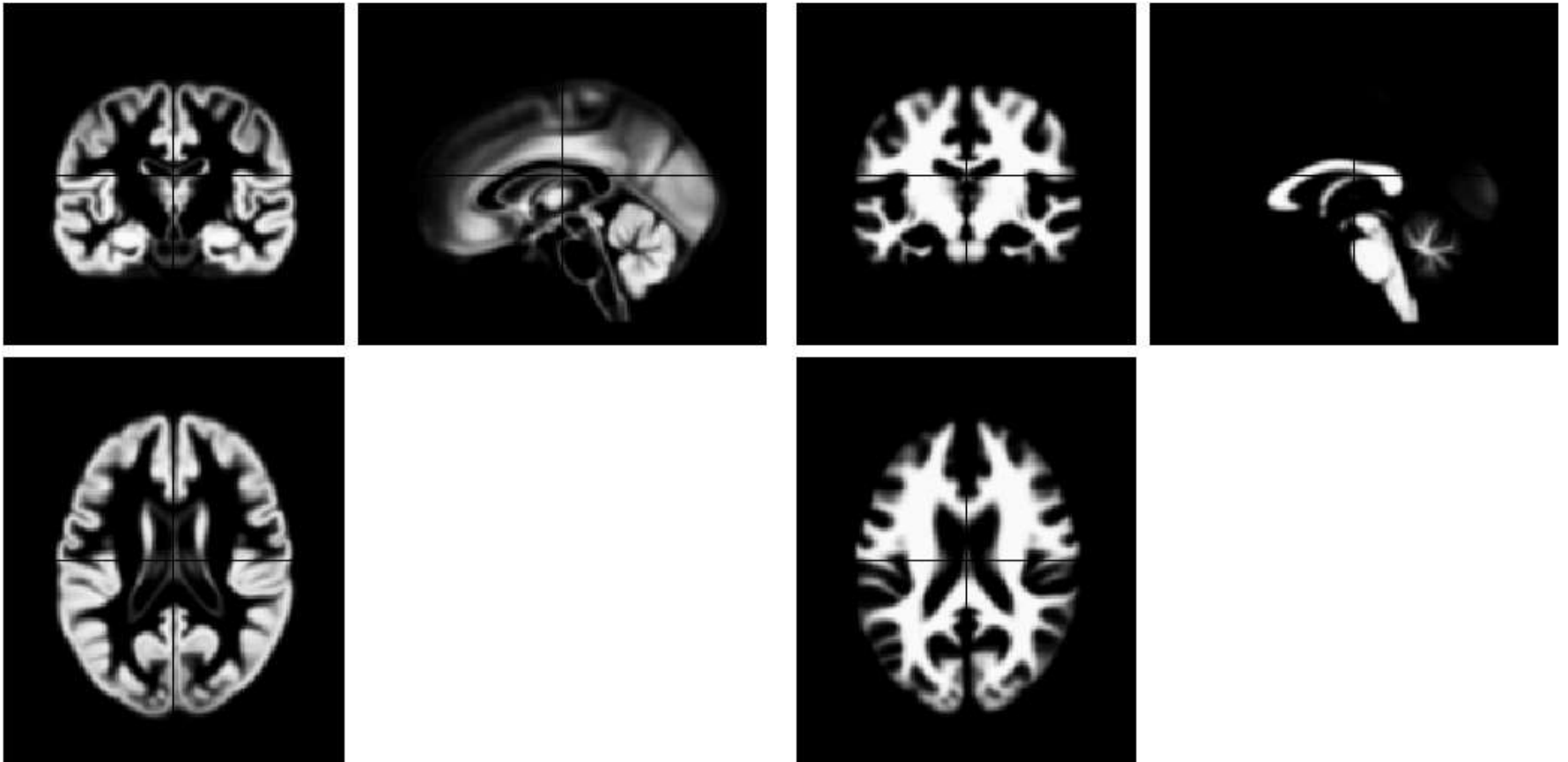
Segmented into GM and WM.

Approximately aligned via rigid-body.



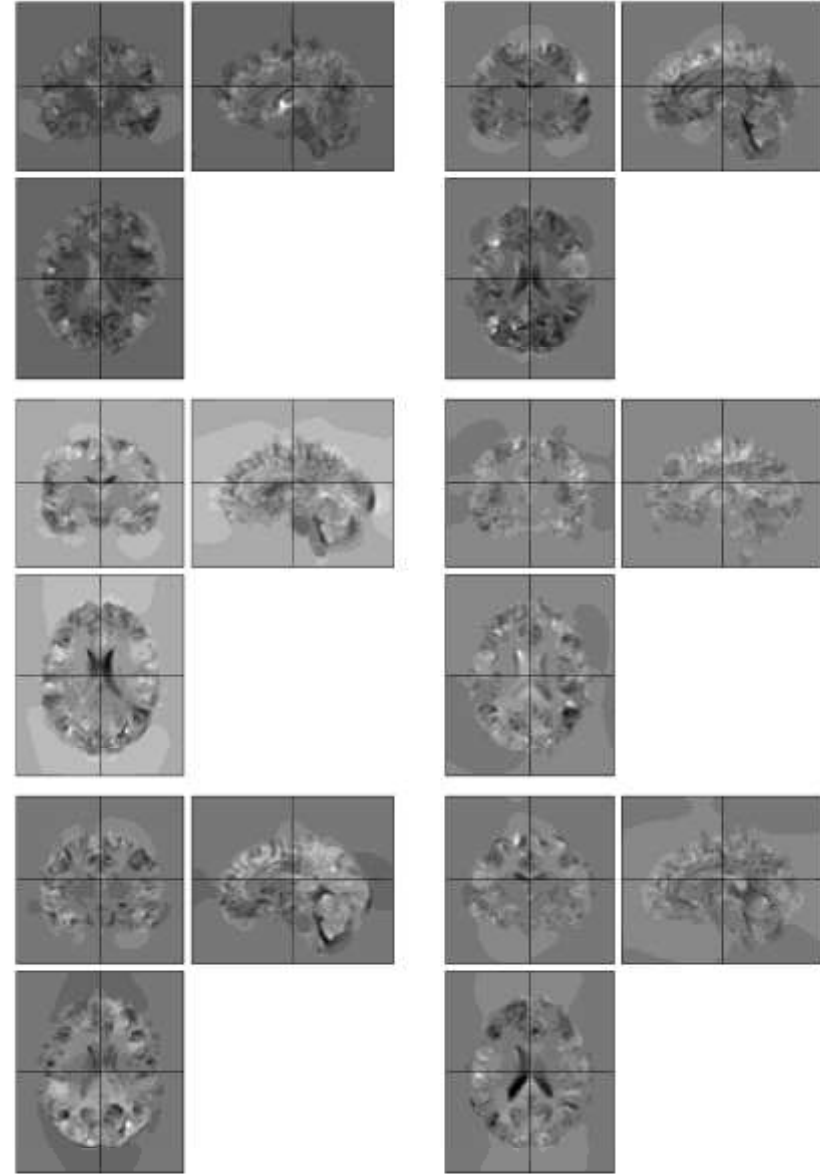
# Diffeomorphic Alignment

All GM and WM were diffeomorphically aligned to their common average-shaped template.



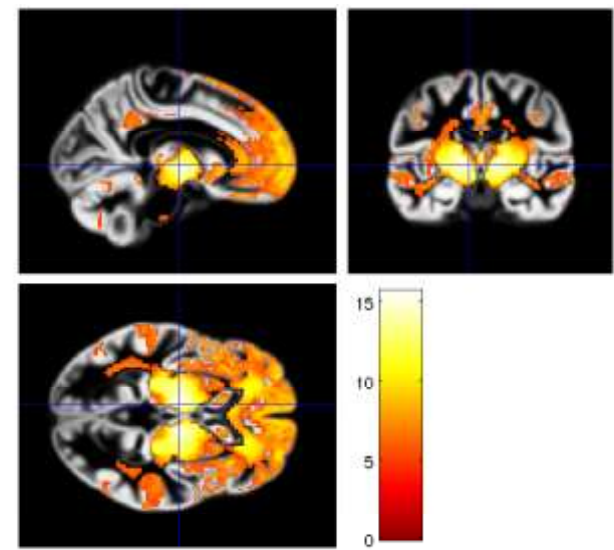
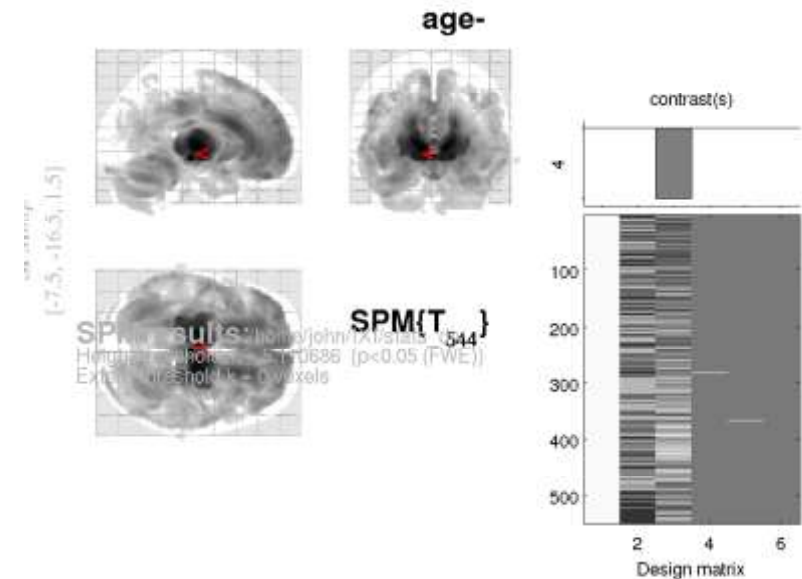
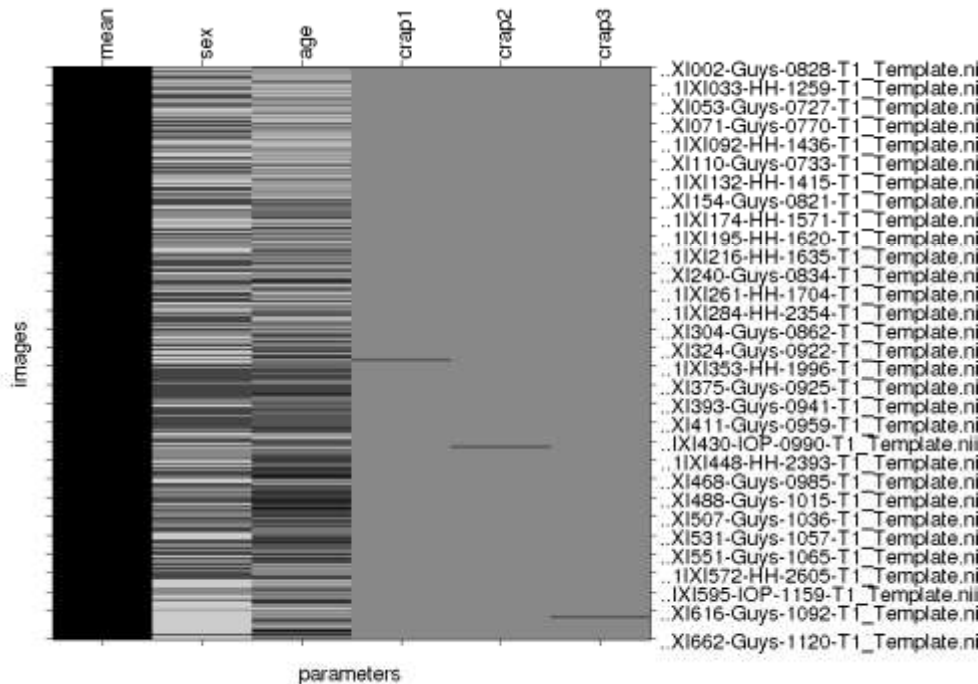
# Divergence Maps

- Used maps of initial velocity divergence.
- Similar to logarithms of Jacobian determinants.
  - Encode a sort of “growth rate”



# Mass-Univariate Analysis – shrinkage with age

## Statistical analysis: Design



Design description...

parameter estimability

Design: Multiple regression

Global calculation: omit

Grand mean scaling: <no grand Mean scaling>

Global normalisation: <no global normalisation>

Parameters: 1 condition, +5 covariate, +0 block, +0 nuisance

6 total, having 6 degrees of freedom

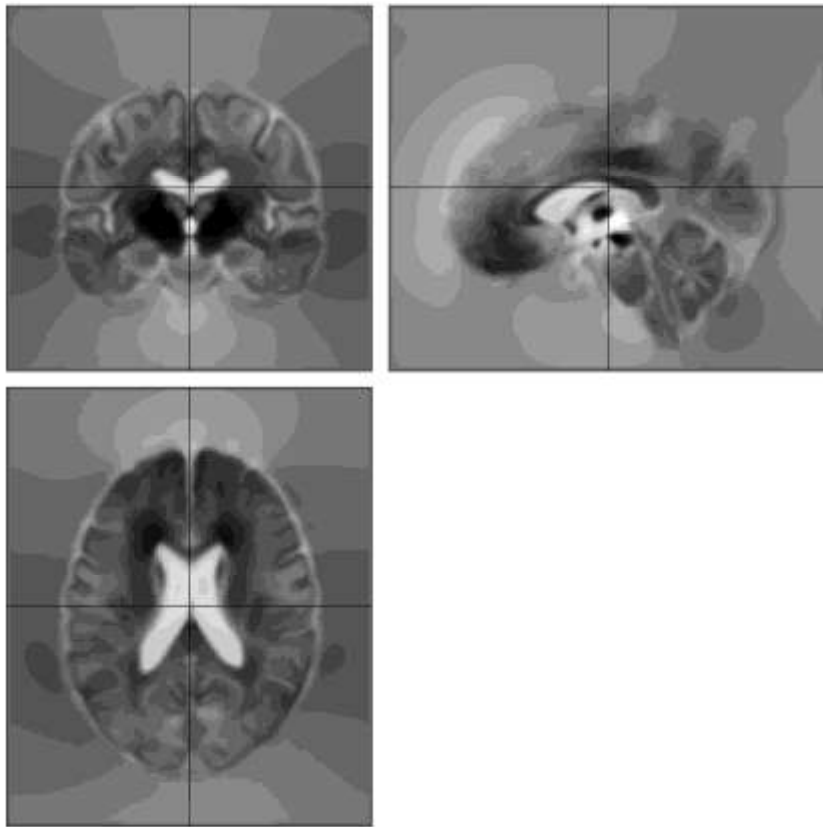
leaving 544 degrees of freedom from 550 images

(gray →  $\beta$  not uniquely specified)

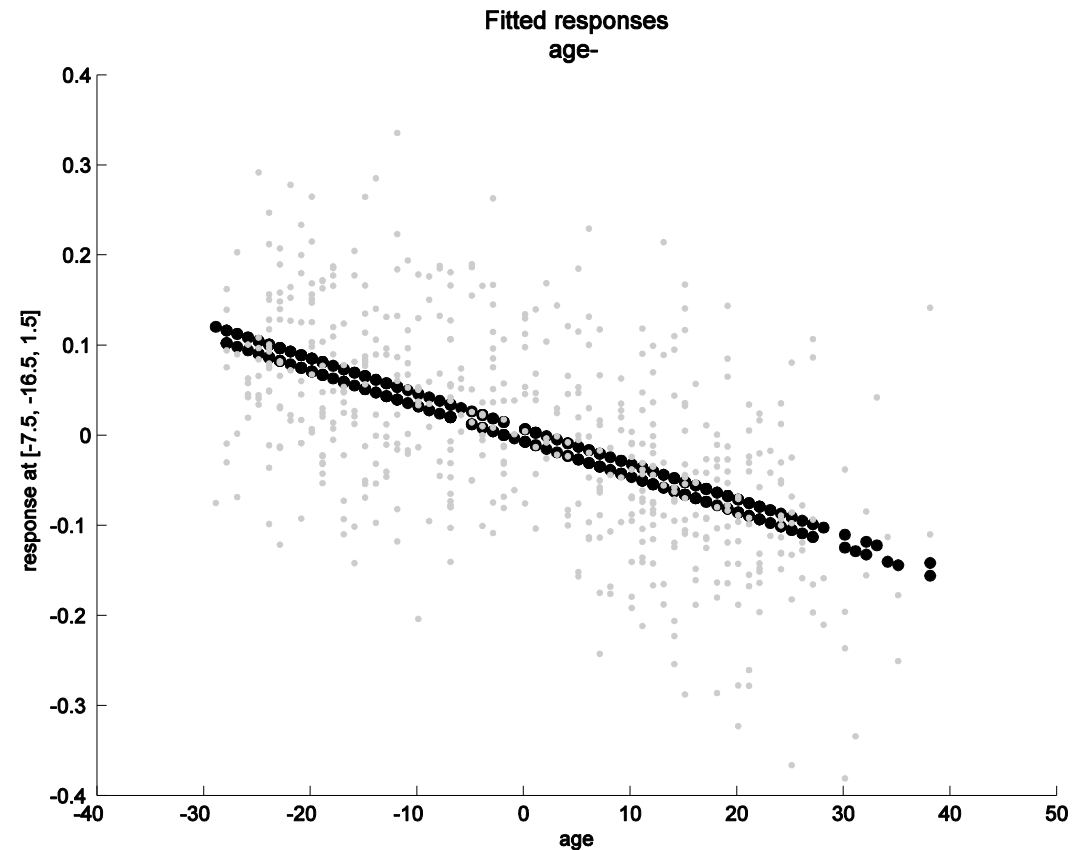


# Large T statistics ( $> 15$ ) – but not very predictive

T Statistic Image



The most predictive single voxel



# Some References

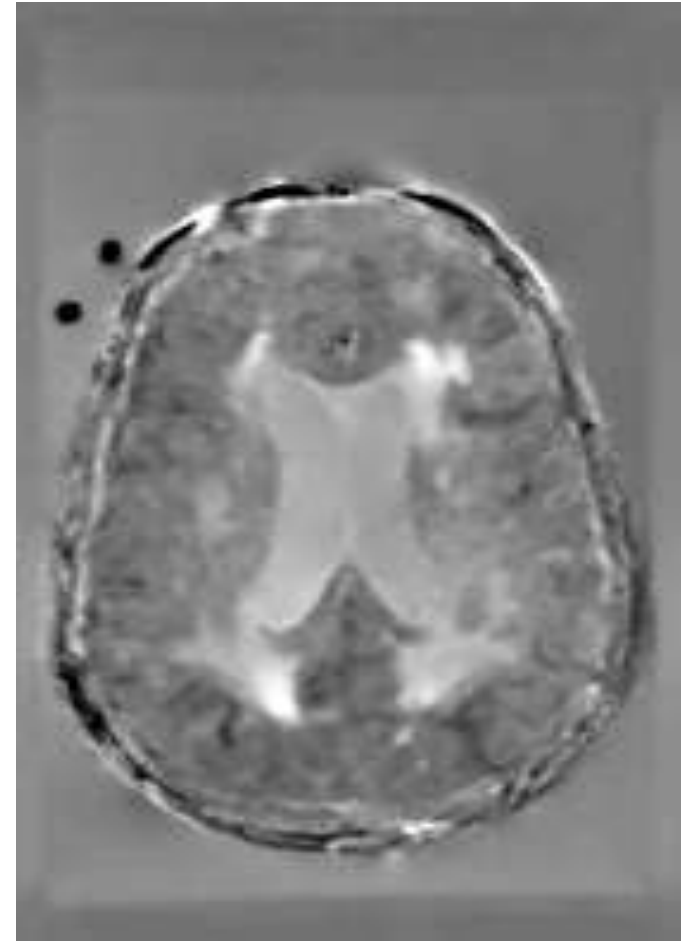
- Ashburner & Friston. “*Unified Segmentation*”. NeuroImage **26**:839-851, 2005.
- Ashburner & Friston. “*Computing Average Shaped Tissue Probability Templates*”. NeuroImage **45**:333-341, 2009.
- Ashburner & Friston. “*Diffeomorphic registration using geodesic shooting and Gauss–Newton optimisation*”. NeuroImage **55**(3):954-967, 2011.

# Overview

- Voxel-Based Morphometry
- Diffeomorphic Registration
- Tensor-Based Morphometry
- **Longitudinal Registration**

# Longitudinal Registration

- Unified model combines:
  - Nonlinear diffeomorphic registration.
  - Rigid-body registration.
  - Intensity inhomogeneity correction.
- All made as mathematically coherent as possible.



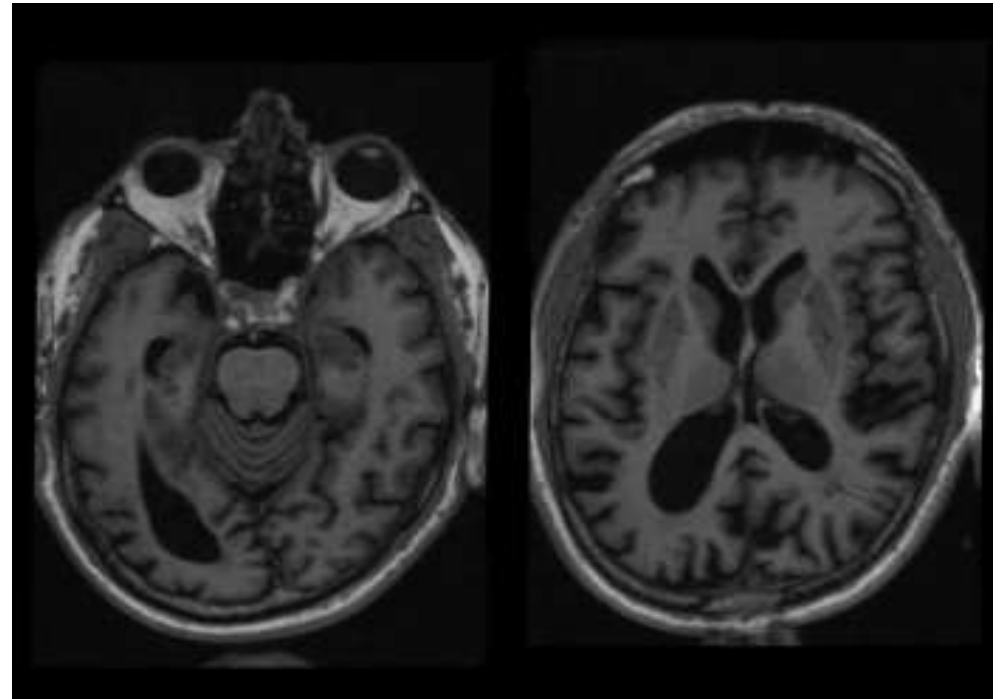
# OASIS Data

## OAS2 0048

66 year old male with dementia (MMSE=19, CDR=1).

Five scans collected over 40 months.

Marcus, D., A. Fotenos, J. Csernansky, J. Morris, and R. Buckner (2010). *Open access series of imaging studies: longitudinal MRI data in nondemented and demented older adults*. Journal of cognitive neuroscience 22 (12), 2677–2684.



# OASIS Data

## OAS2 0048

66 year old male with dementia (MMSE=19, CDR=1).

Five scans collected over 40 months.

Difference between time point and first scan.



# OASIS Data

## OAS2 0048

66 year old male with dementia (MMSE=19, CDR=1).

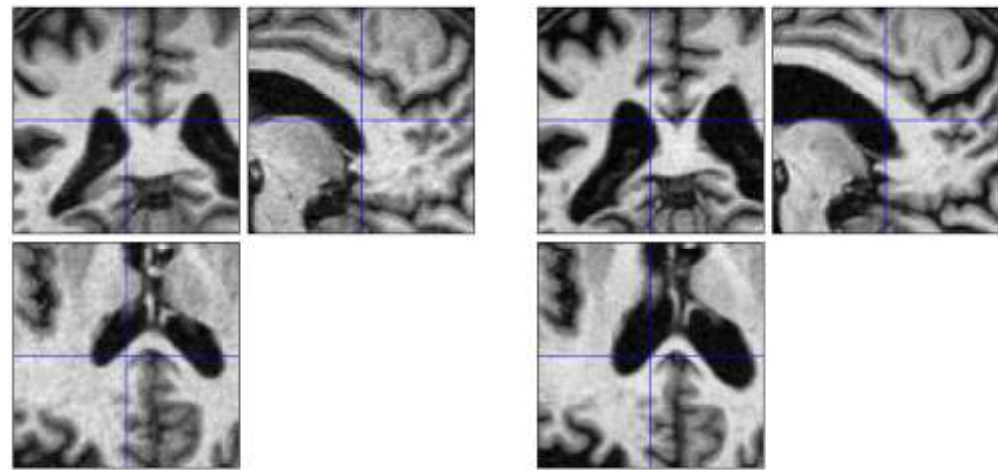
Five scans collected over 40 months.

Expansion/contraction.



# Two Longitudinal Scans

Two scans taken 6 years apart  
(after rigid registration).

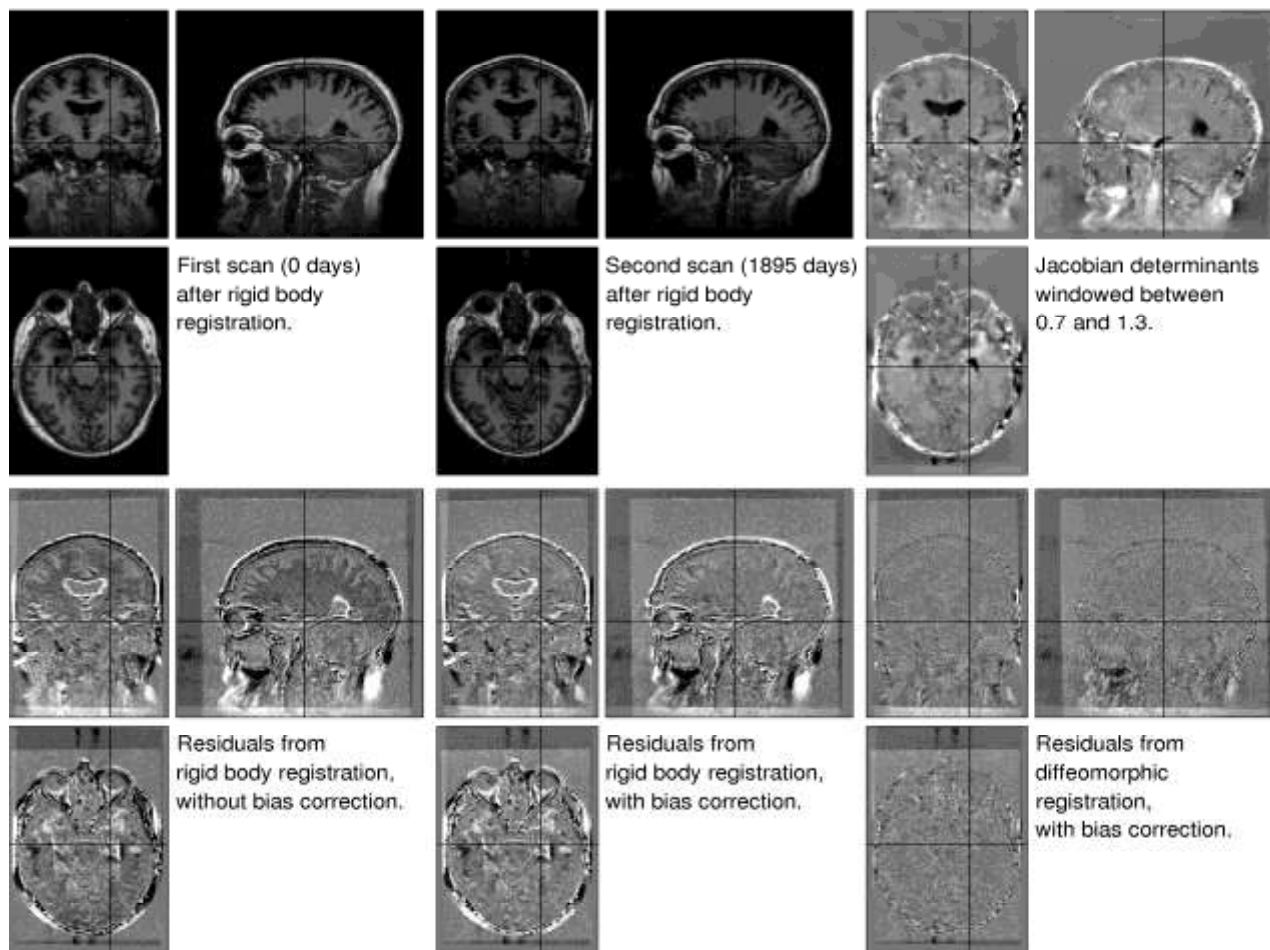




# Oasis Data

## OAS2 0002

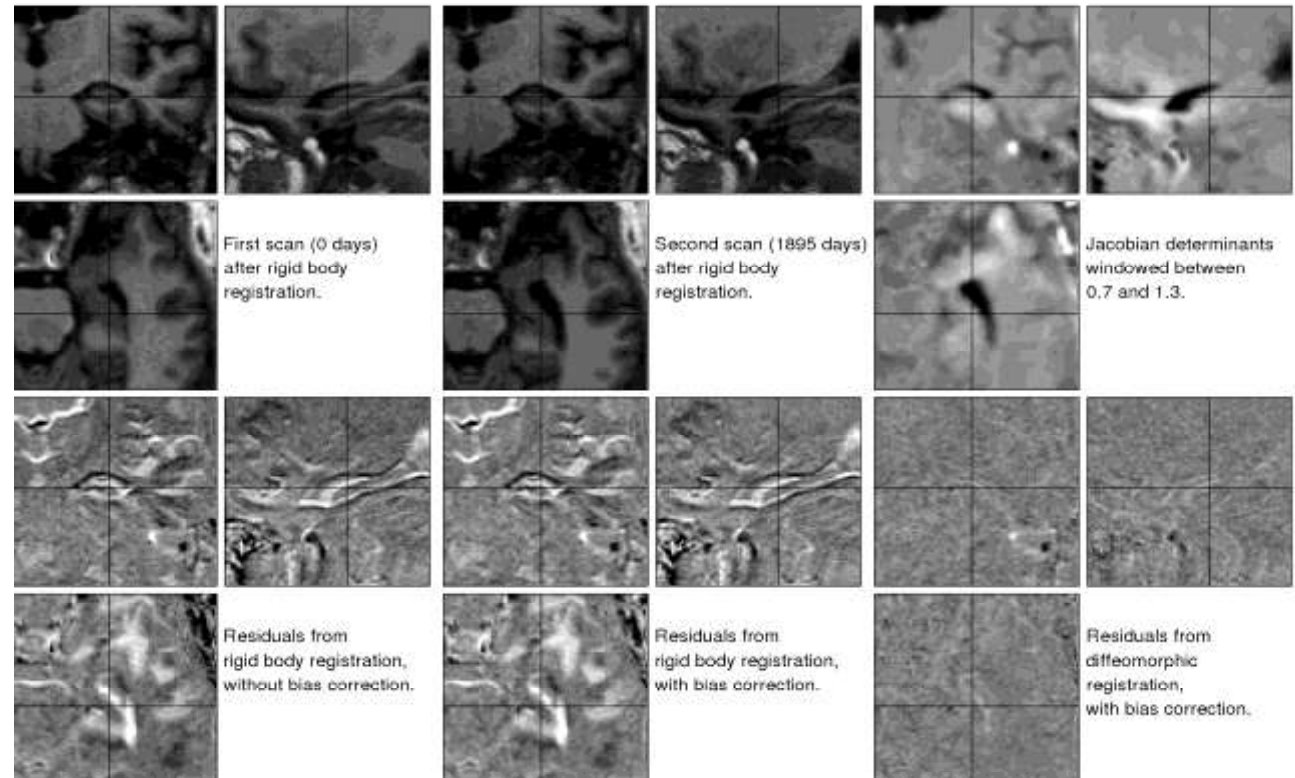
75 year old male,  
with MCI  
(MMSE=22,  
CDR=0.5).



# Oasis Data

## OAS2 0002

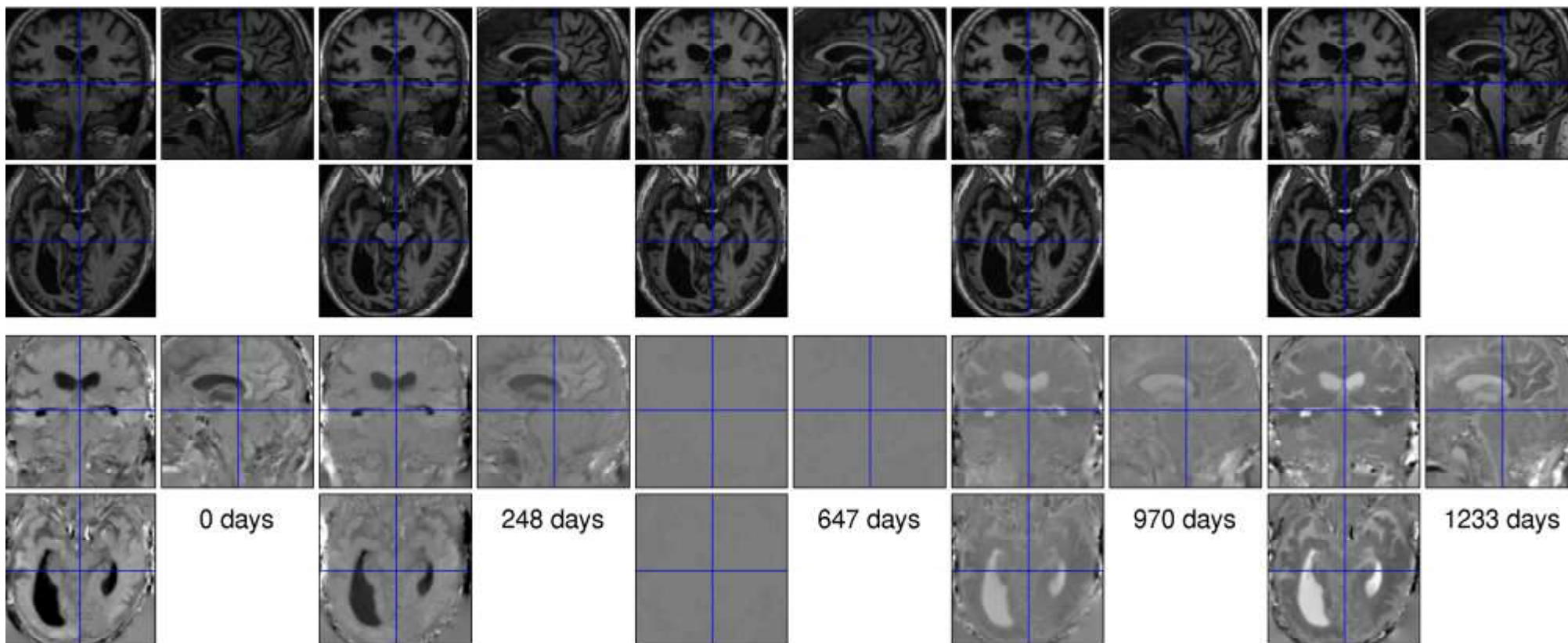
75 year old male,  
with MCI  
(MMSE=22,  
CDR=0.5).



# Oasis Data

## OAS2 0048

66 year old male, with MCI (MMSE=19, CDR=1).



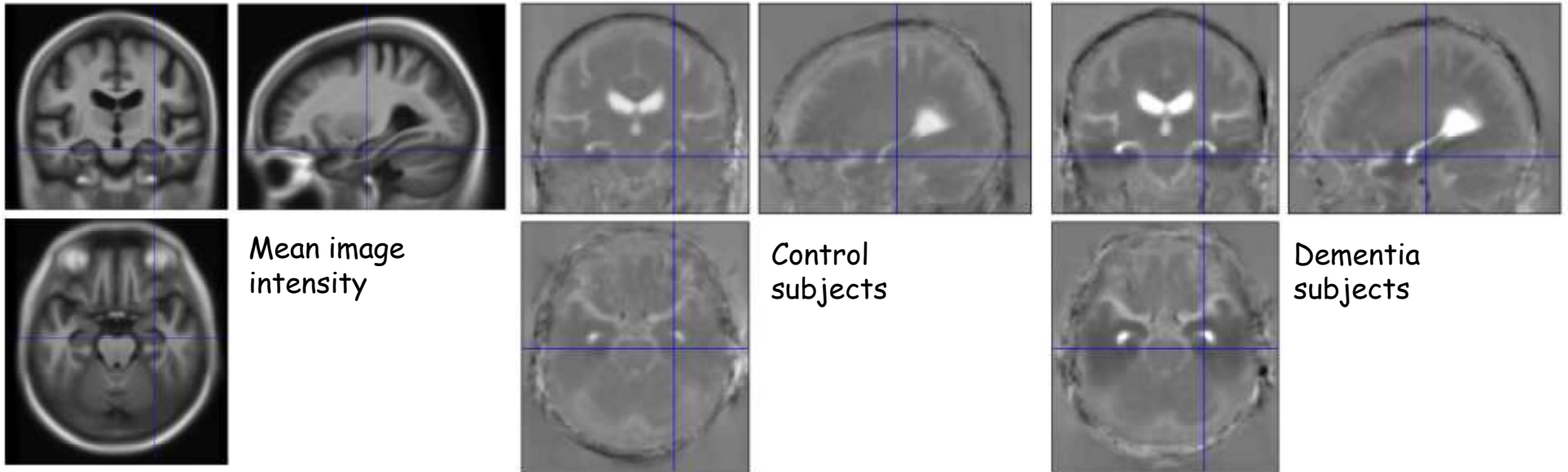
# Oasis Data

Data from first 82 subjects (OAS2 0001 to OAS2 0099).

Computed average expansion/contraction rates for each subject.

Warped all data to common anatomical space.

Generated averages.



# References

- [Ashburner & Ridgway \(2013\)](#). *Symmetric diffeomorphic modelling of longitudinal structural MRI*. *Frontiers in Brain Imaging Methods* 6(197).

