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.

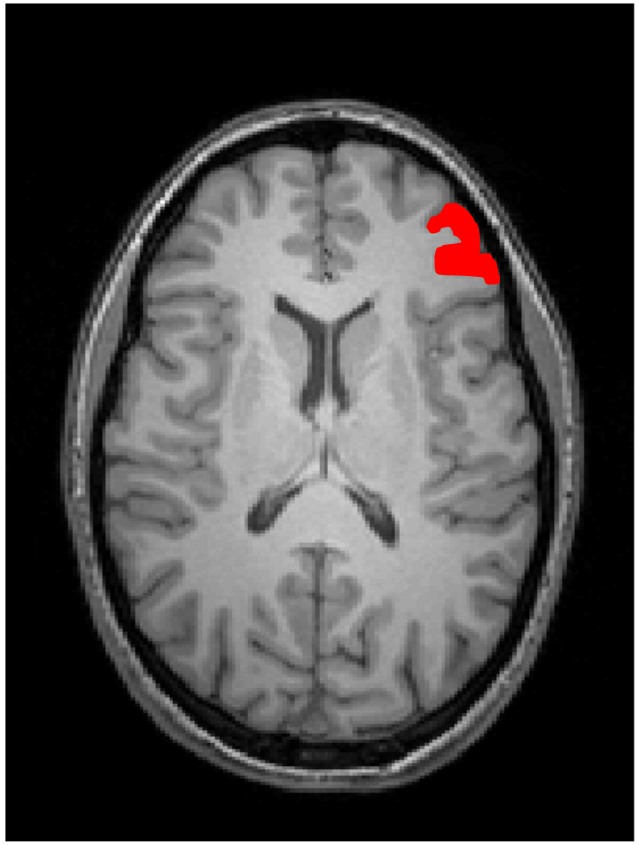
Overview

- **Voxel-Based Morphometry**
- Diffeomorphic Registration
- Tensor-Based Morphometry
- Multivariate Approaches
- Scalar Momentum
- Some Evaluations
- Longitudinal Registration

Voxel-Based Morphometry

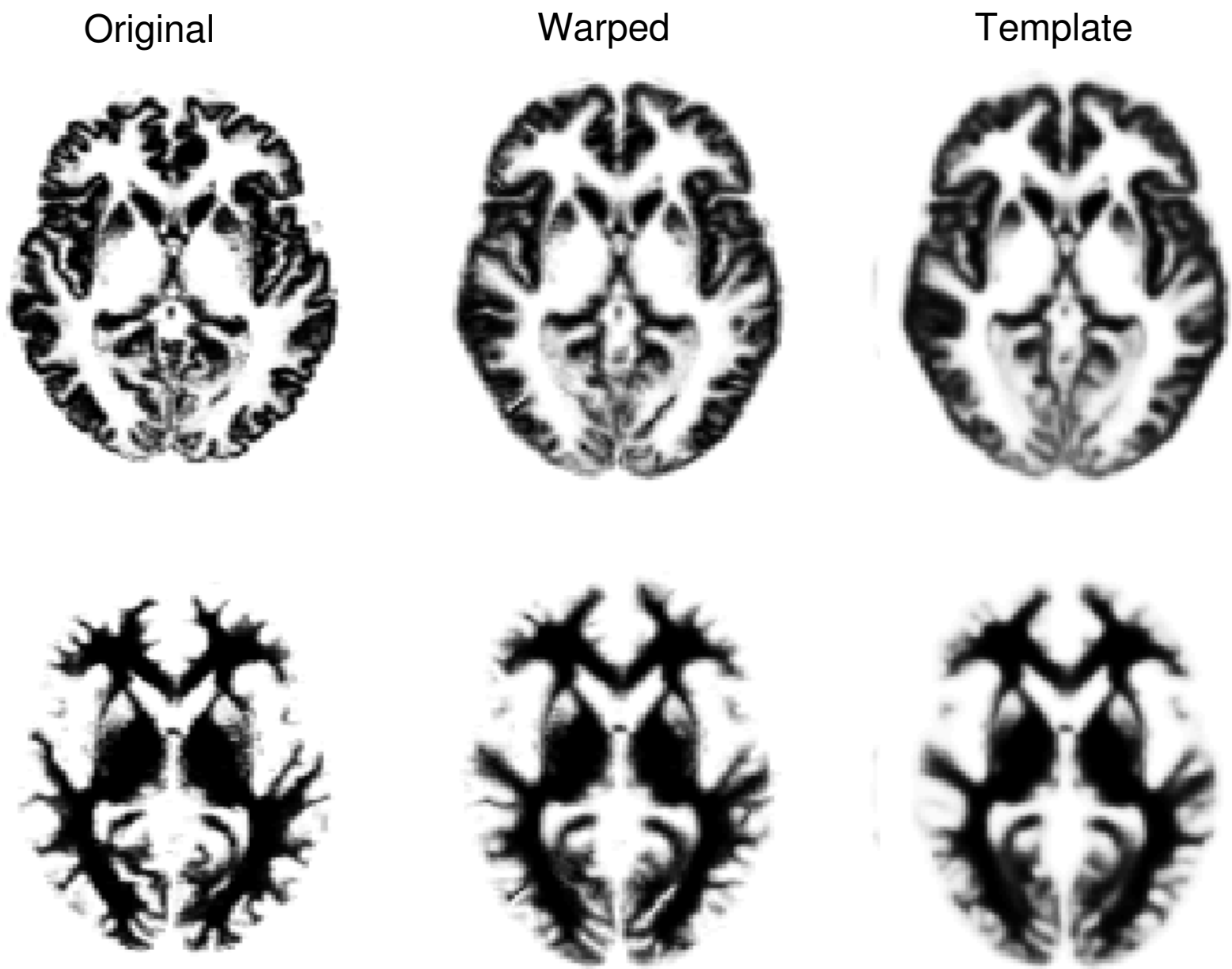
- Produce a map of statistically significant differences among populations of subjects.
  - e.g. compare a patient group with a control group.
  - or identify correlations with age, test-score etc.
- The data are pre-processed to sensitise the tests to regional tissue volumes.
  - Usually grey or white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

Volumetry

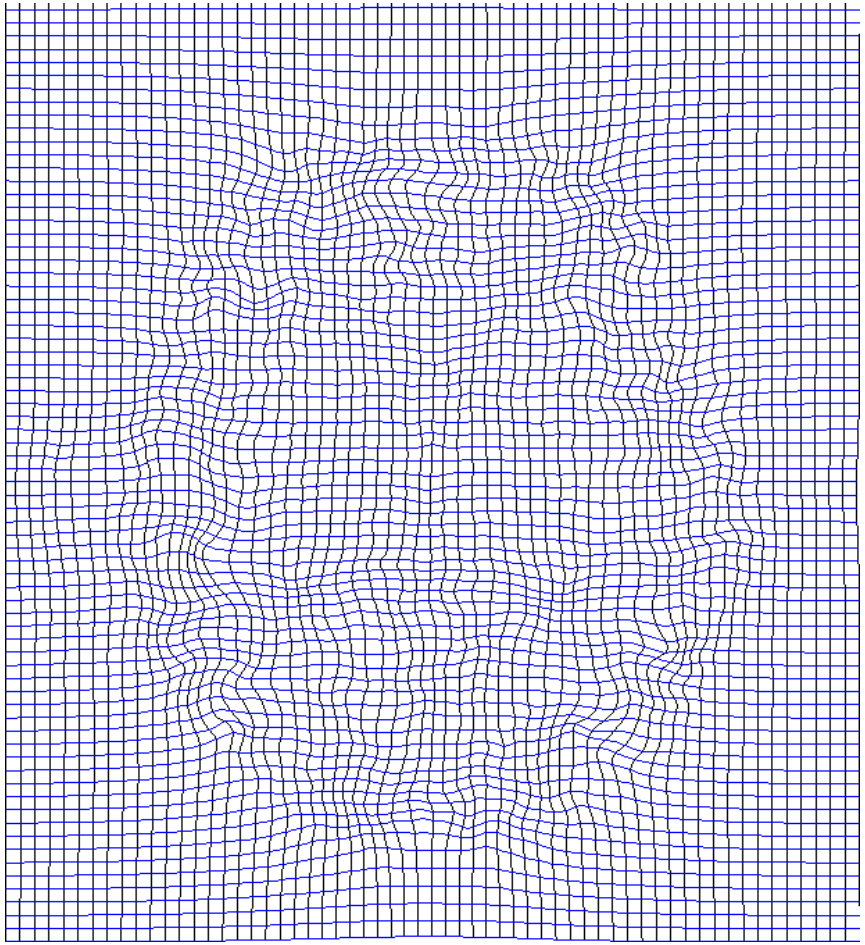


T1-Weighted MRI

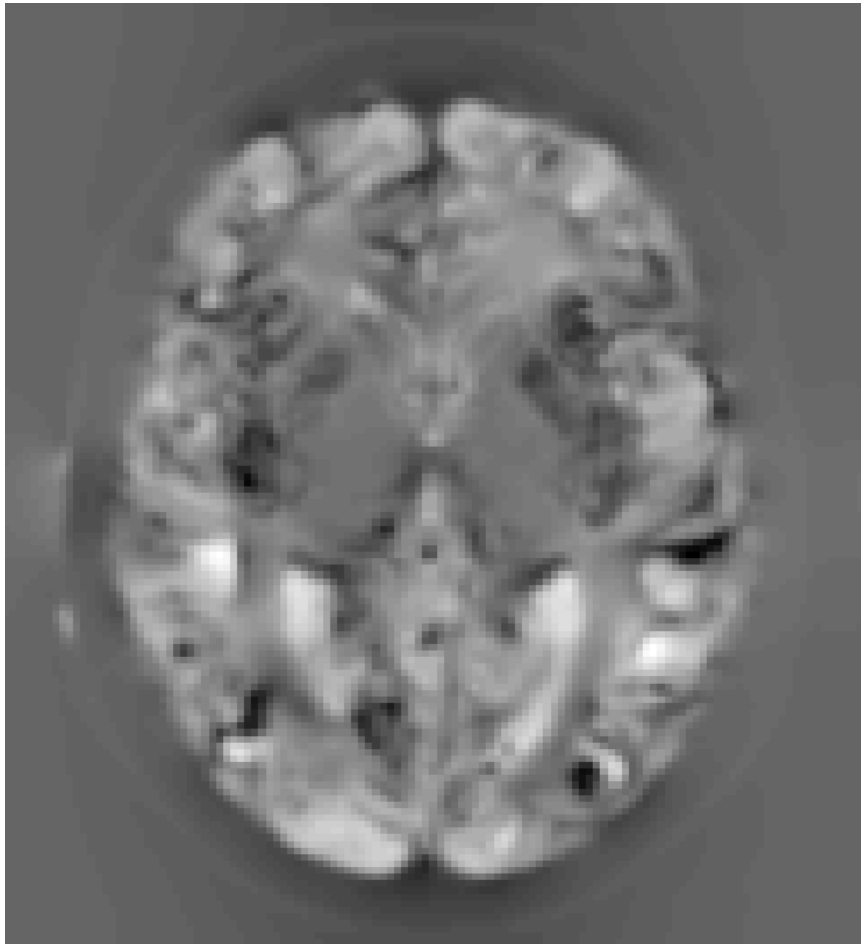
Grey Matter


Original
Warped
Template

“Modulation” – change of variables.



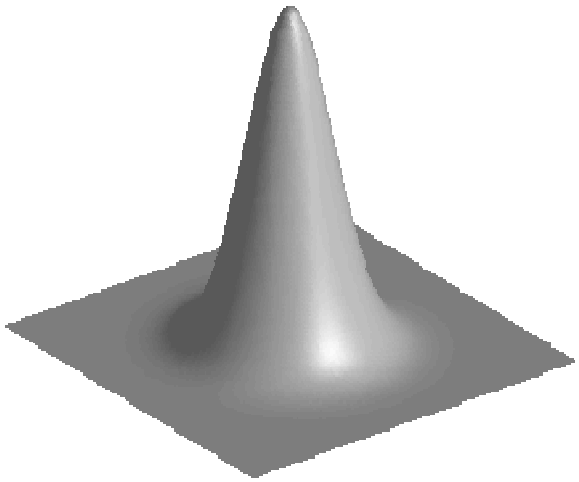
Deformation Field



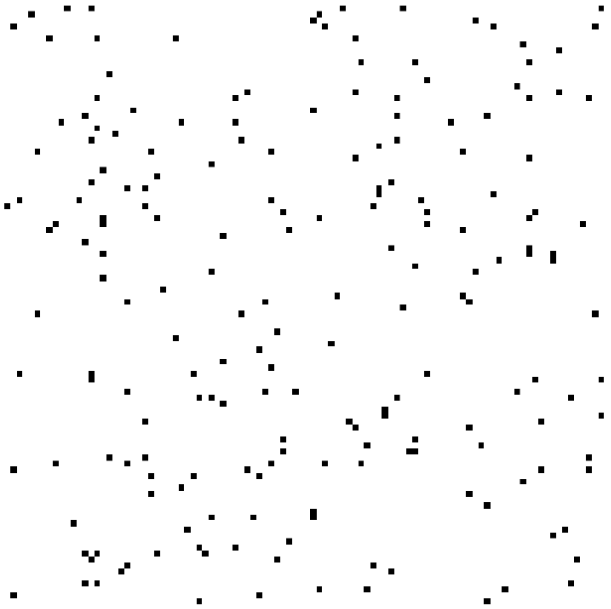
Jacobians determinants
Encode relative volumes.

Smoothing

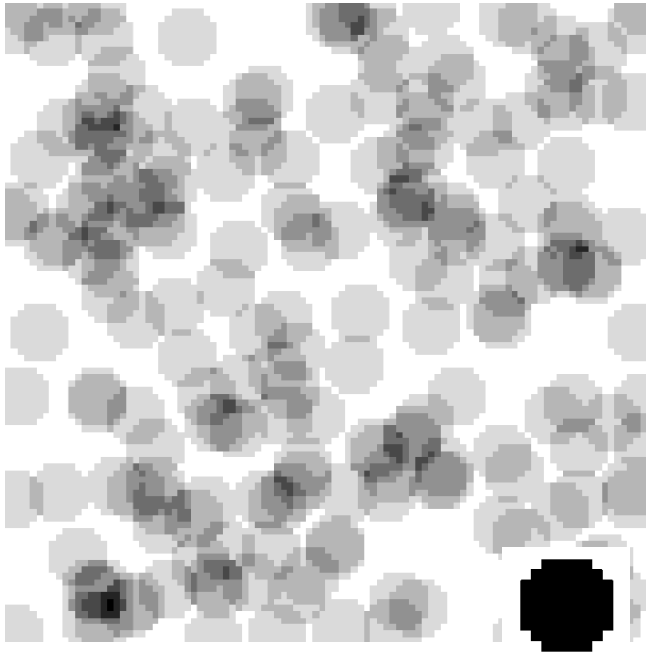
Each voxel after smoothing effectively becomes the result of applying a weighted region of interest (ROI).



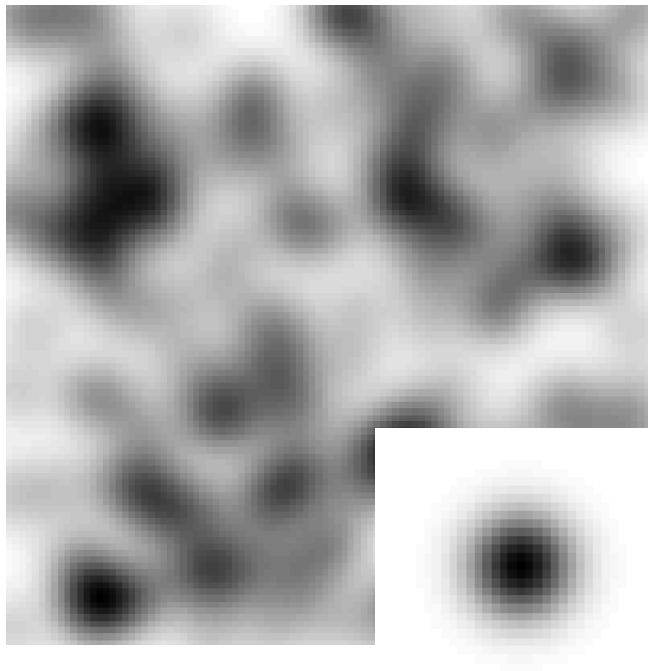
Before convolution



Convolved with a circle

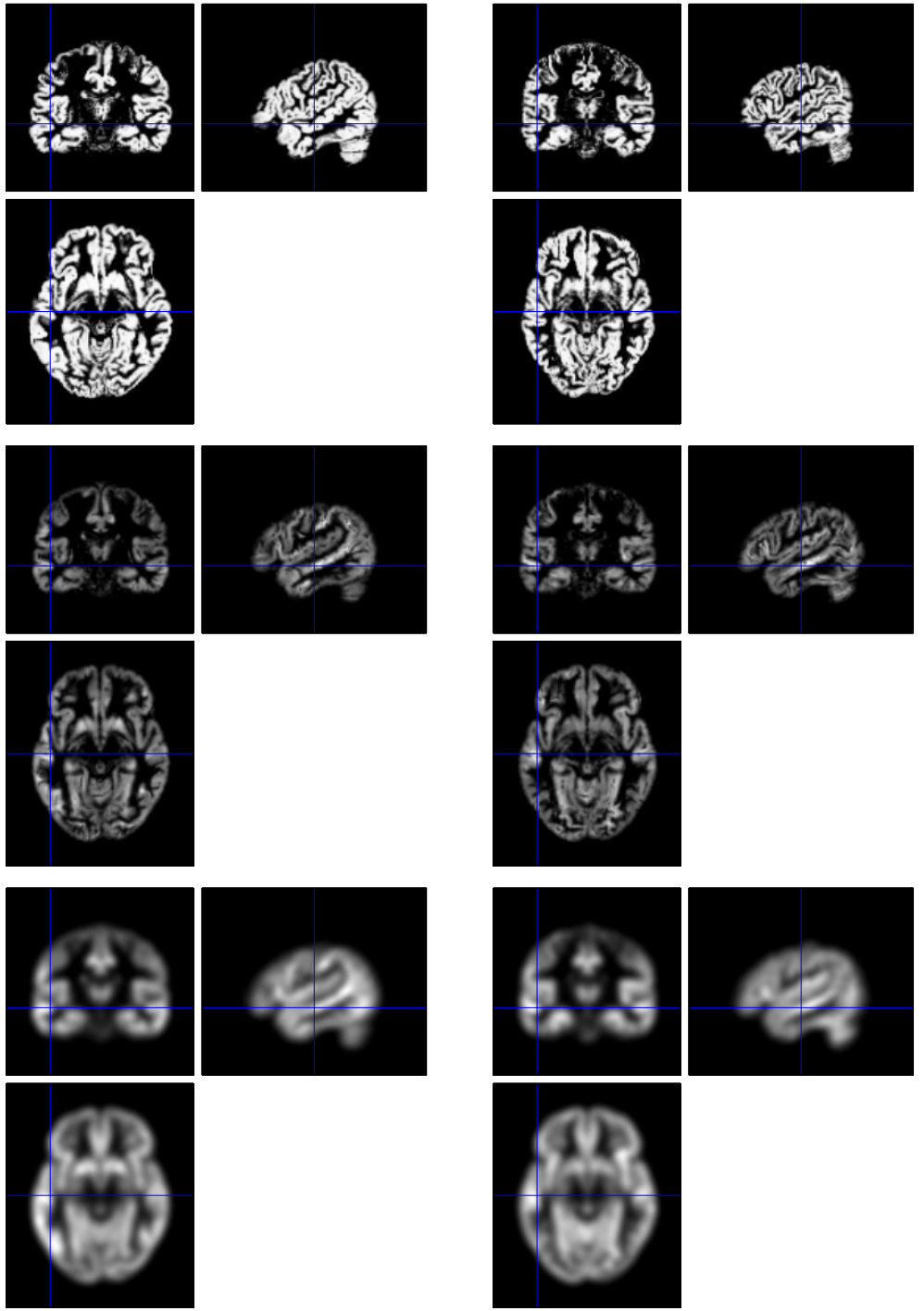


Convolved with a Gaussian

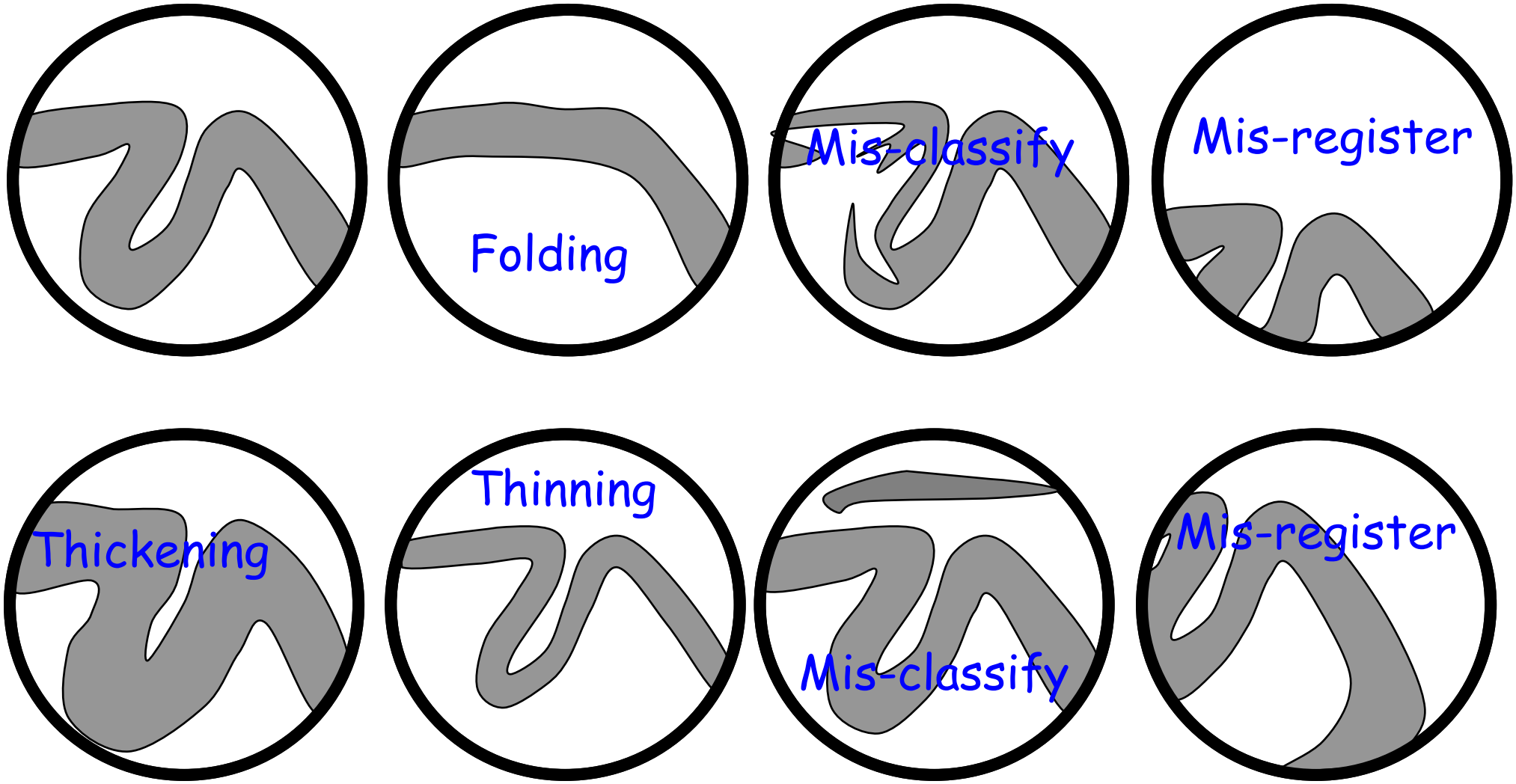


VBM Pre-processing in SPM12

- 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.

Overview

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- **Diffeomorphic Registration**
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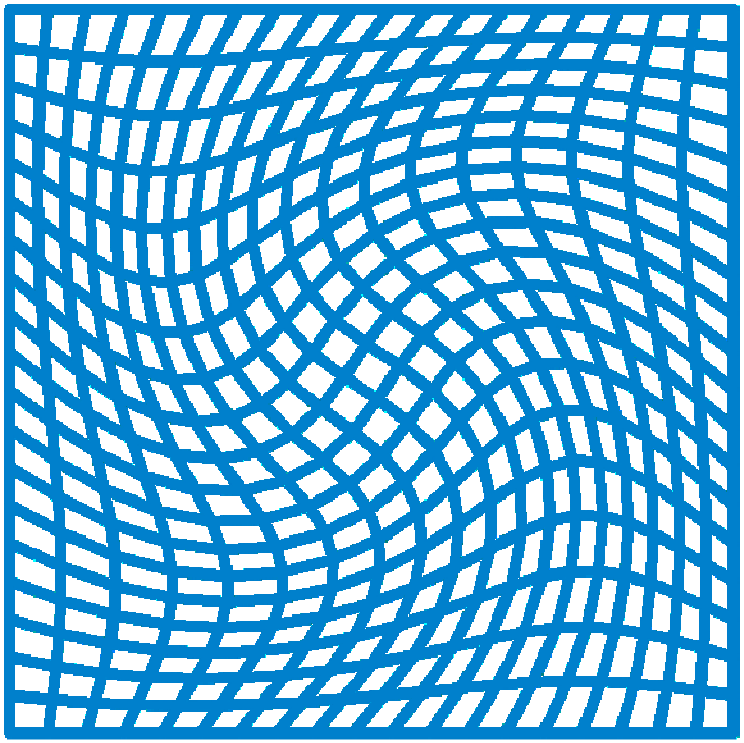
- Multivariate Approaches
- Scalar Momentum
- Some Evaluations
- Longitudinal Registration

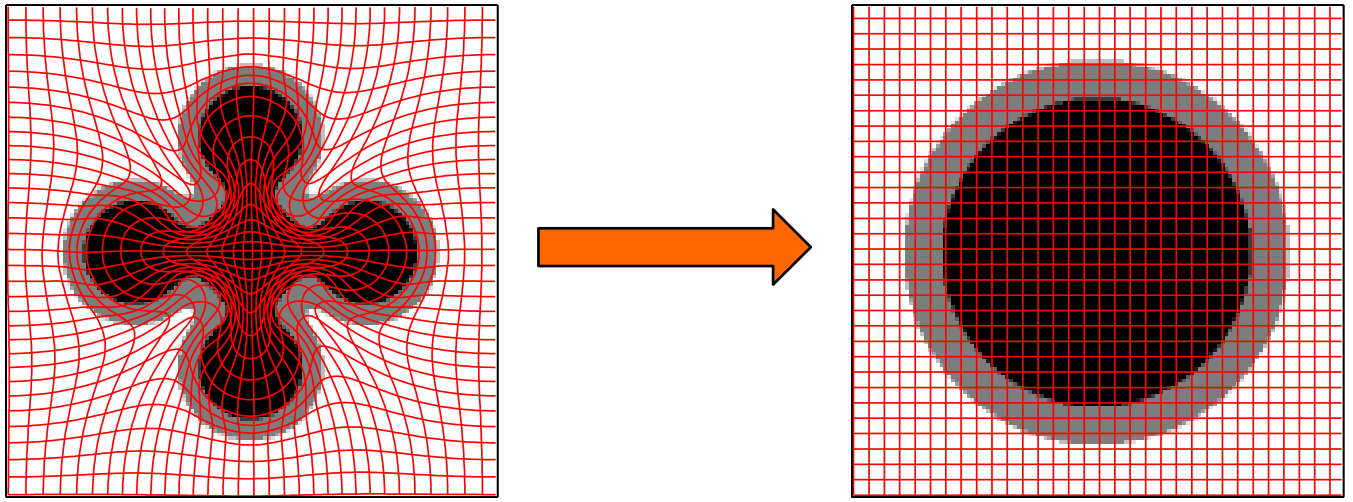
Diffeomorphism

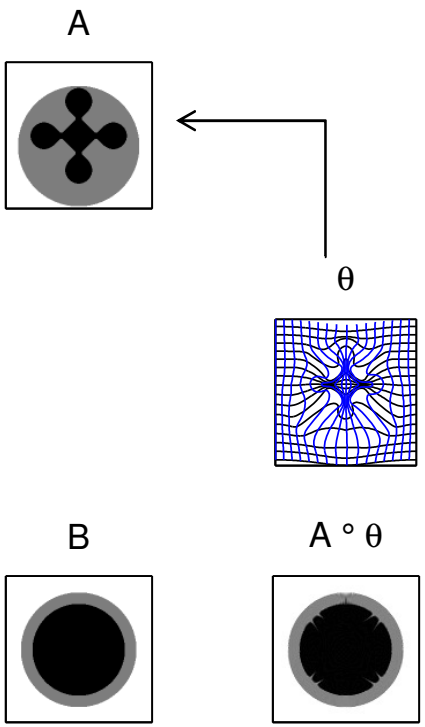
In mathematics, a diffeomorphism is an isomorphism in the category of smooth manifolds. It is an invertible function that maps one differentiable manifold to another, such that both the function and its inverse are smooth.

Wikipedia



Deformations





Composition

Small Deformation Approximation

The composition:

$$\vartheta \circ \varphi$$

Would be approximated with:

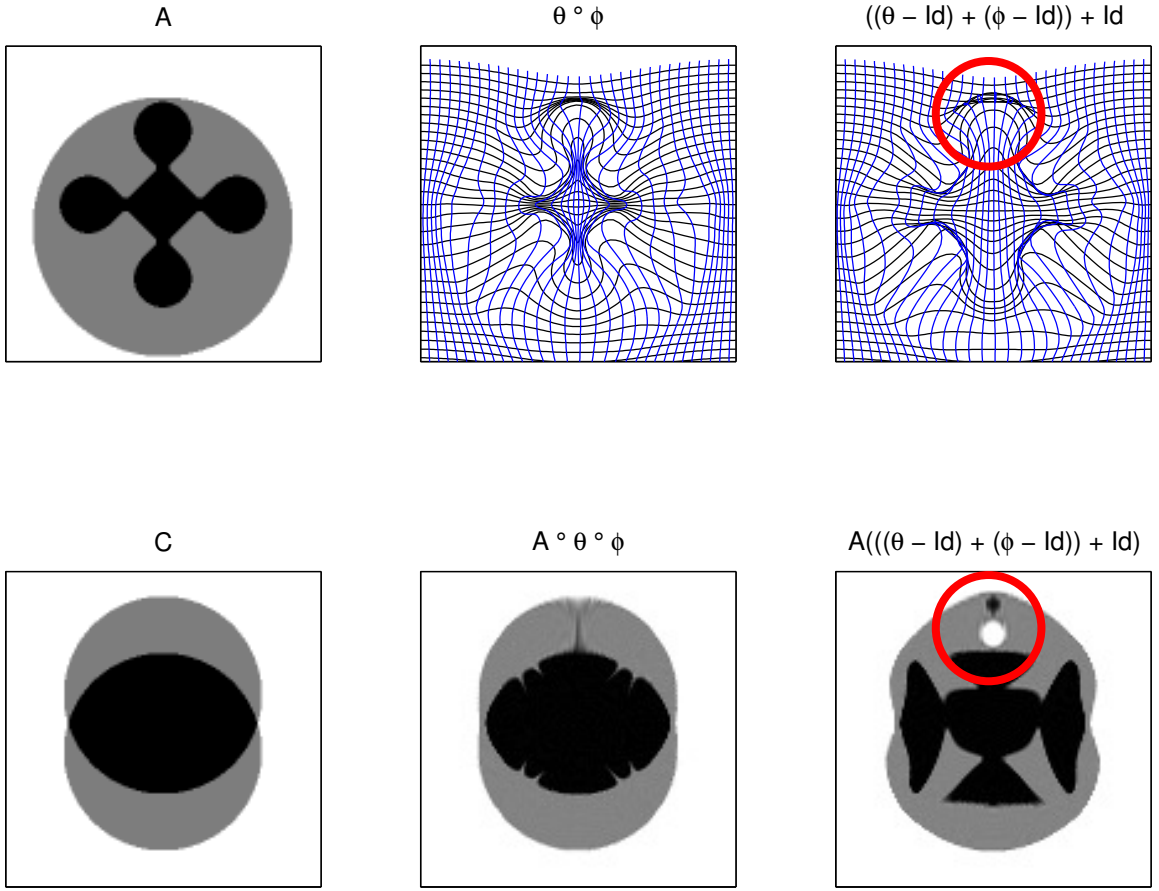
$$Id + ((\vartheta - Id) + (\varphi - Id))$$

The inversion:

$$\varphi^{-1}$$

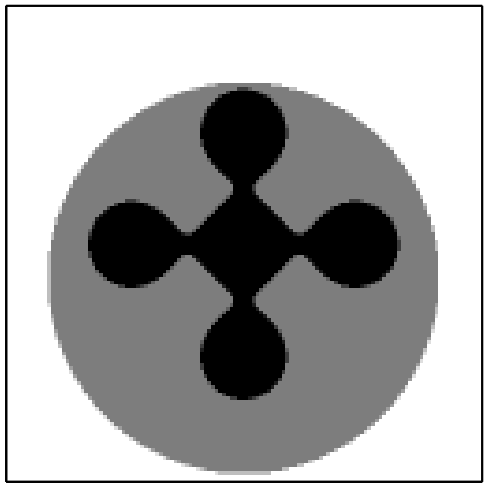
Would be approximated with:

$$Id - (\varphi - Id)$$

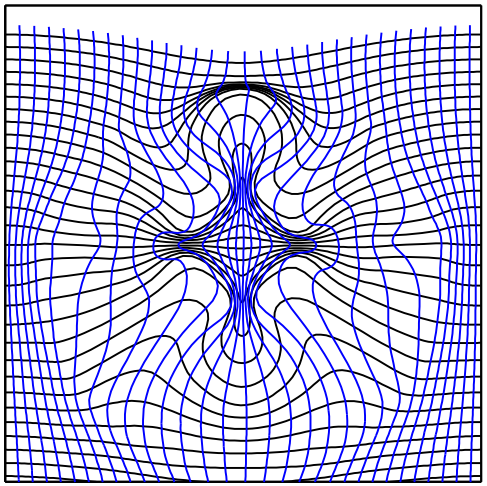


Not good approximations for large deformations.

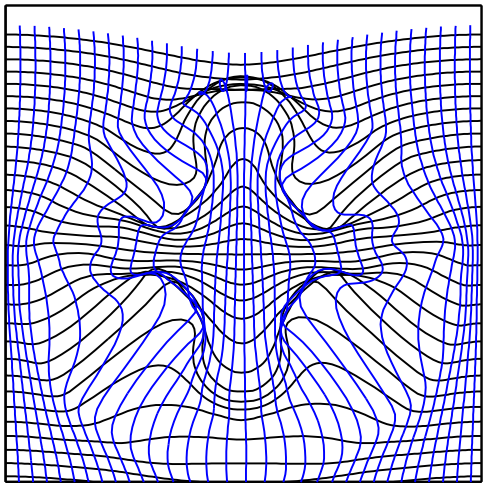
A



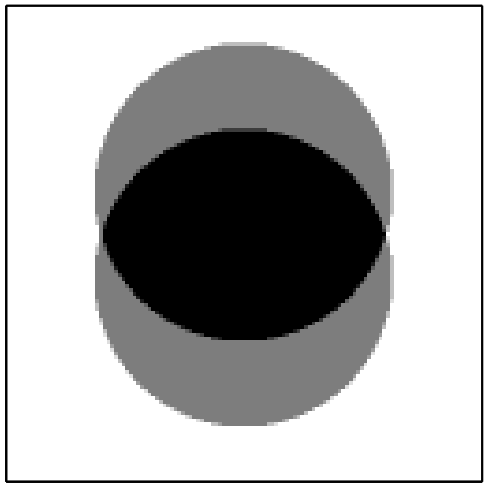
$\theta \circ \phi$



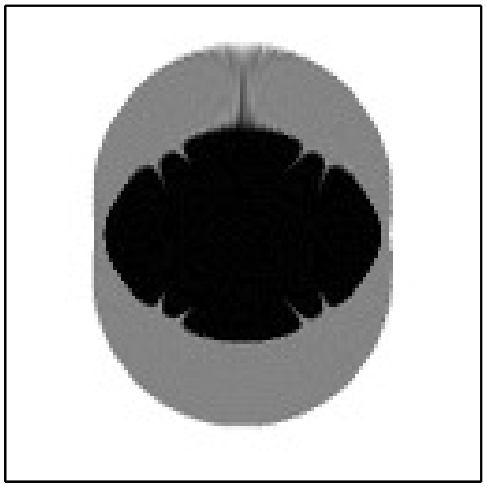
$((\theta - \mathrm{Id}) + (\phi - \mathrm{Id})) + \mathrm{Id}$



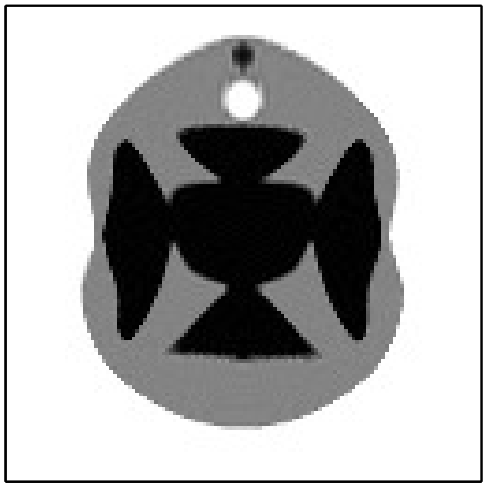
C



$A \circ \theta \circ \phi$



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



Diffeomorphic Image Registration

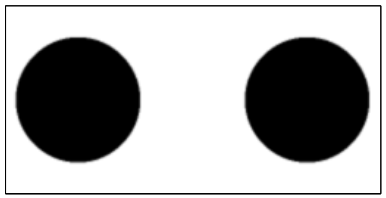
- Minimises two terms:

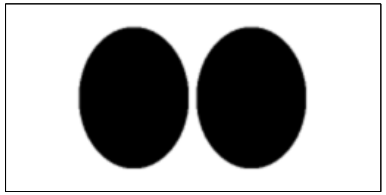
1. A measure of distance between images
2. A measure of the amount of distortion.

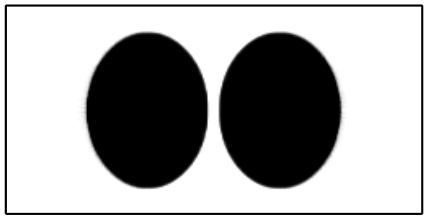
Because we can not simply add displacement fields, large deformations are generated by composing many small deformations.

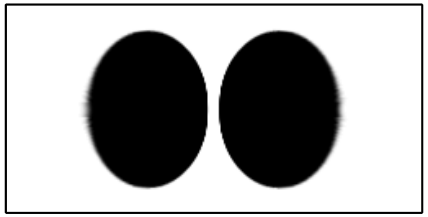
The amount of distortion is computed by summing up the distortion measures from the small displacements.

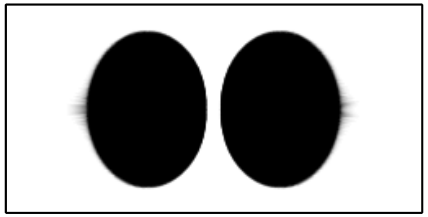
Effect of Different Distortion Measures

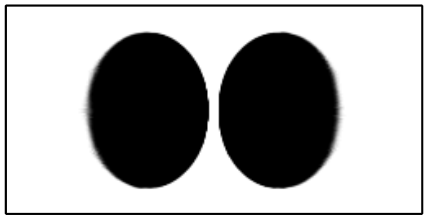


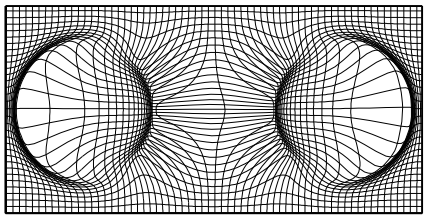


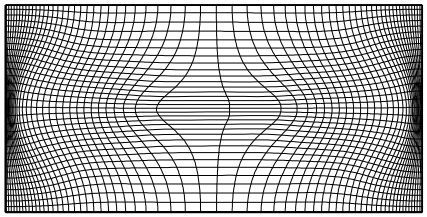


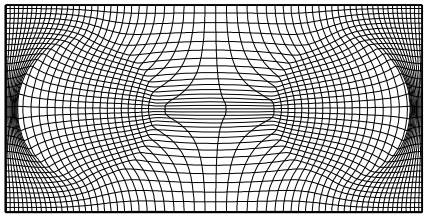


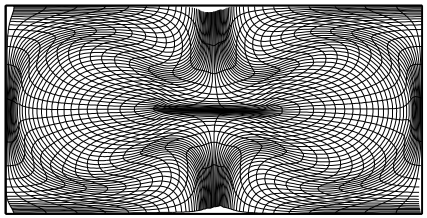


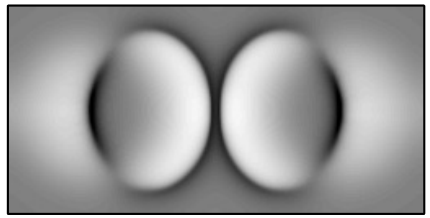


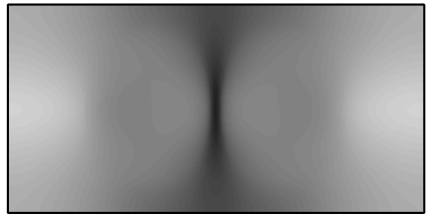


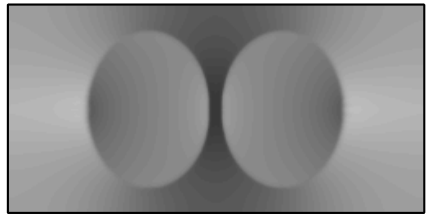












Two diffeomorphic approaches in SPM

Dartel.

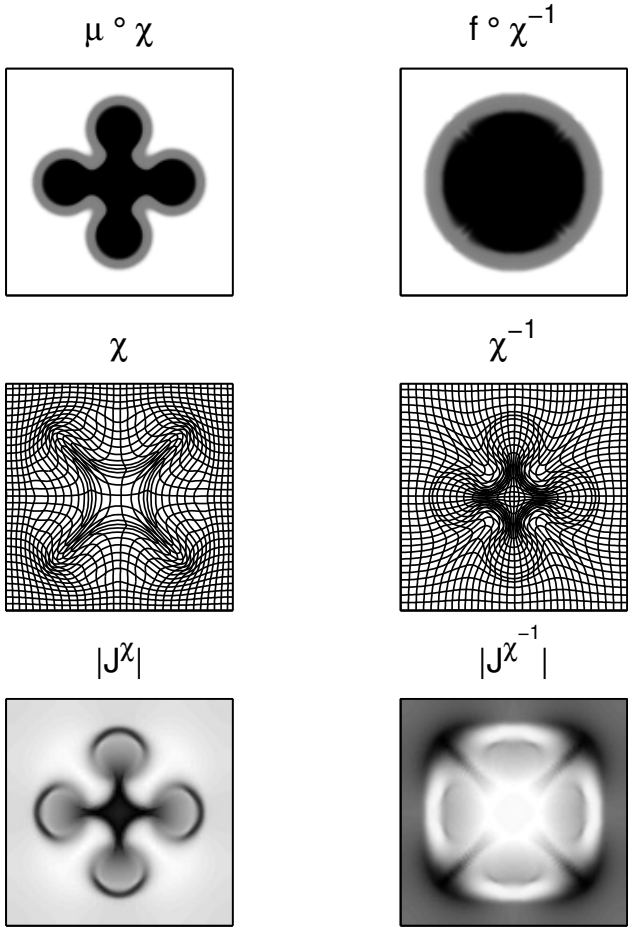
- Uses the same small deformation composed multiple times.
- Faster than Geodesic Shooting.
- Gives similar deformations to Geodesic Shooting.
- Currently more additional utilities.

Geodesic Shooting

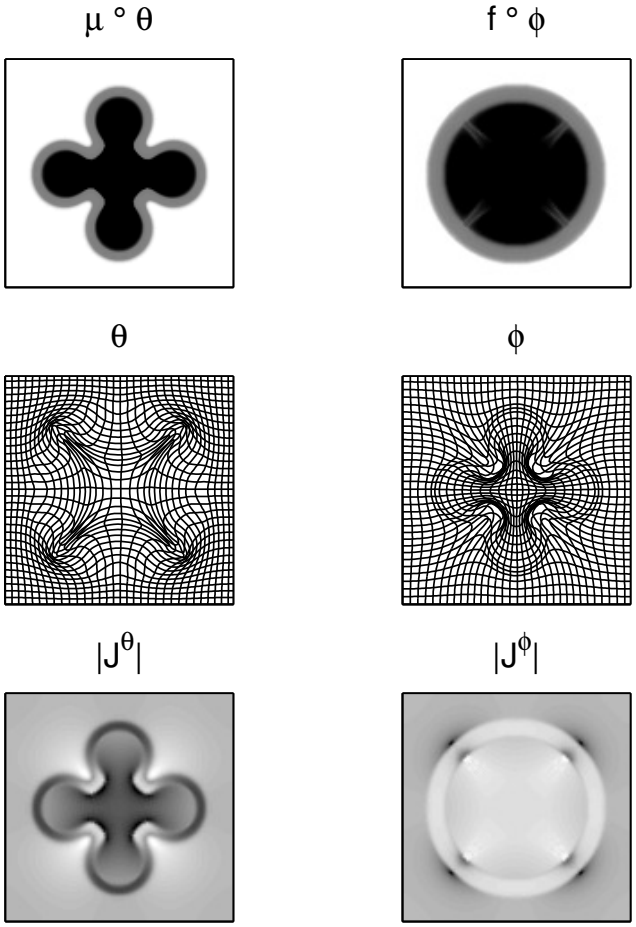
- Uses the optimal series of small deformations, which are composed together.
- More mathematically correct than Dartel.
- Gives nicer maps of volume change than Dartel.
- Likely to replace Dartel in future.

Dartel & GS Compared

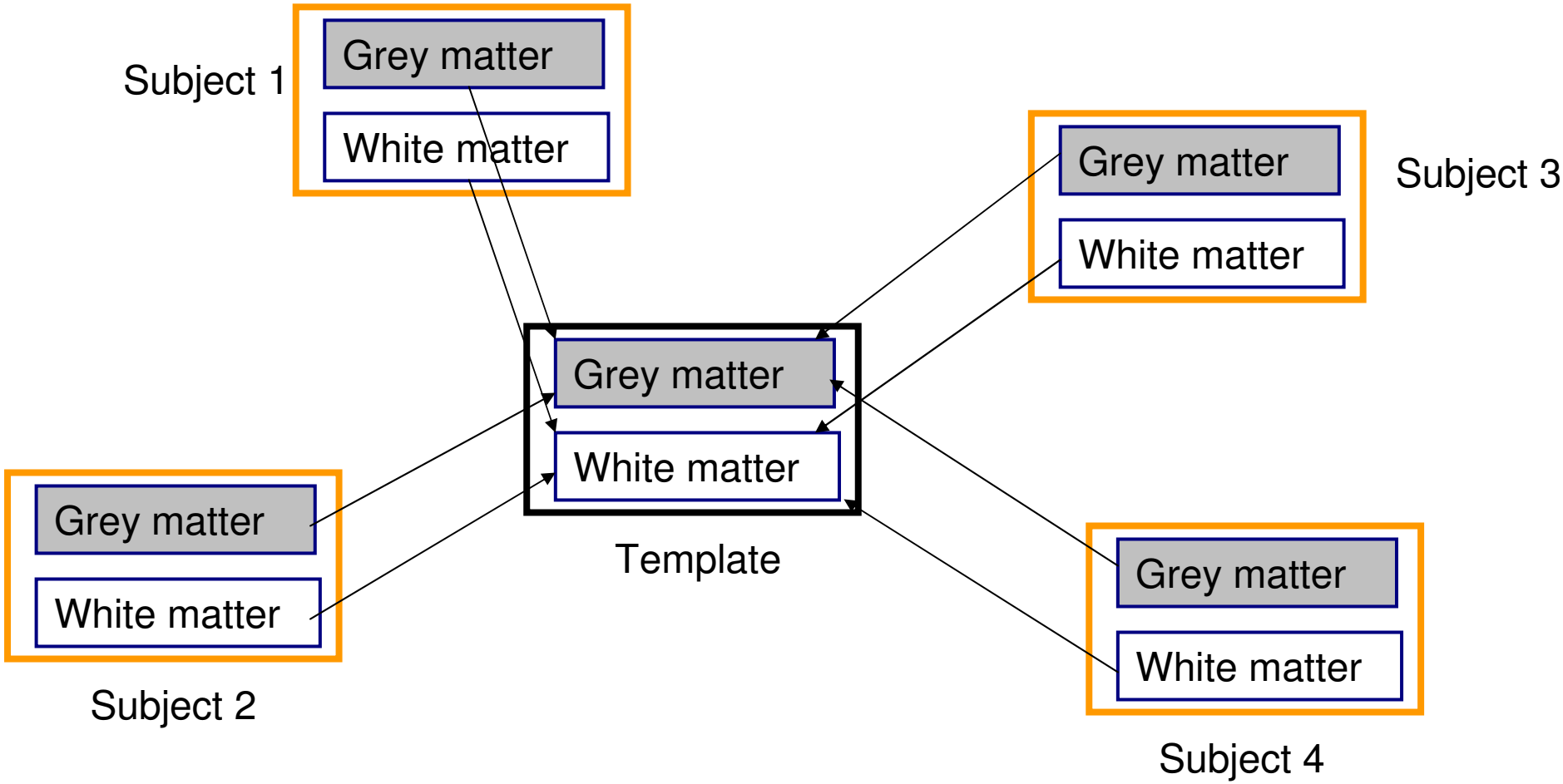
Dartel



Geodesic Shooting



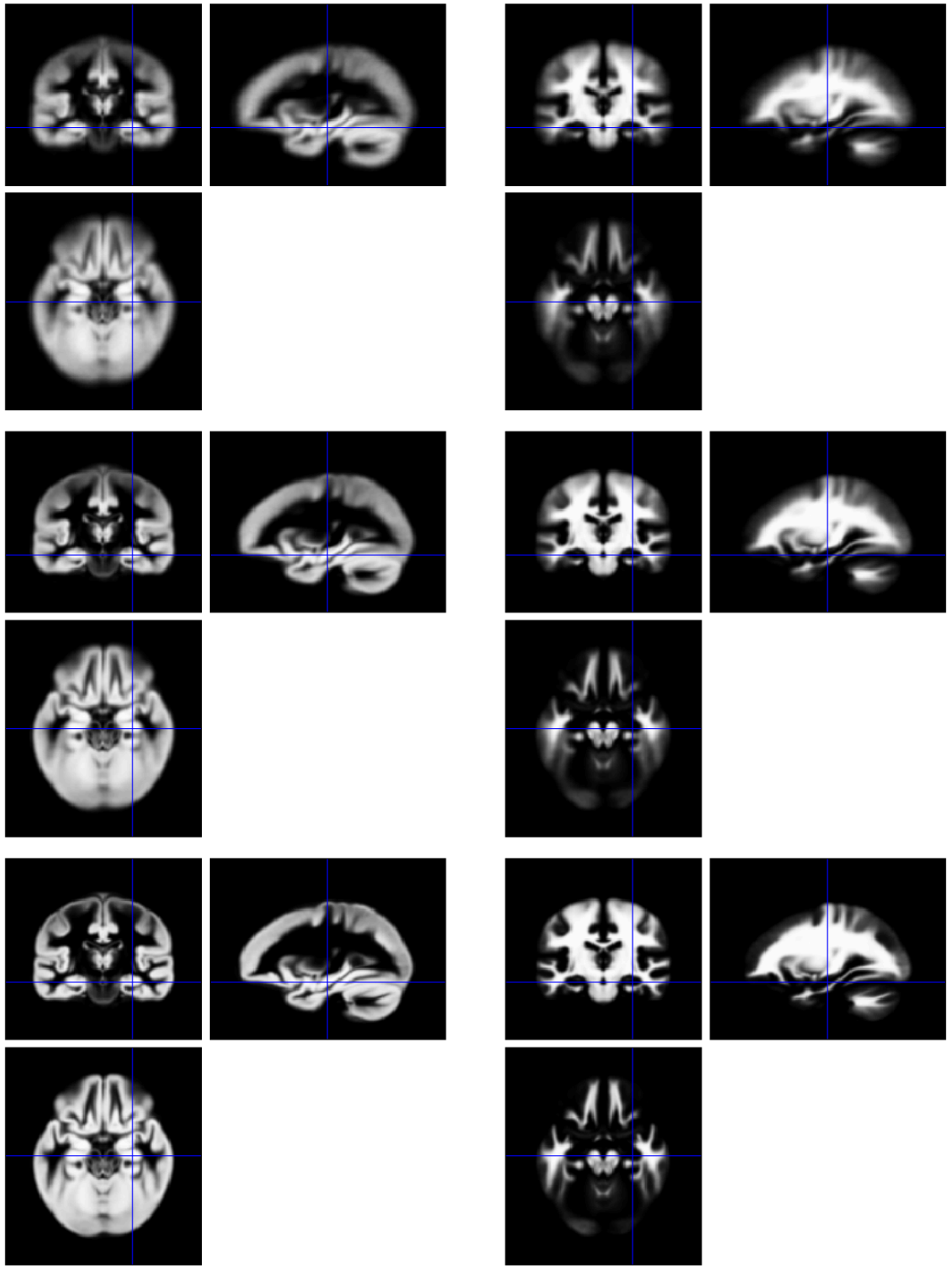
Simultaneous registration of GM to GM and WM to WM



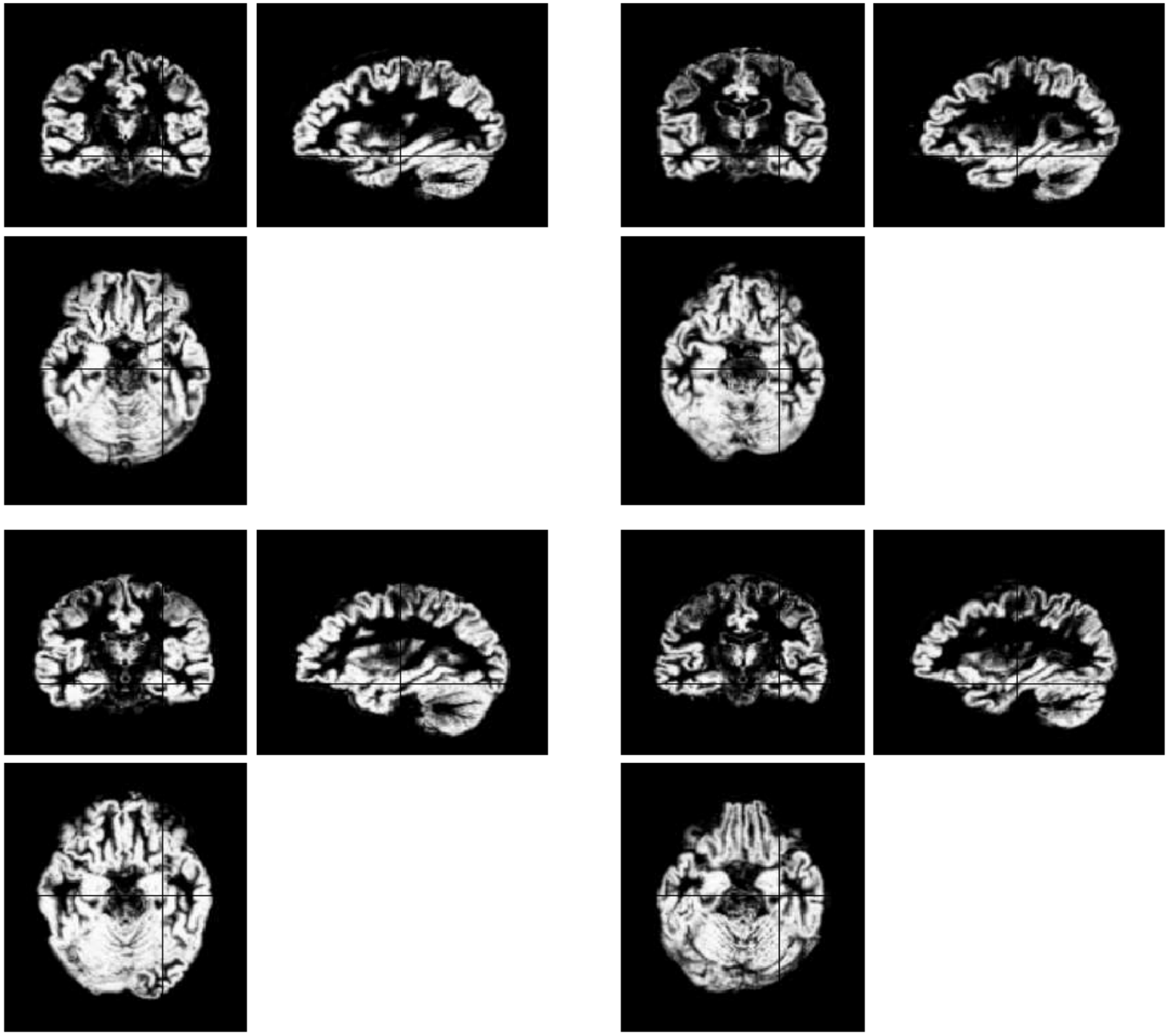
Template

Iteratively generated from all subjects in study

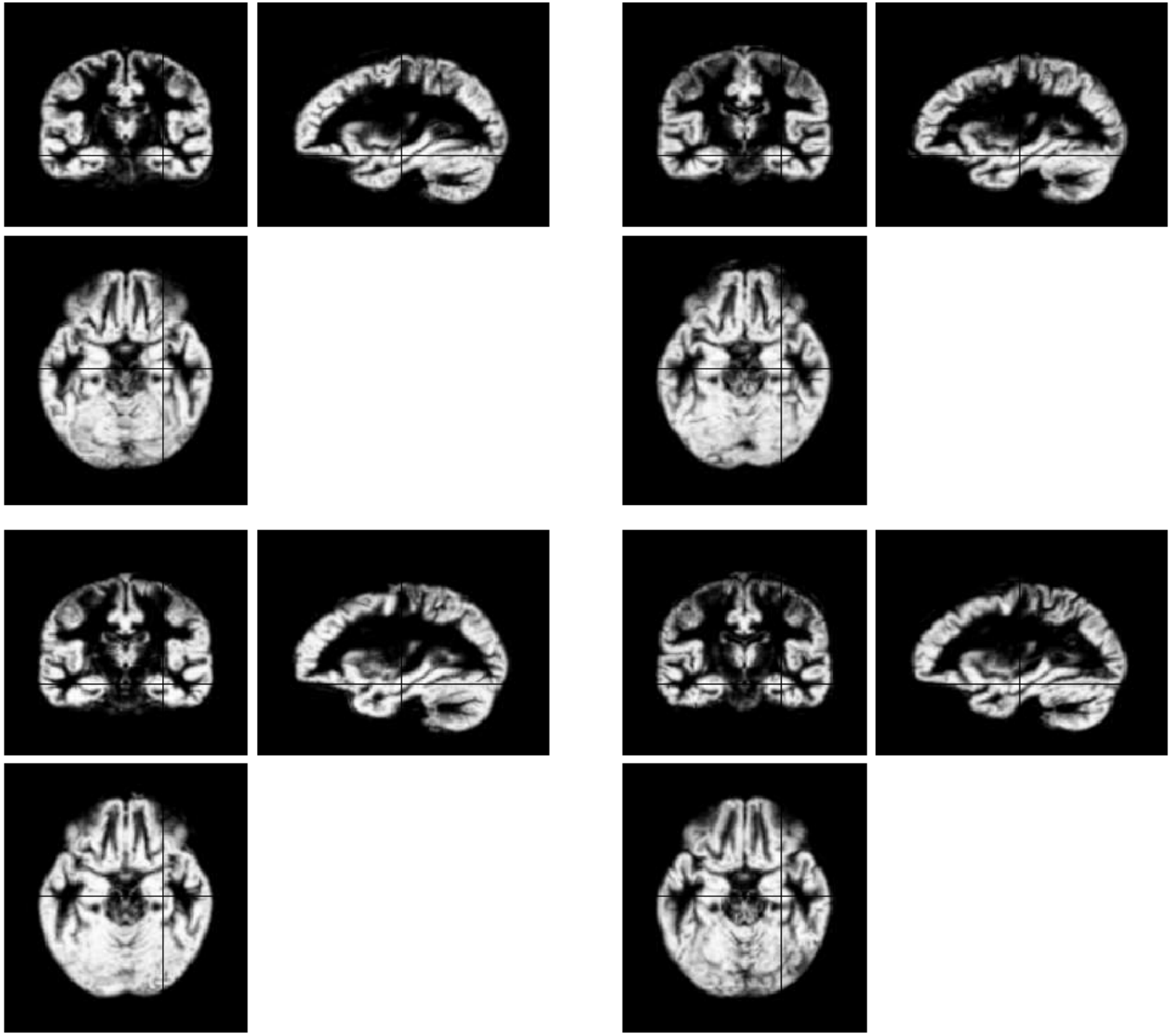
Begin with rigidly aligned tissue probability maps

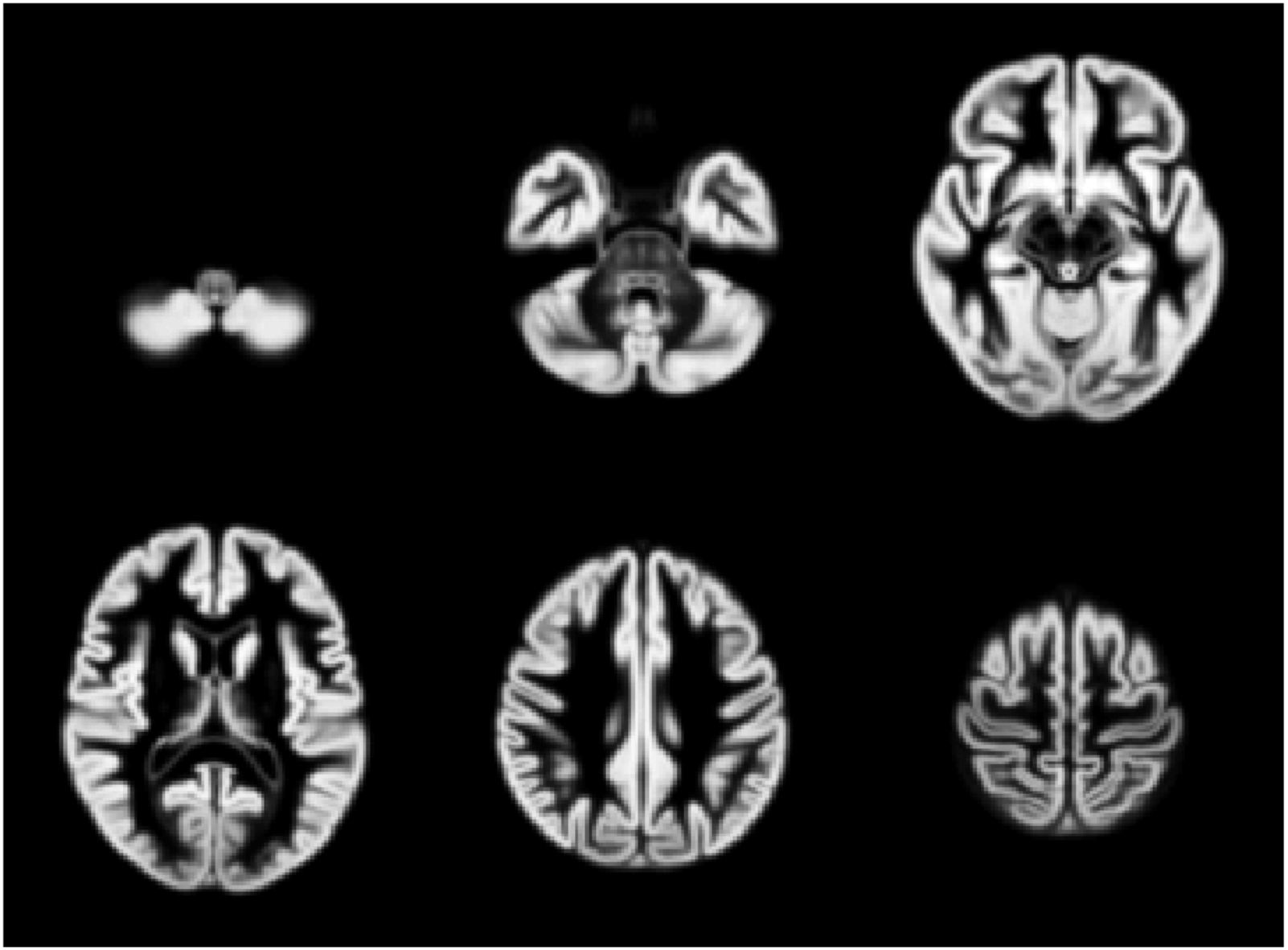


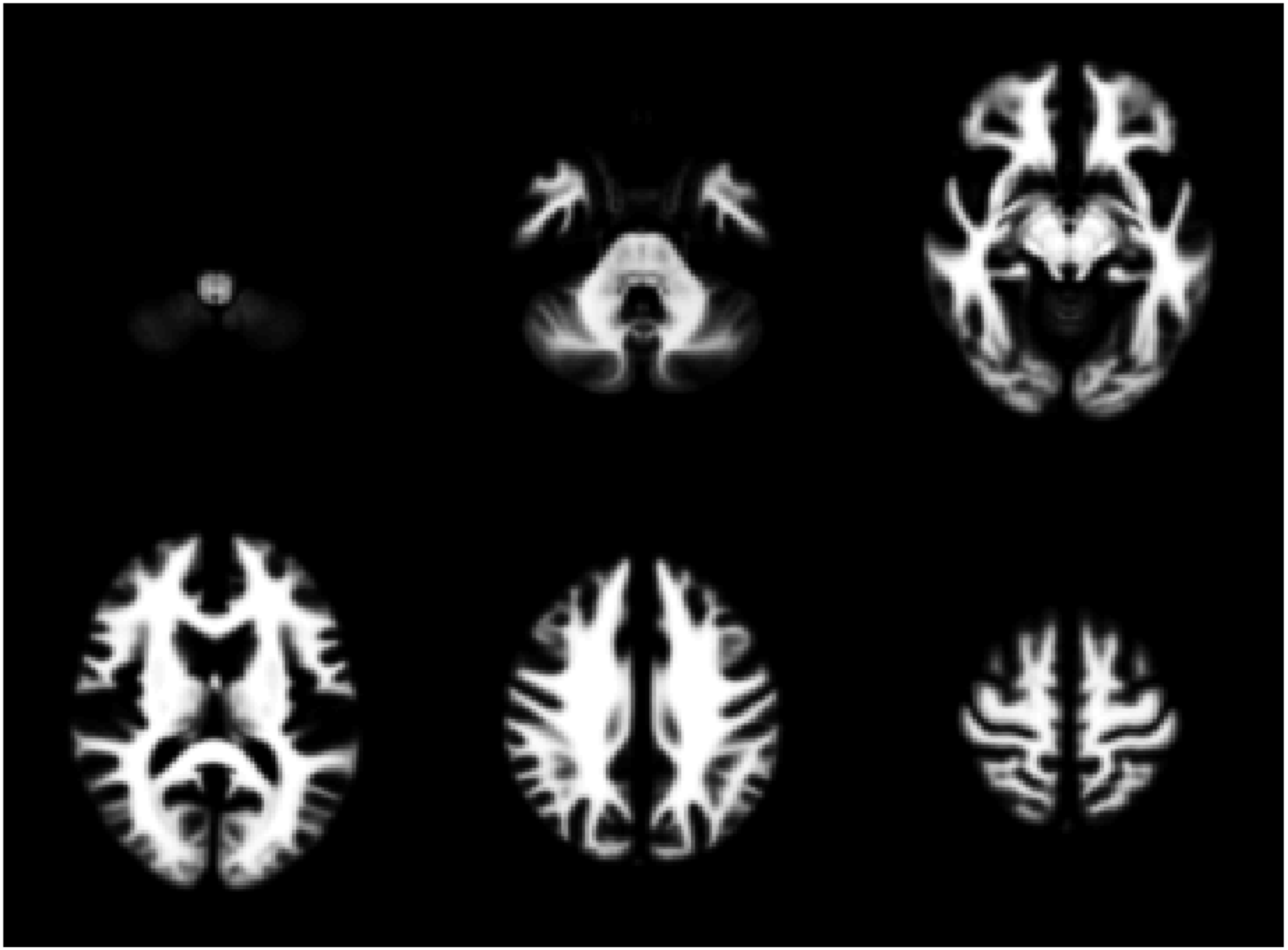
Initial
GM images

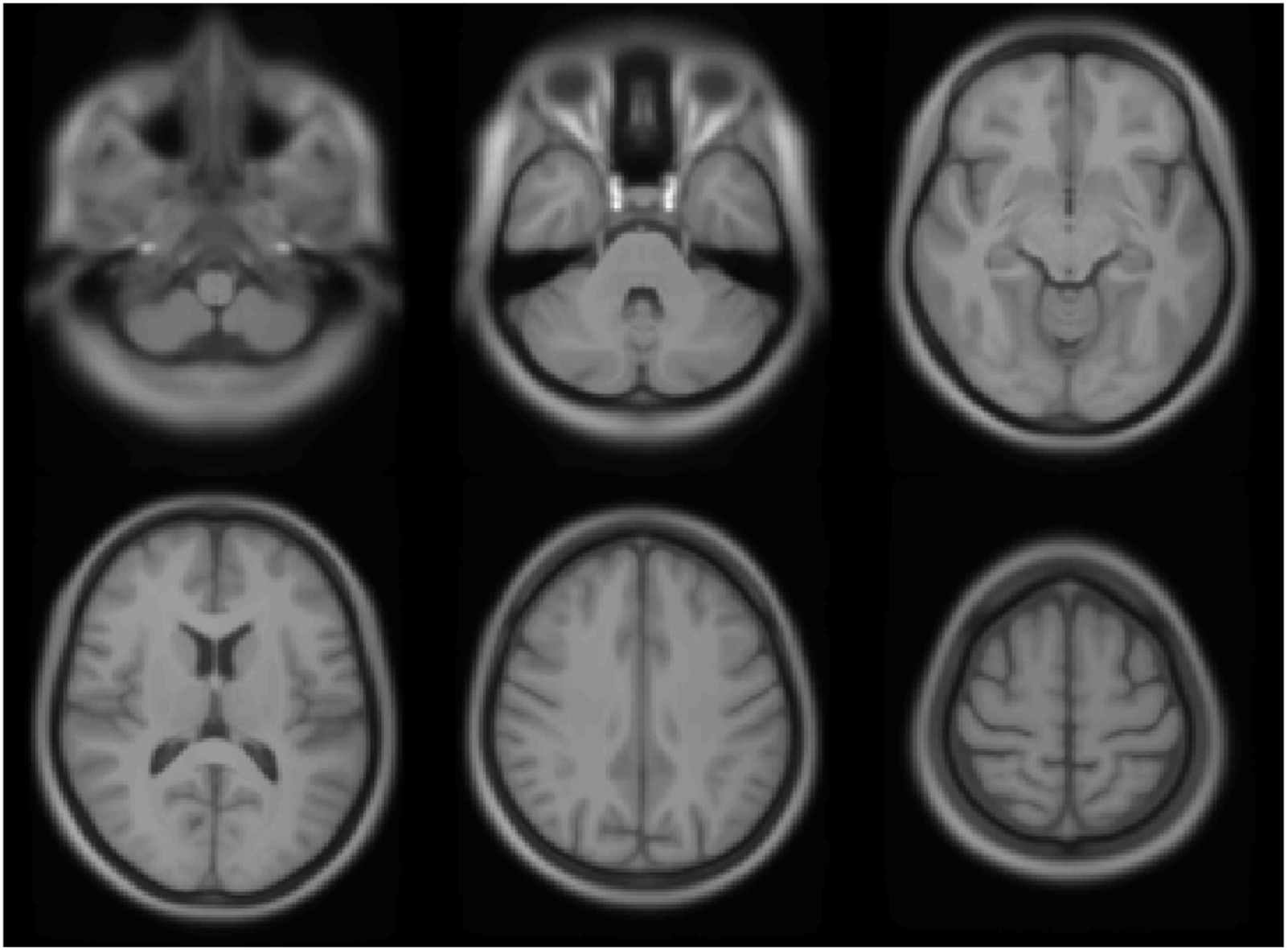


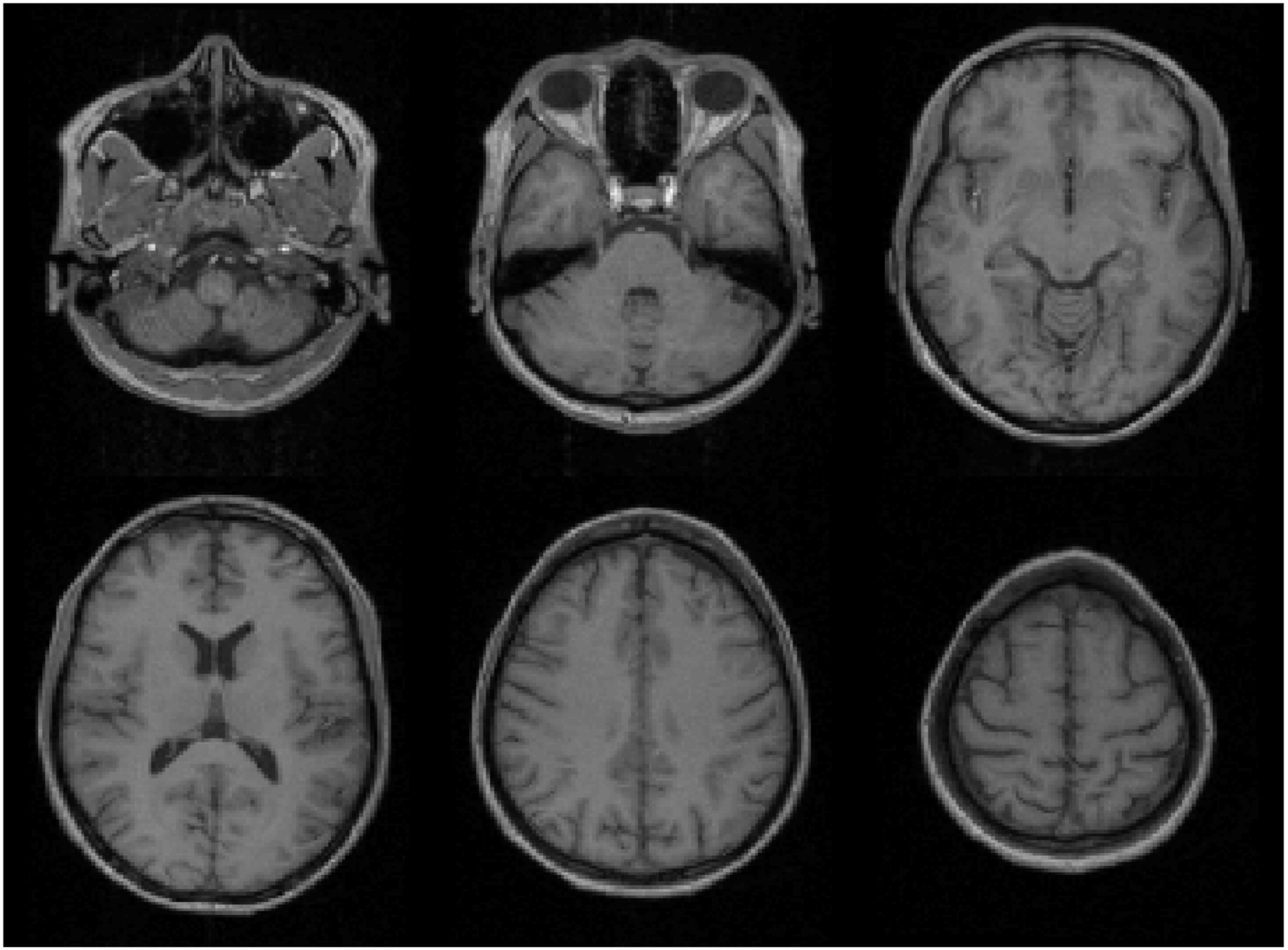
Warped
GM images

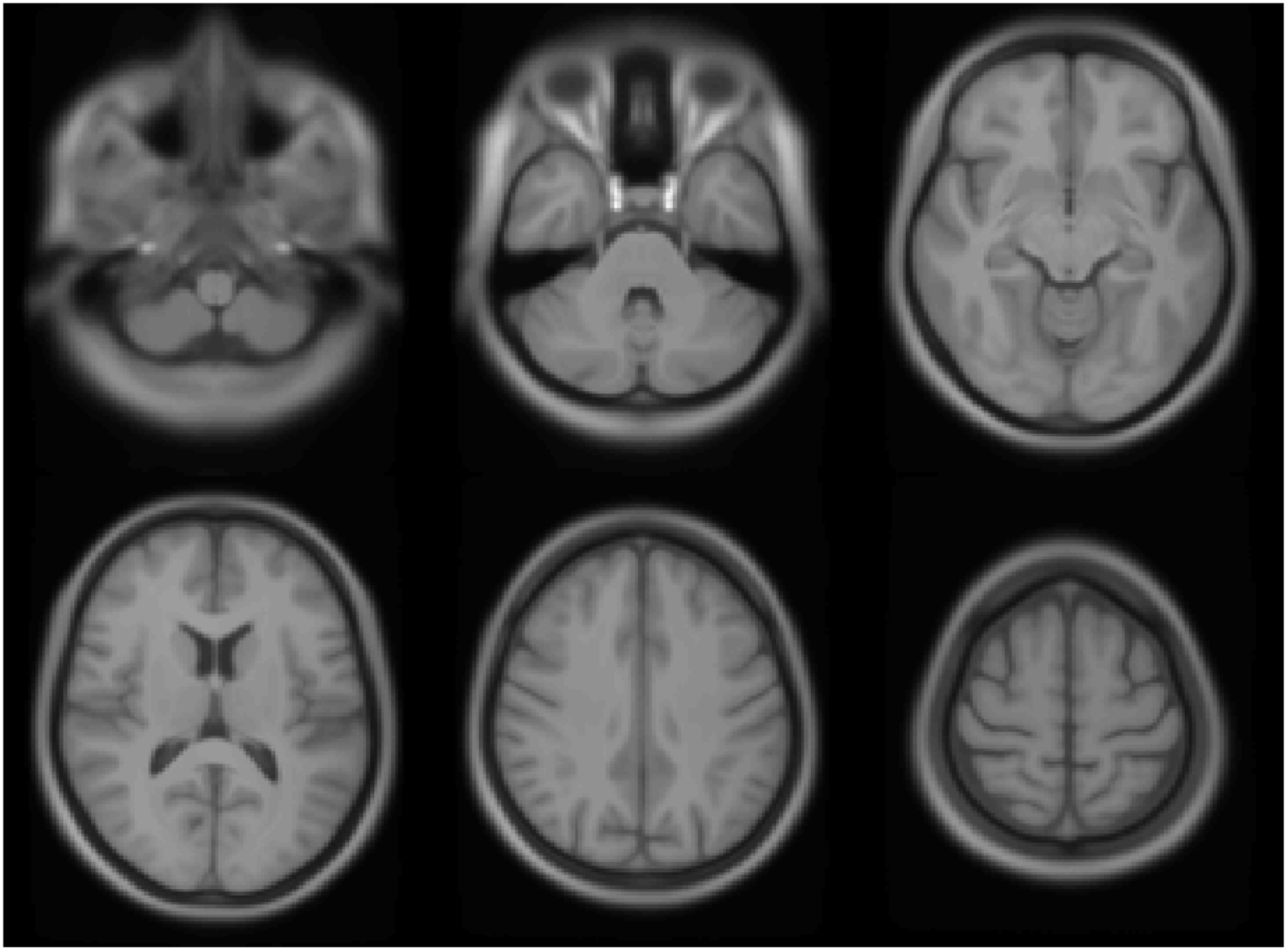


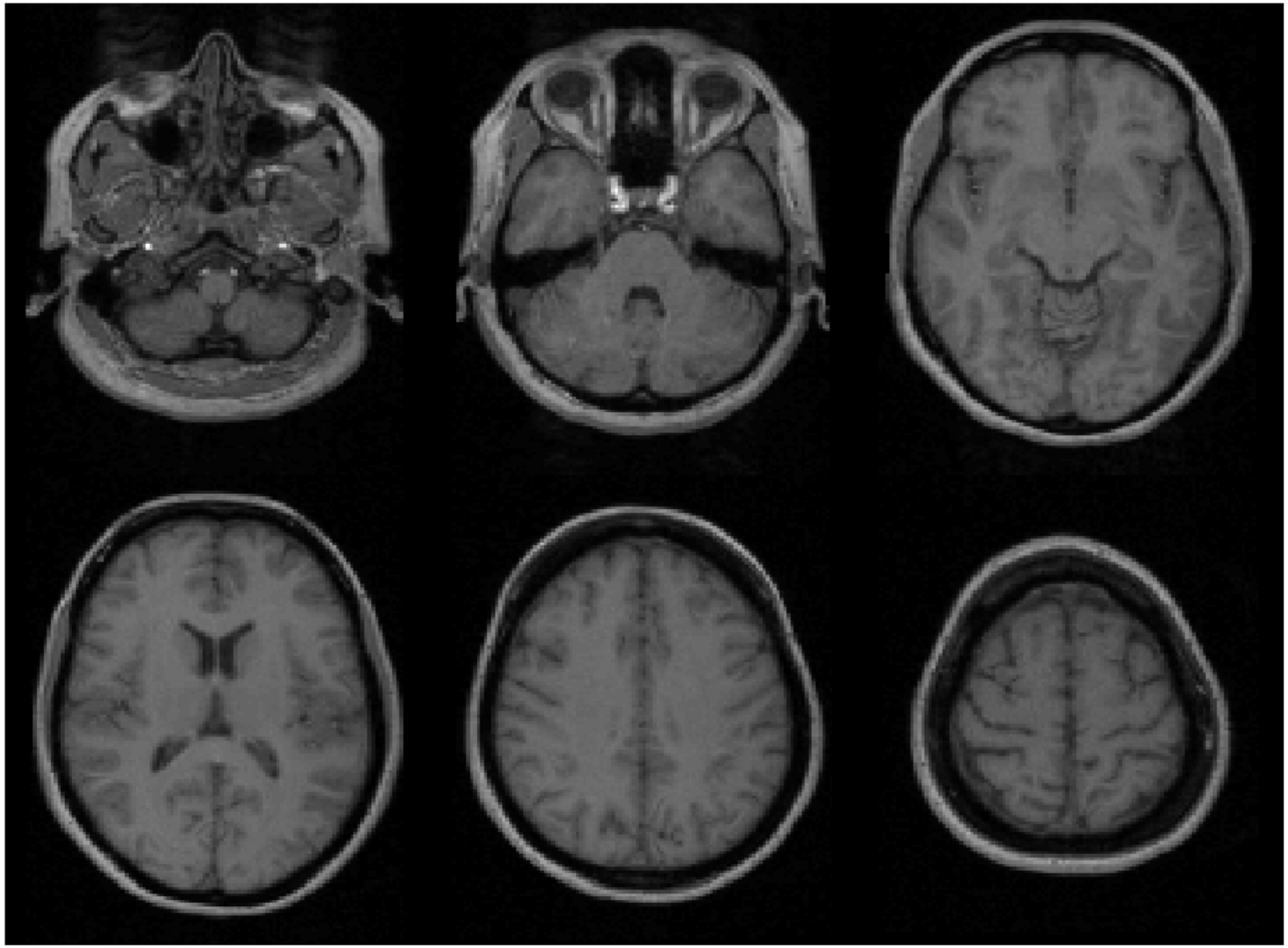


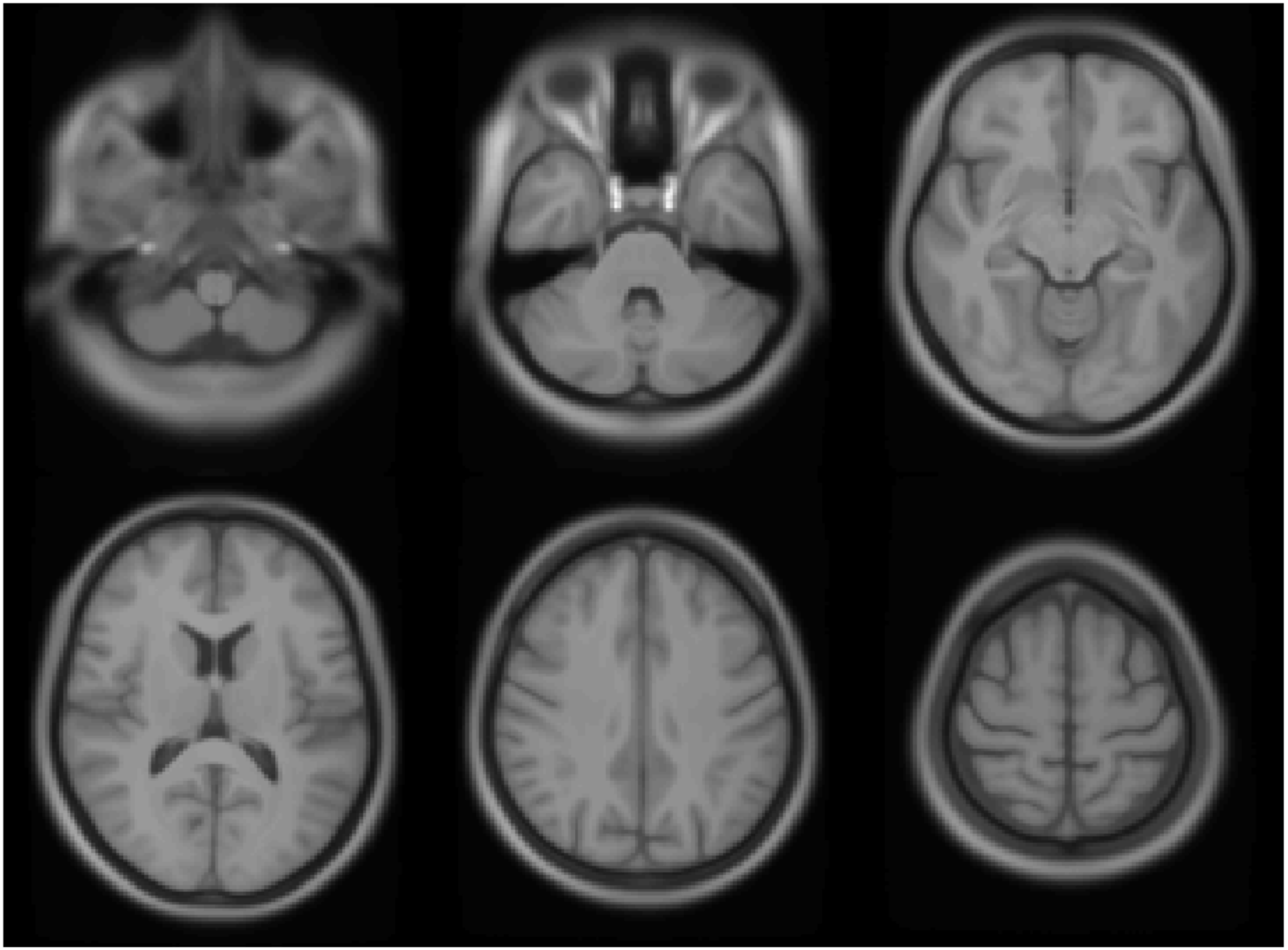


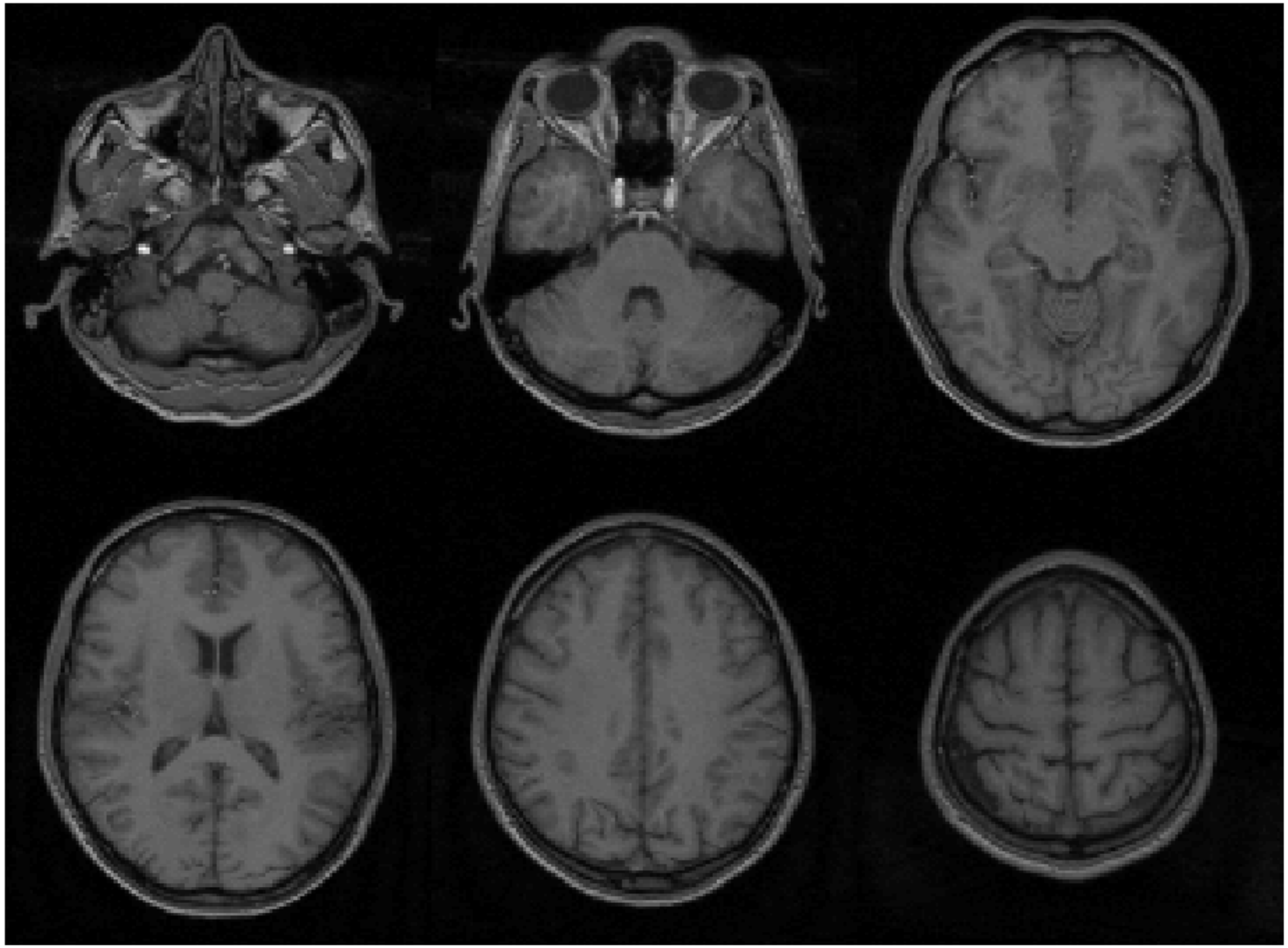


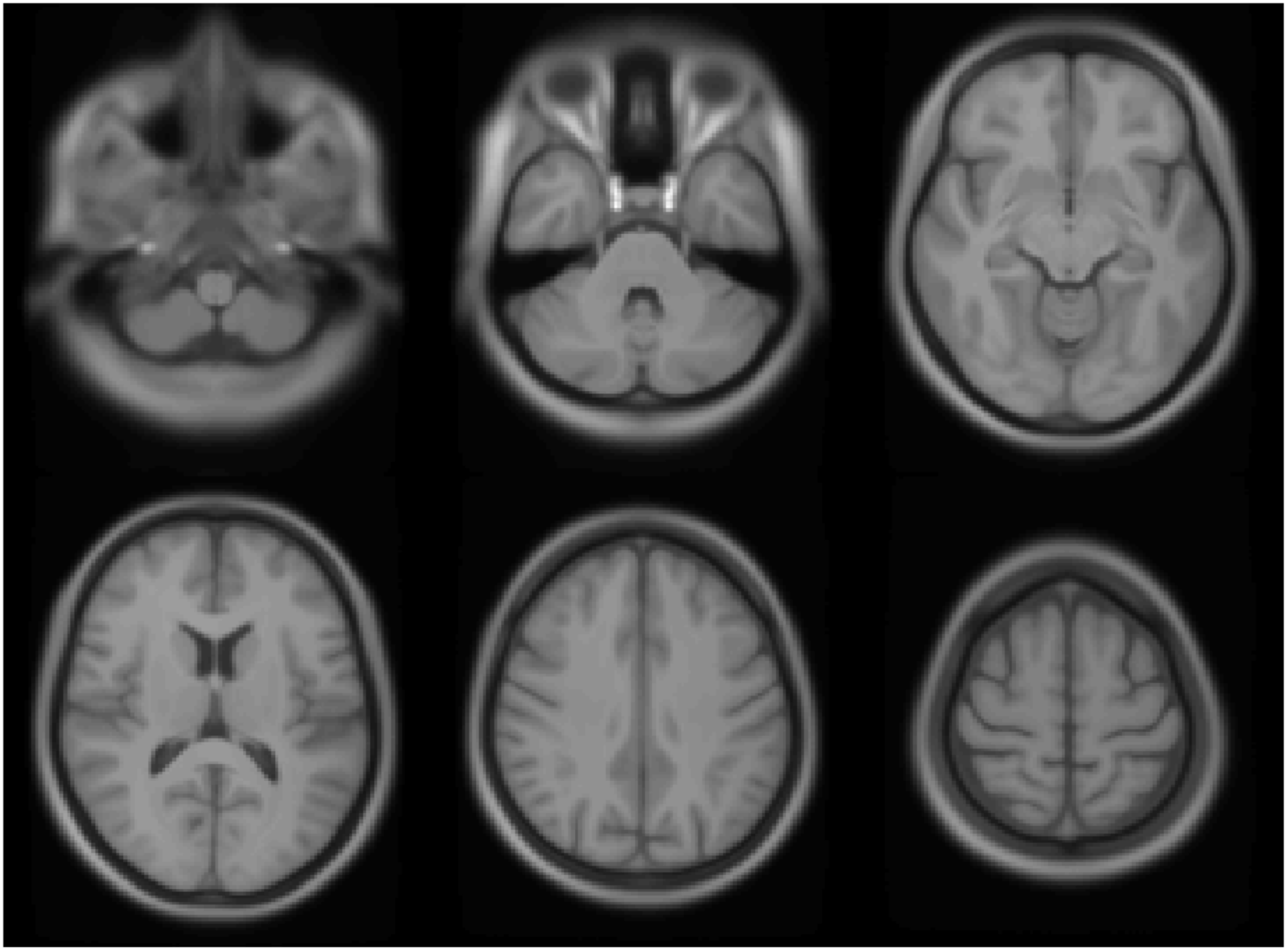


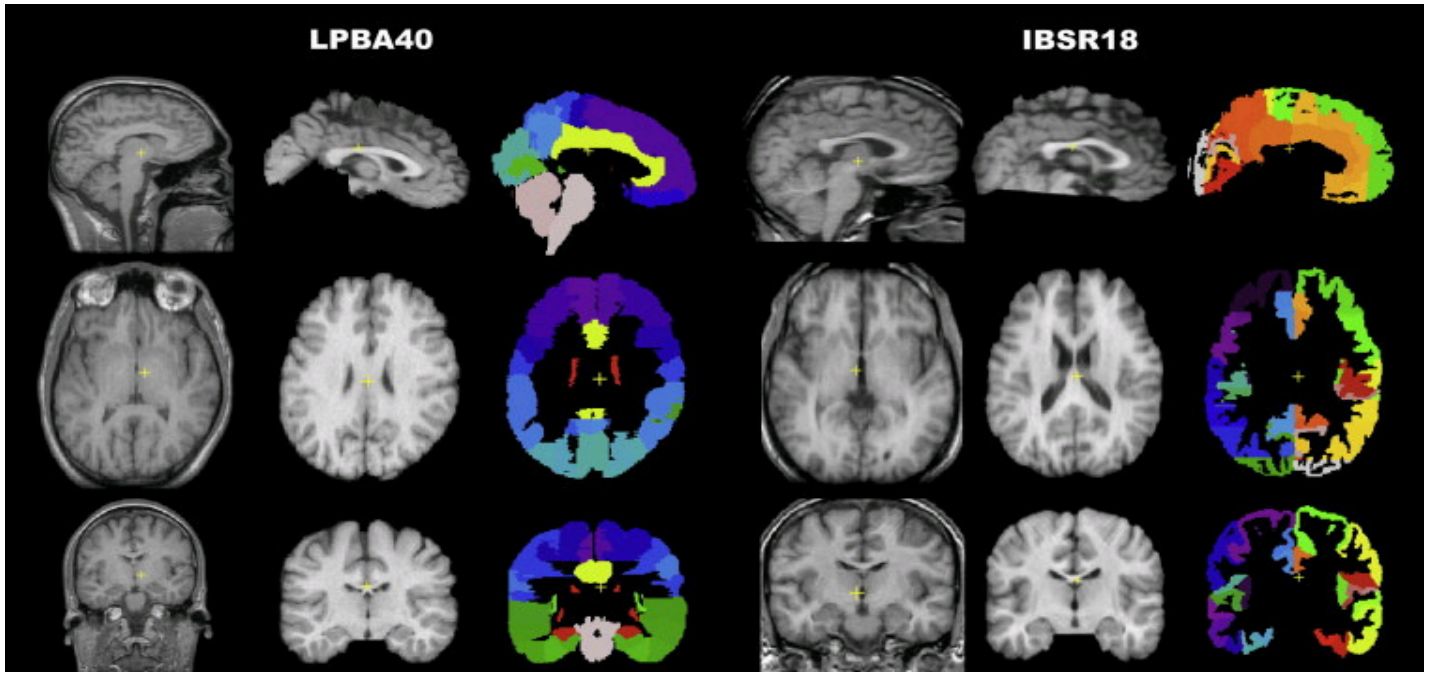




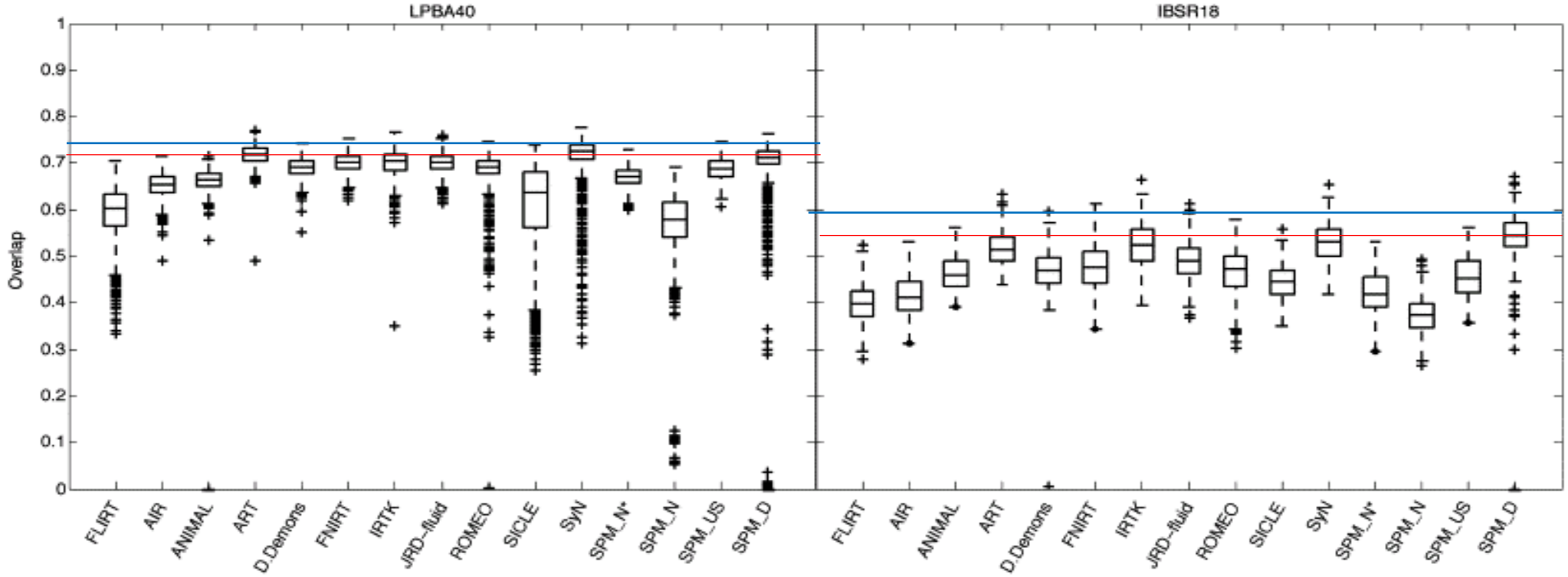


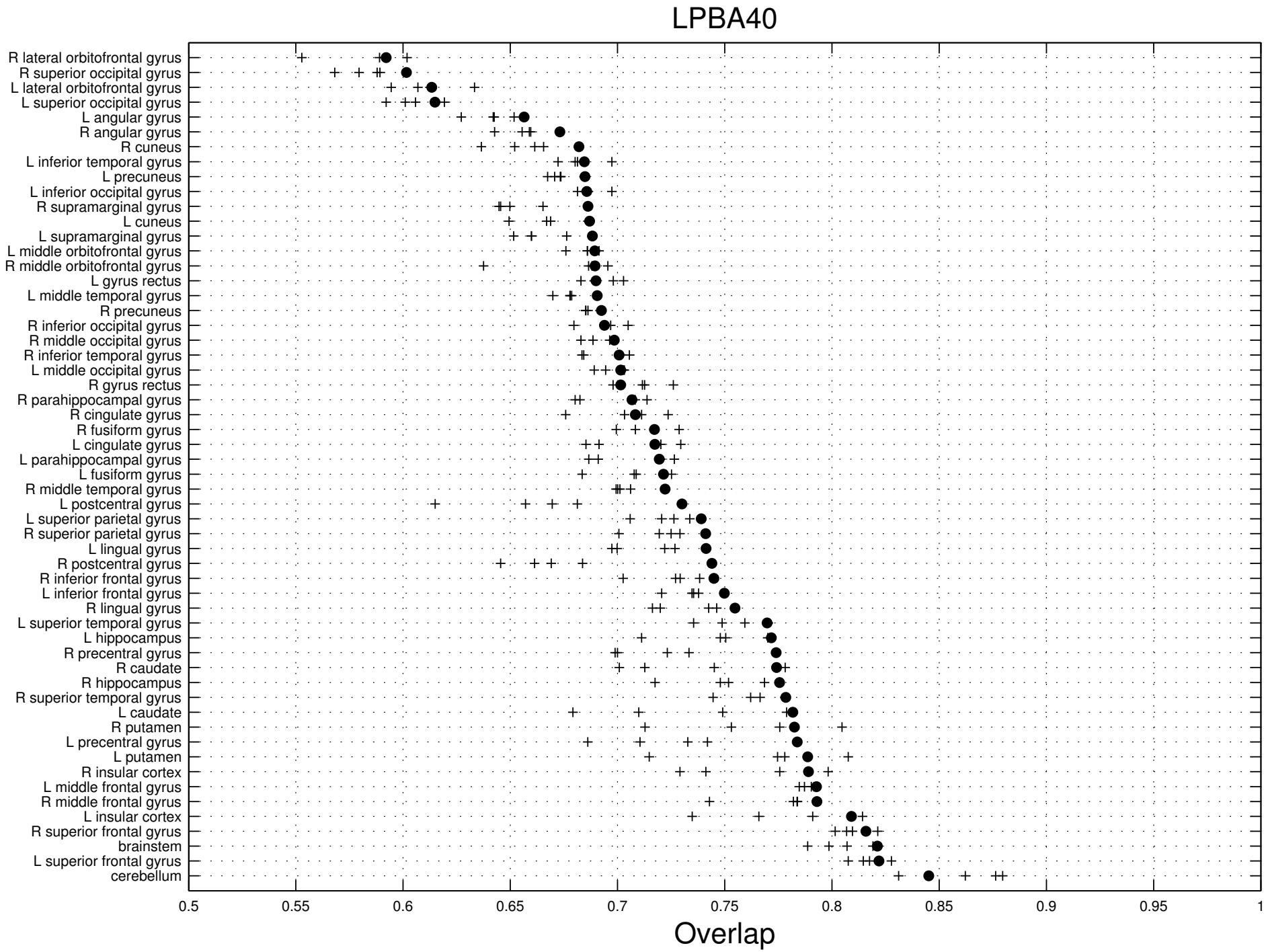






Evaluations of nonlinear registration algorithms




LPBA40
R lateral orbitofrontal gyrus
R superior occipital gyrus
L lateral orbitofrontal gyrus
L superior occipital gyrus
L angular gyrus
R angular gyrus
R cuneus
L inferior temporal gyrus
L precuneus
L inferior occipital gyrus
R supramarginal gyrus
L cuneus
L supramarginal gyrus
L middle orbitofrontal gyrus
R middle orbitofrontal gyrus
L gyrus rectus
L middle temporal gyrus
R precuneus
R inferior occipital gyrus
R middle occipital gyrus
R inferior temporal gyrus
L middle occipital gyrus
R gyrus rectus
R parahippocampal gyrus
R cingulate gyrus
R fusiform gyrus
L cingulate gyrus
L parahippocampal gyrus
L fusiform gyrus
R middle temporal gyrus
L postcentral gyrus
L superior parietal gyrus
R superior parietal gyrus
L lingual gyrus
R postcentral gyrus
R inferior frontal gyrus
L inferior frontal gyrus
R lingual gyrus
L superior temporal gyrus
L hippocampus
R precentral gyrus
R caudate
R hippocampus
R superior temporal gyrus
L caudate
R putamen
L precentral gyrus
L putamen
R insular cortex
L middle frontal gyrus
R middle frontal gyrus
L insular cortex
R superior frontal gyrus
brainstem
L superior frontal gyrus
cerebellum
0.5
0.55
0.6
0.65
0.7
0.75
0.8
0.85
0.9
0.95
1
Overlap

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.

$$1.01 \times 1.01 = 1.0201$$

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

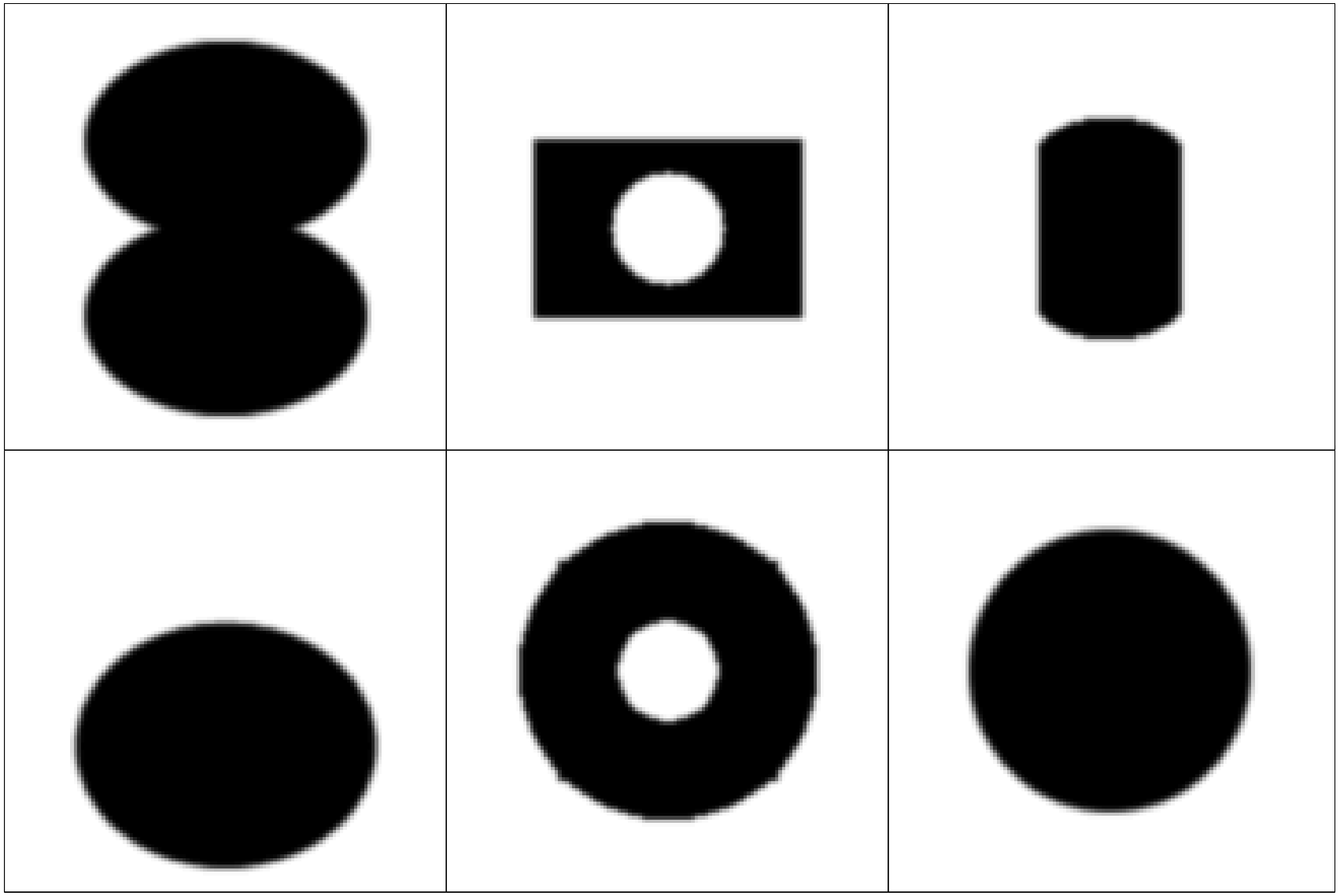
Some References

- 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.

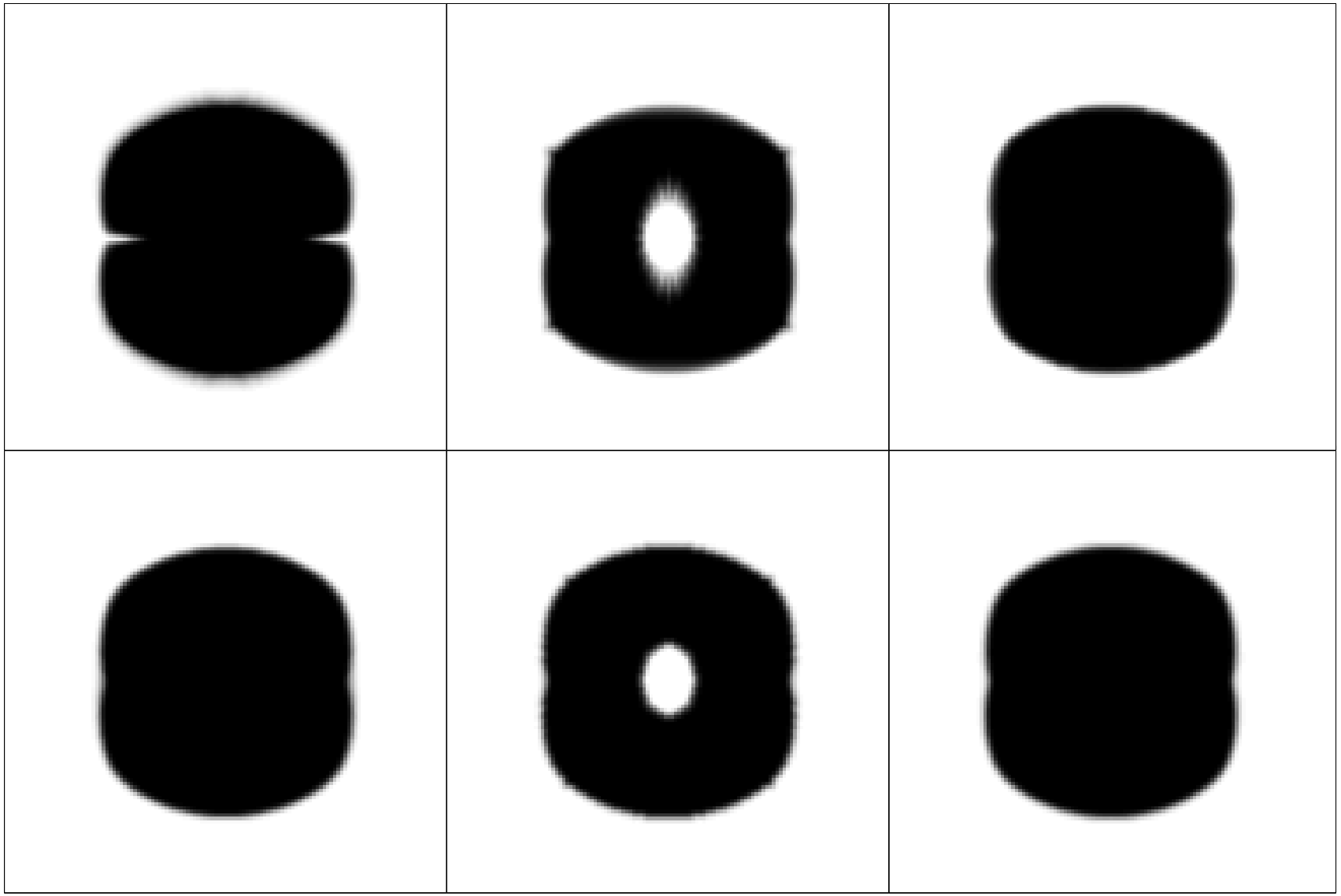
Overview

- Voxel-Based Morphometry
- Diffeomorphic Registration
- **Tensor-Based Morphometry**
- Multivariate Approaches
- Scalar Momentum
- Some Evaluations
- Longitudinal Registration

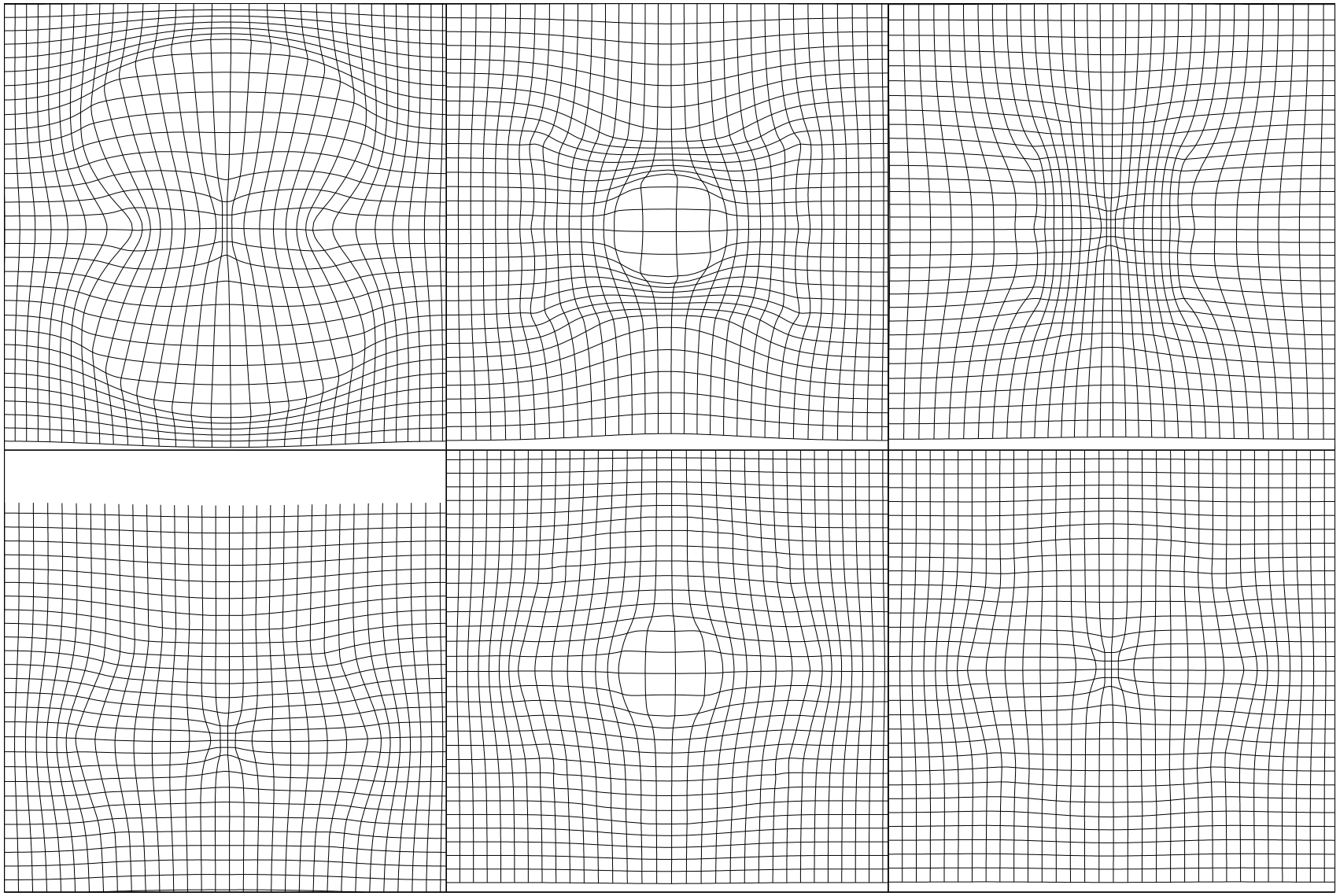
Some 2D Shapes



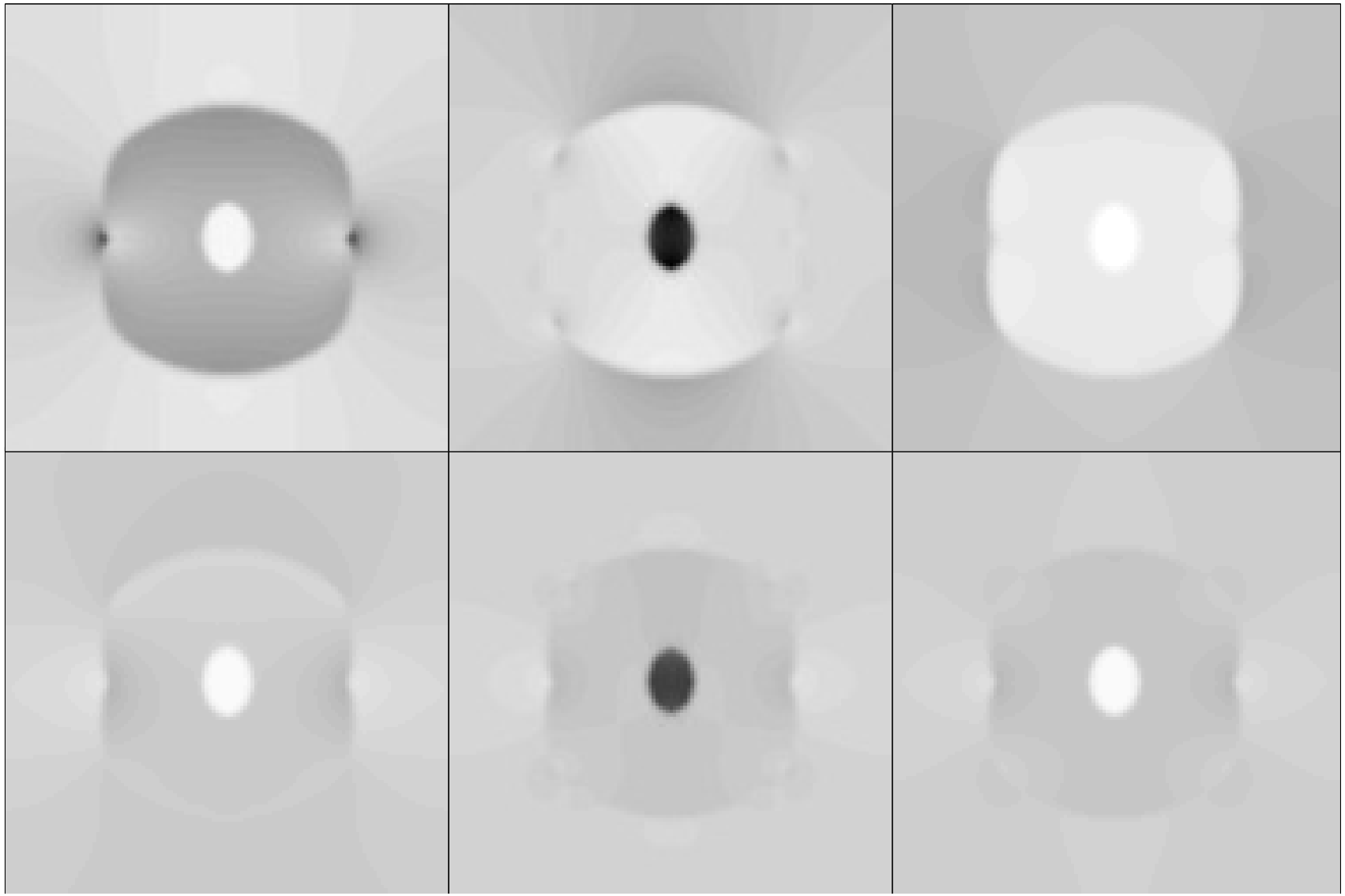
Shapes aligned to their average



These were the deformations for that



and these are the Jacobian determinants



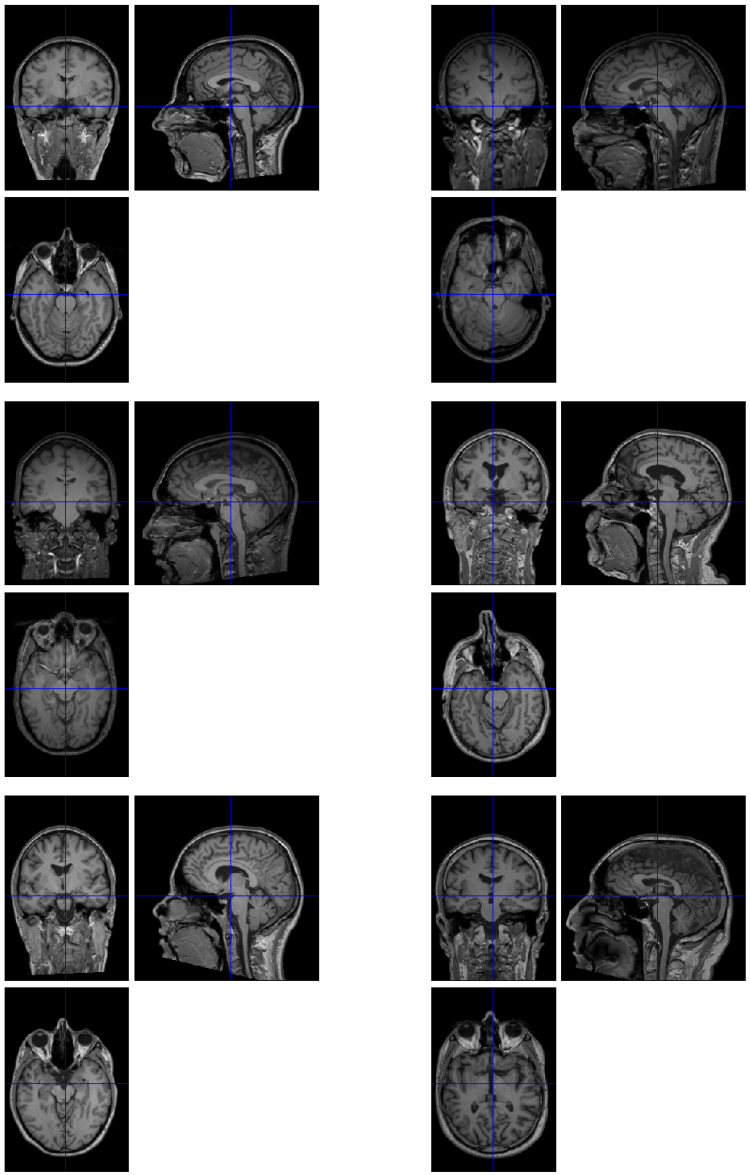
Cross-Sectional Data

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

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

Data from three different hospitals in London:

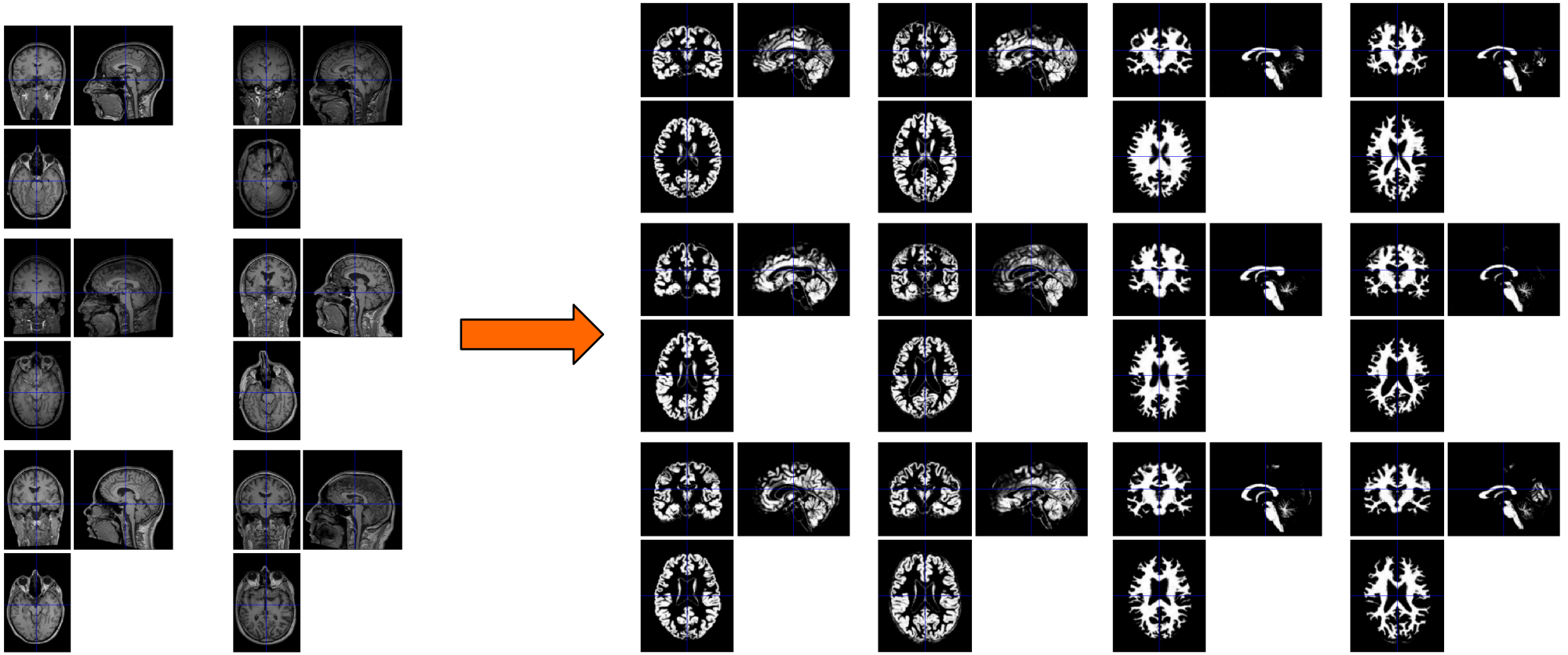
- Hammersmith Hospital using a Philips 3T system
- Guy's Hospital using a Philips 1.5T system
- Institute of Psychiatry using a GE 1.5T system5T system



Segmentation

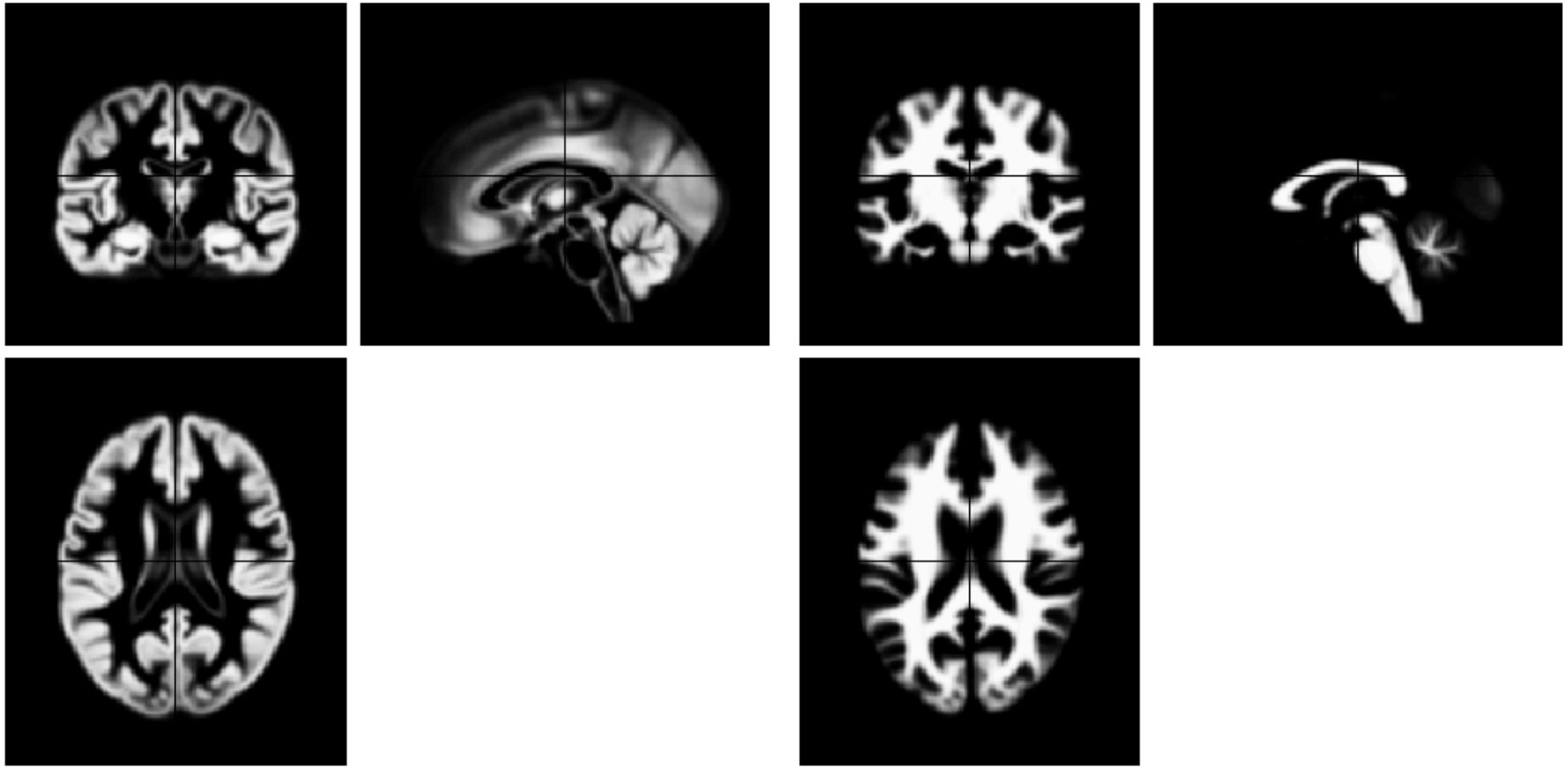
Segmented into GM and WM.

Approximately aligned via rigid-body.



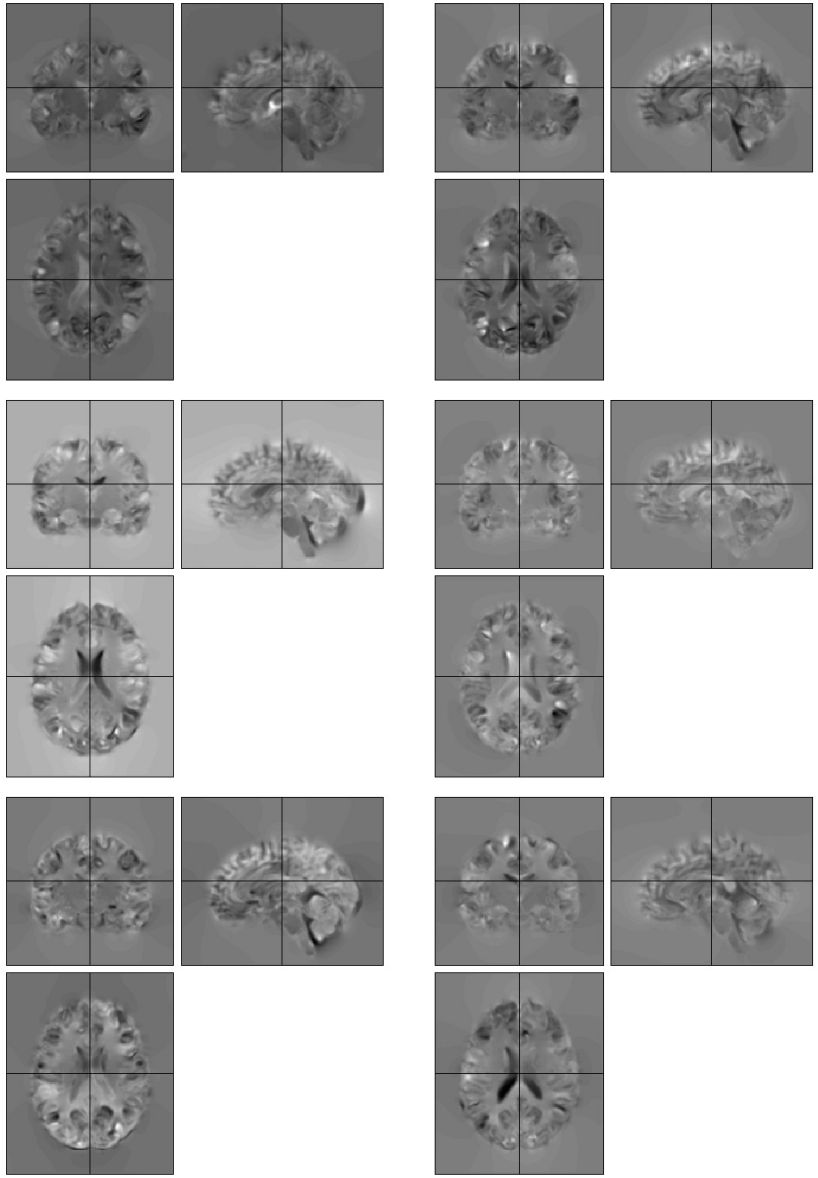
Diffeomorphic Alignment

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

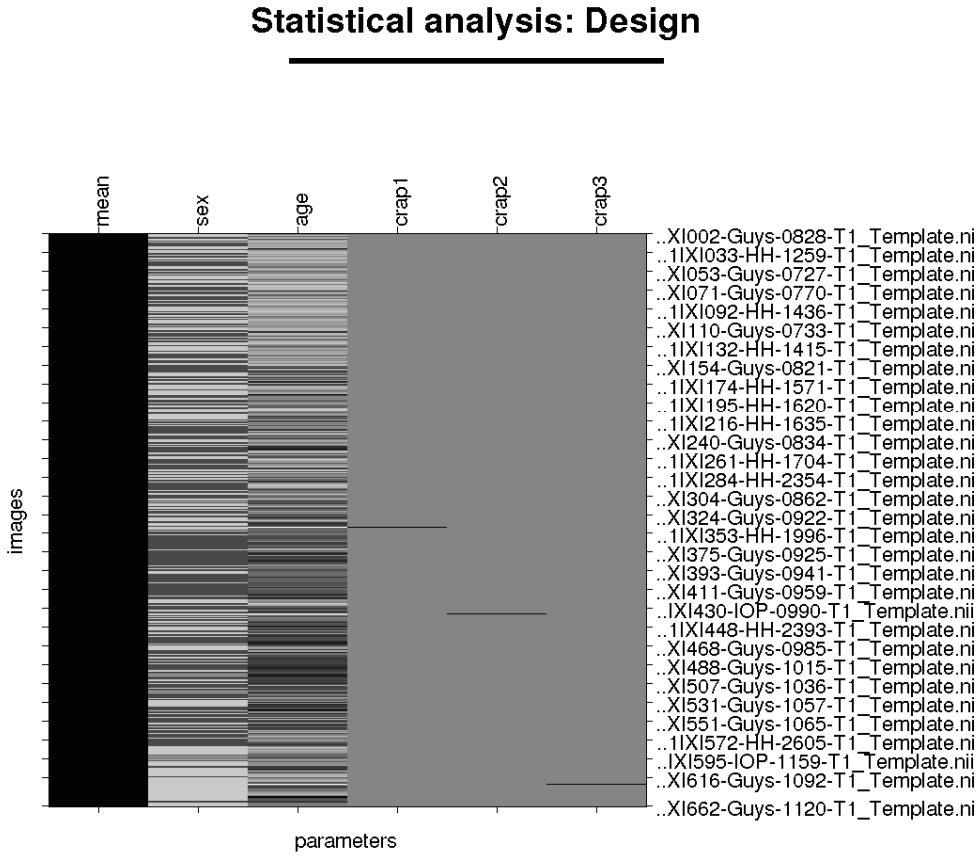


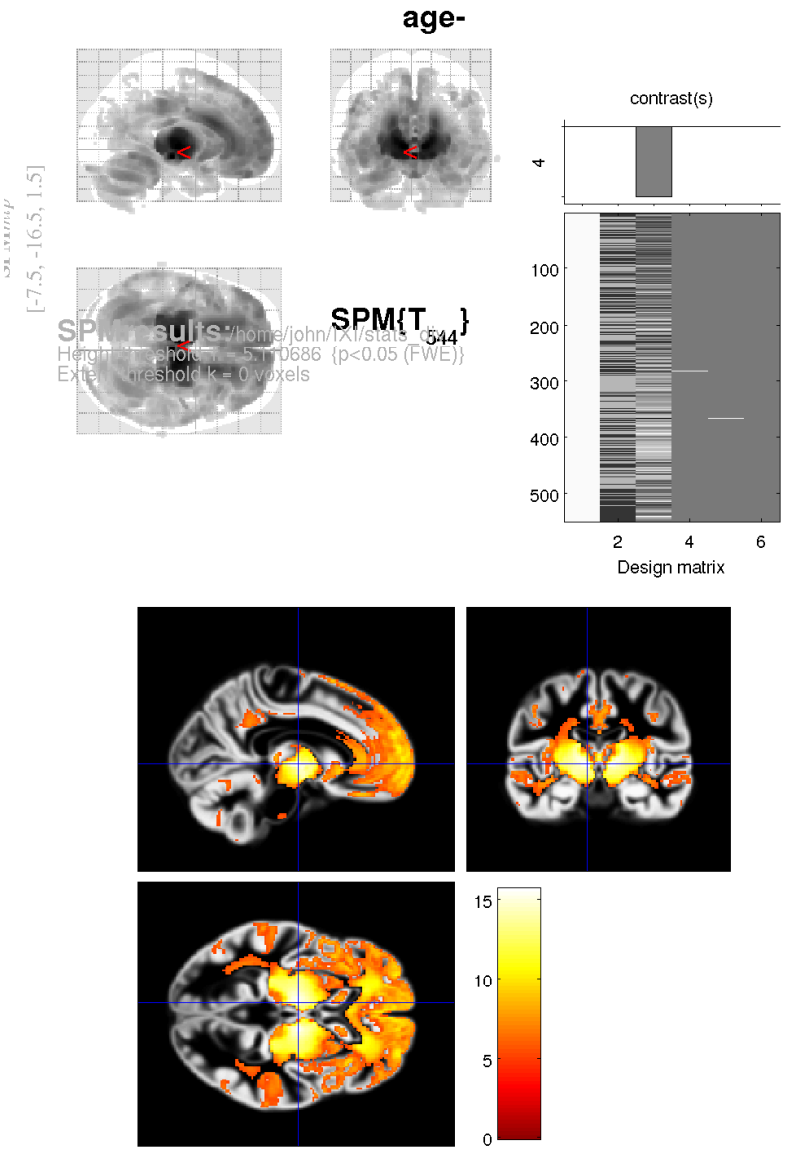
Divergence Maps

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



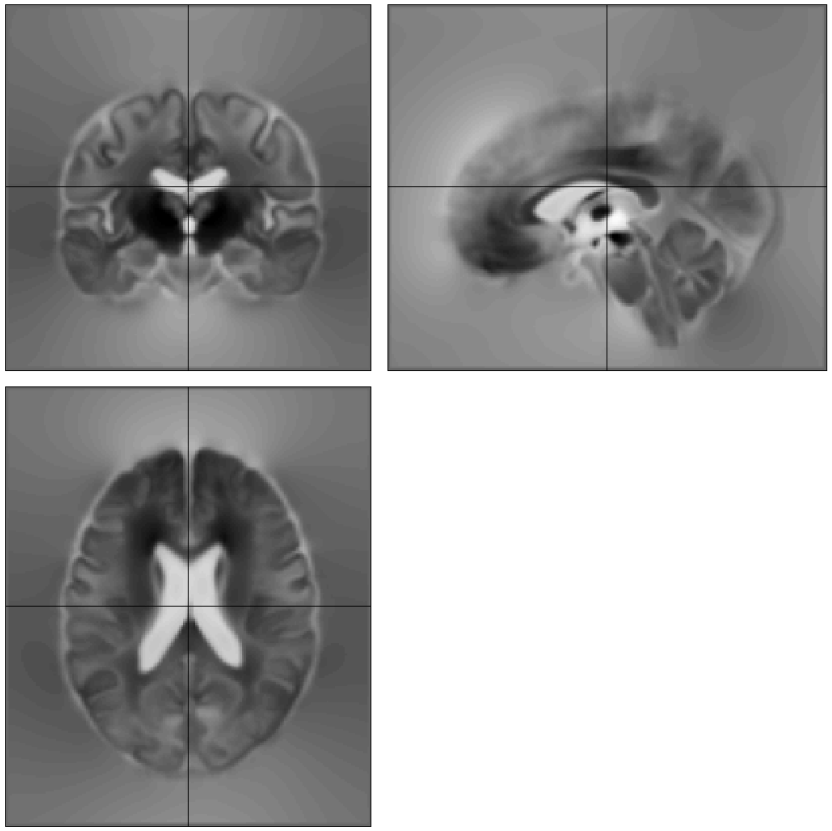
Mass-Univariate Analysis – shrinkage with age



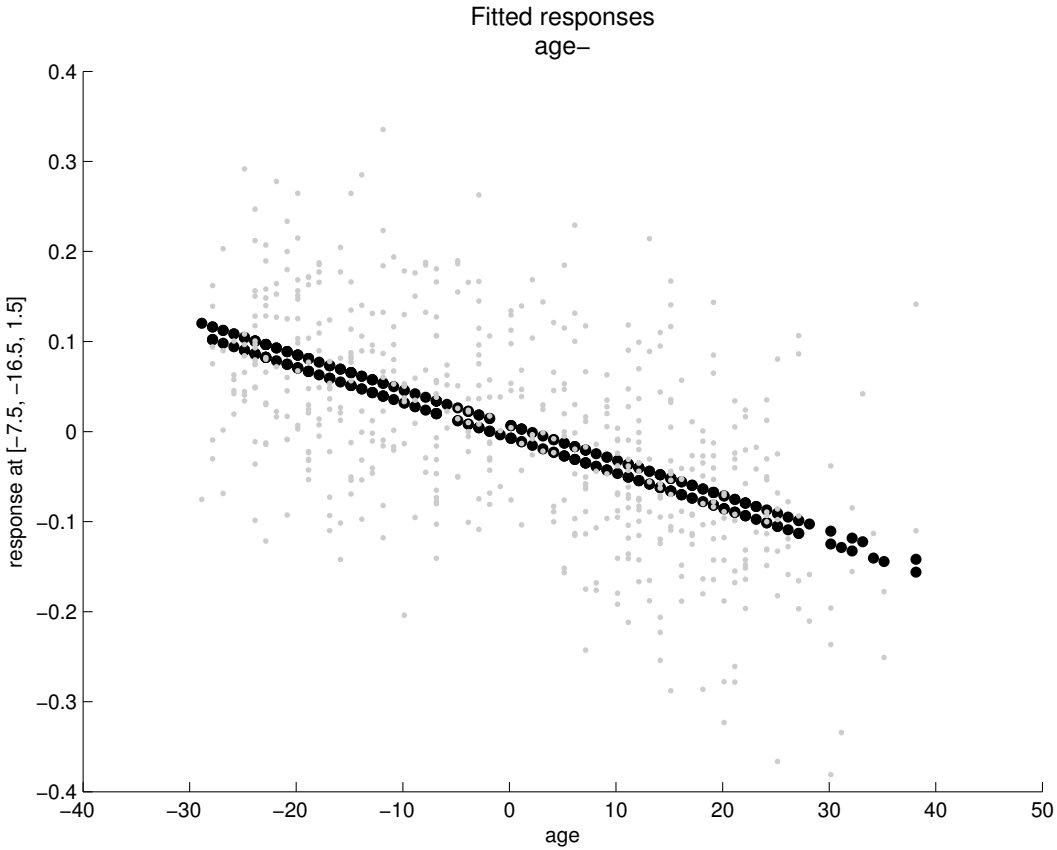


Large T statistics (> 15) – but not very predictive

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

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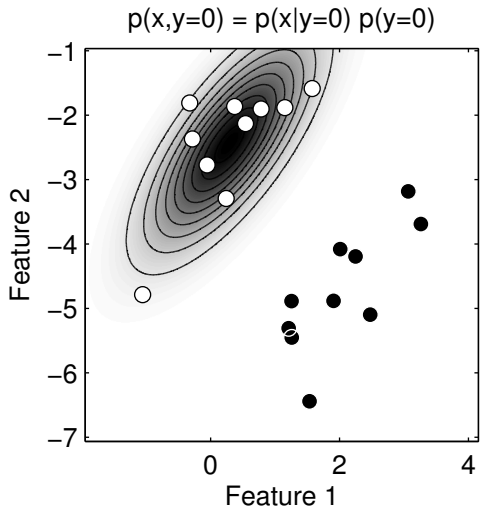
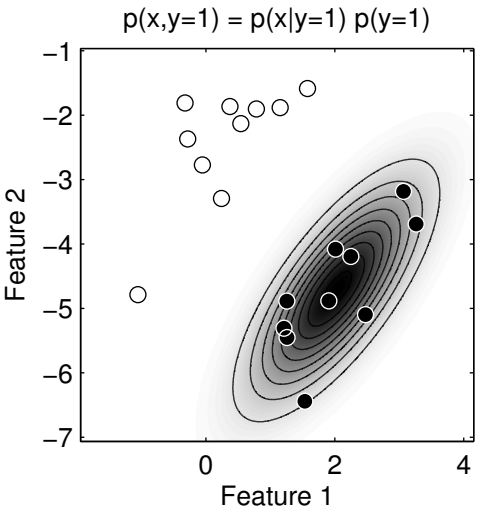
Multivariate models of form

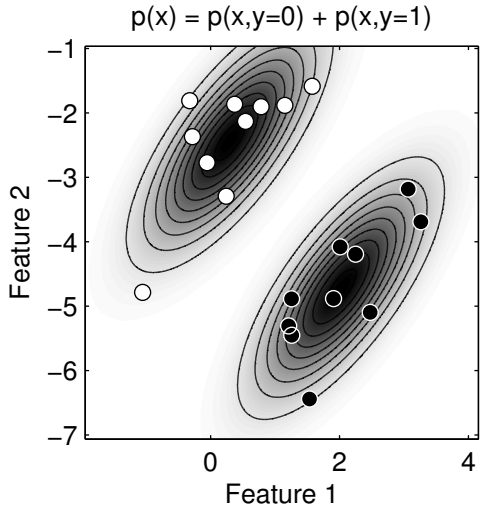
- In theory, assumptions about structural covariance among brain regions are more biologically plausible.
  - Form determined (in part) by spatio-temporal modes of gene expression.
- Empirical evidence in (eg)
  - Mechelli, Friston, Frackowiak & Price. *Structural covariance in the human cortex*. Journal of Neuroscience 25(36):8303-8310 (2005).
- We should work with the most accurate modelling assumptions available.
  - If a model is accurate, it will make accurate predictions.

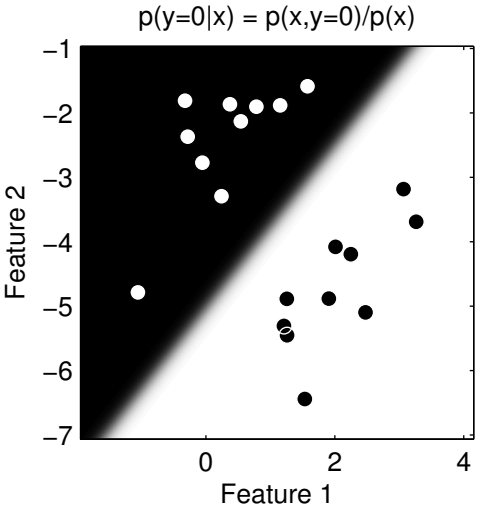
Fisher's Linear Discriminant Analysis

- A multivariate model.
- Special case of canonical variates analysis.
- A **generative model**.



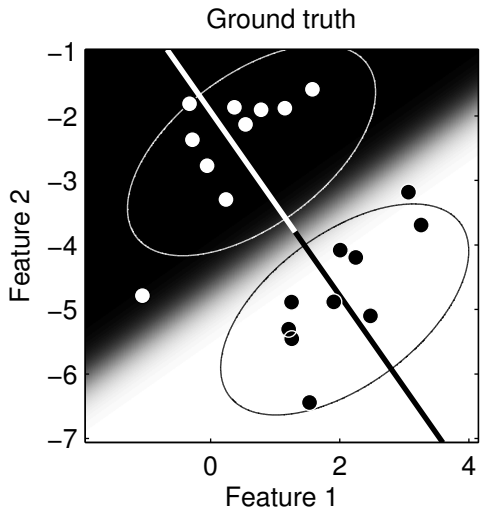


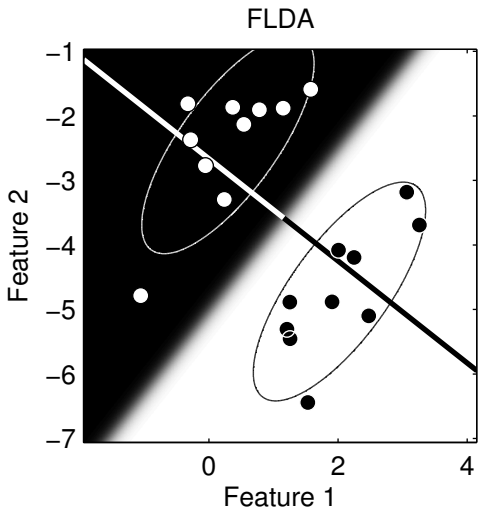


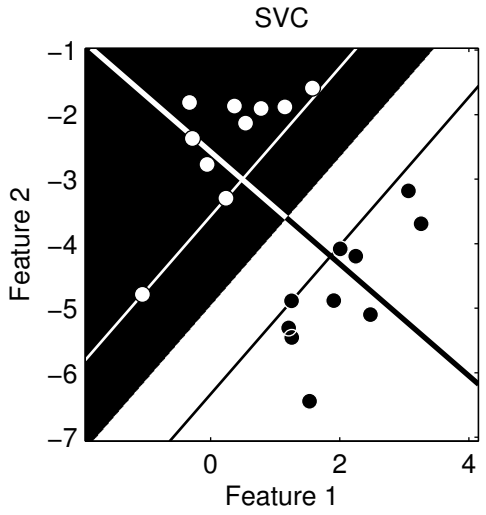


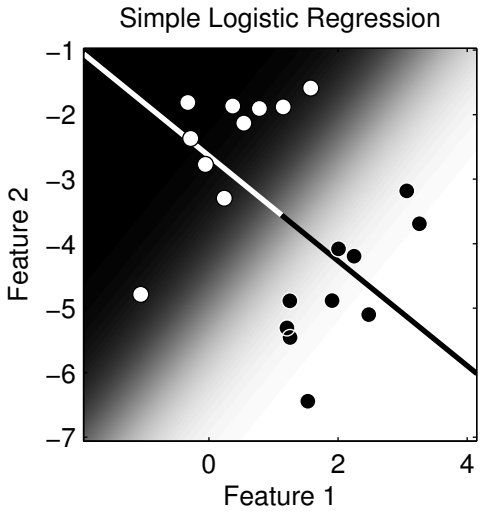
Other linear discrimination approaches

- Can also use **discriminative models**.
- Anatomical differences are encoded by the vector orthogonal to the separating hyper-plane.
- The most accurate model of difference is the one that best separates the groups.



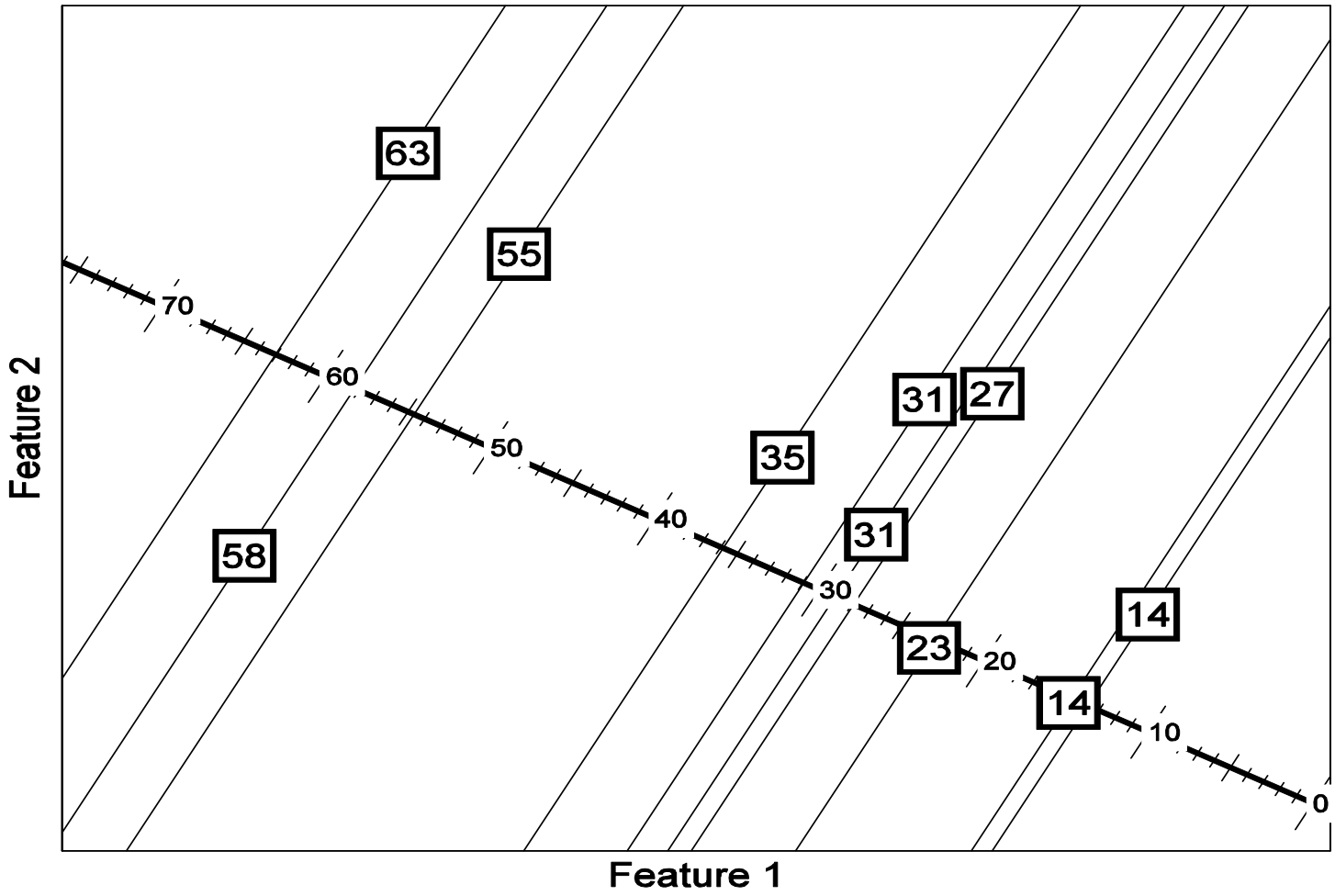






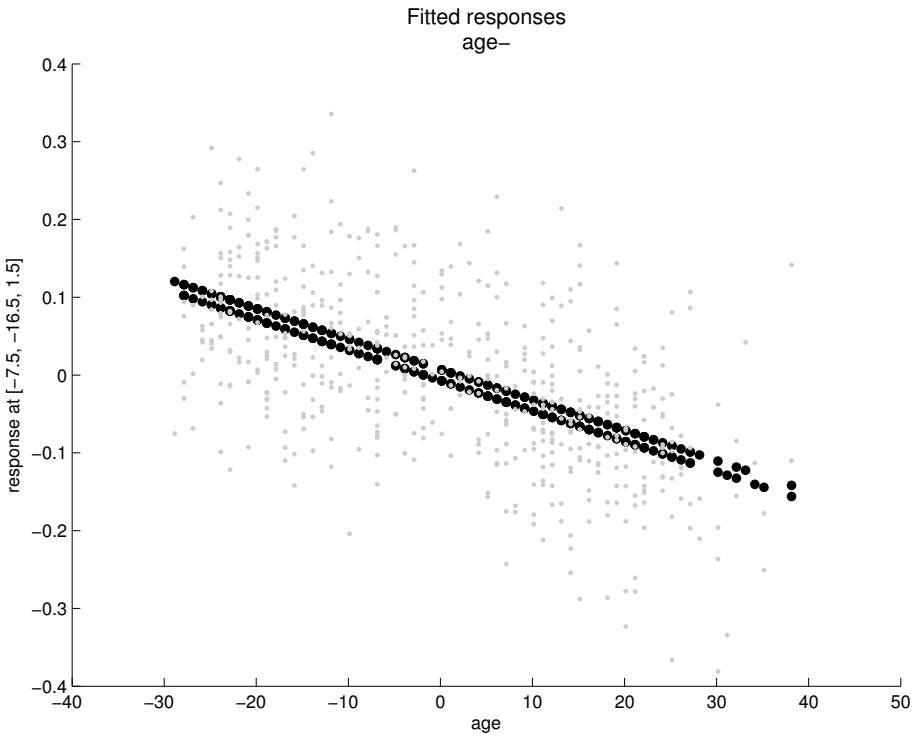
Regression

- For predicting a continuous variable

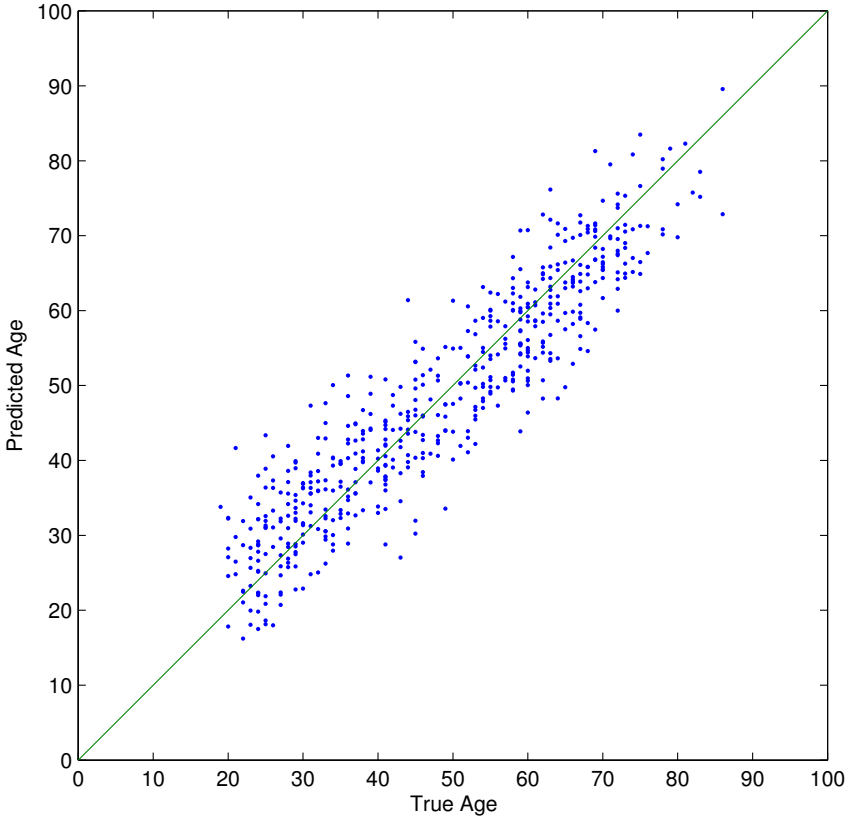


Predicting Age – univariate v multivariate

Single Voxel



Combining All Voxels



Weight Map

For linear classifiers, predictions are made by:

$$y = a_1 \times x_1 + a_2 \times x_2 + a_3 \times x_3 + \ldots + b$$

where: y is the prediction

x_1, x_2, x_3 etc are voxels in the image to classify

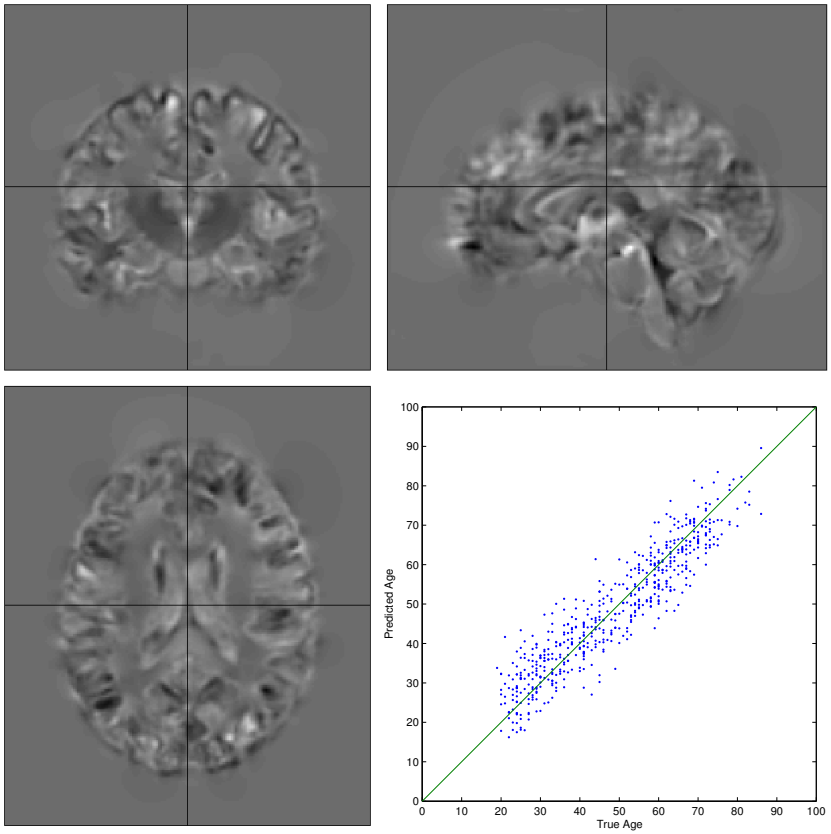
a_1, a_2, a_3 etc are voxels in a weight map

b is a constant offset.

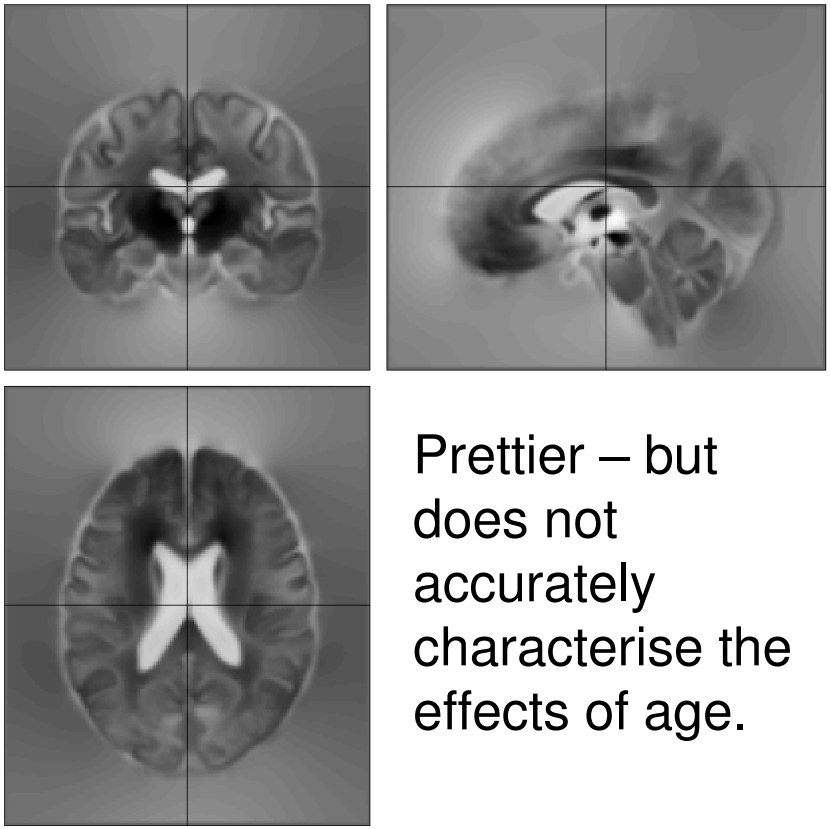
The weight map can be visualised

Maps

Multivariate weight map



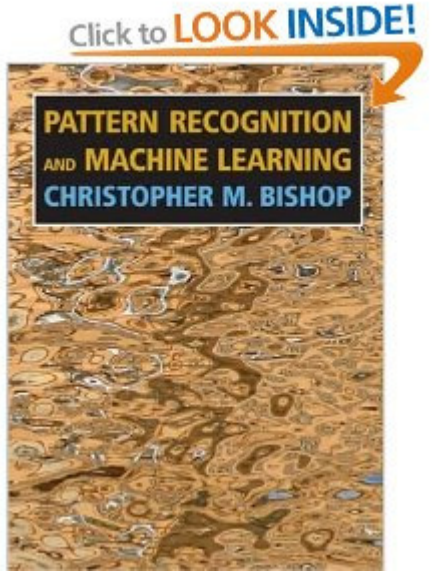
Simple T statistic image

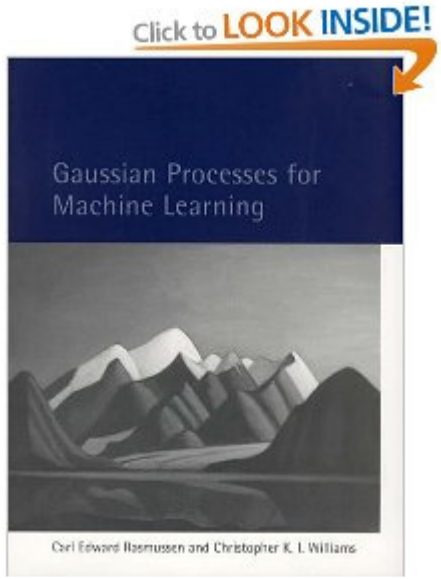


Prettier – but does not accurately characterise the effects of age.

Some References

- Bishop. *Pattern Recognition and Machine Learning*. 2006.
- Rasmussen & Williams. *Gaussian Processes for Machine Learning*. MIT Press, 2006. ISBN-10 0-262-18253-X, ISBN-13 978-0-262-18253-9. http://www.gaussianprocess.org/gpml/
- Ashburner & Klöppel. "*Multivariate models of inter-subject anatomical variability*". NeuroImage 56(2):422-439, 2011.





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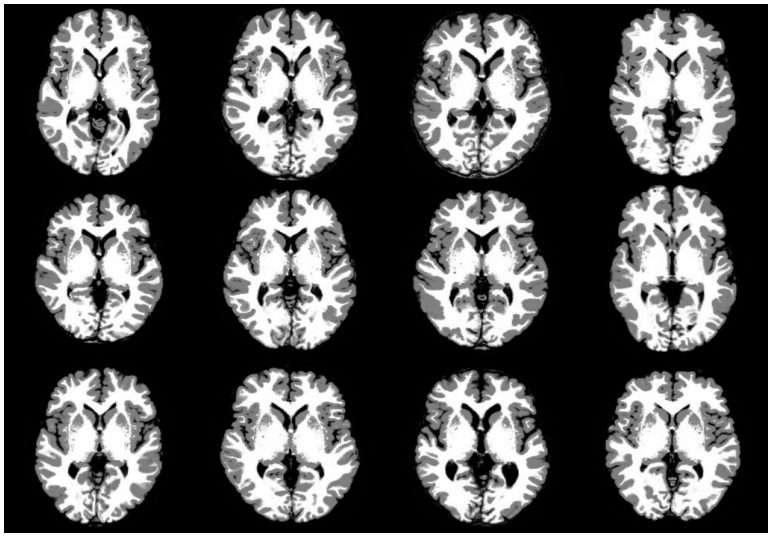
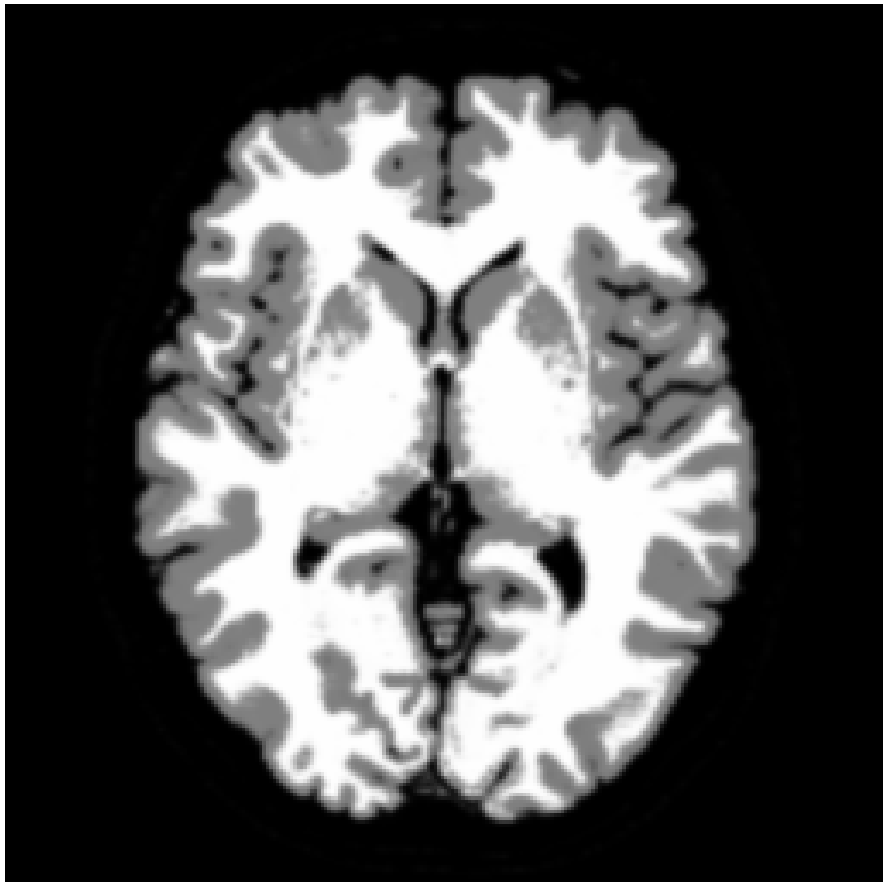
Distances

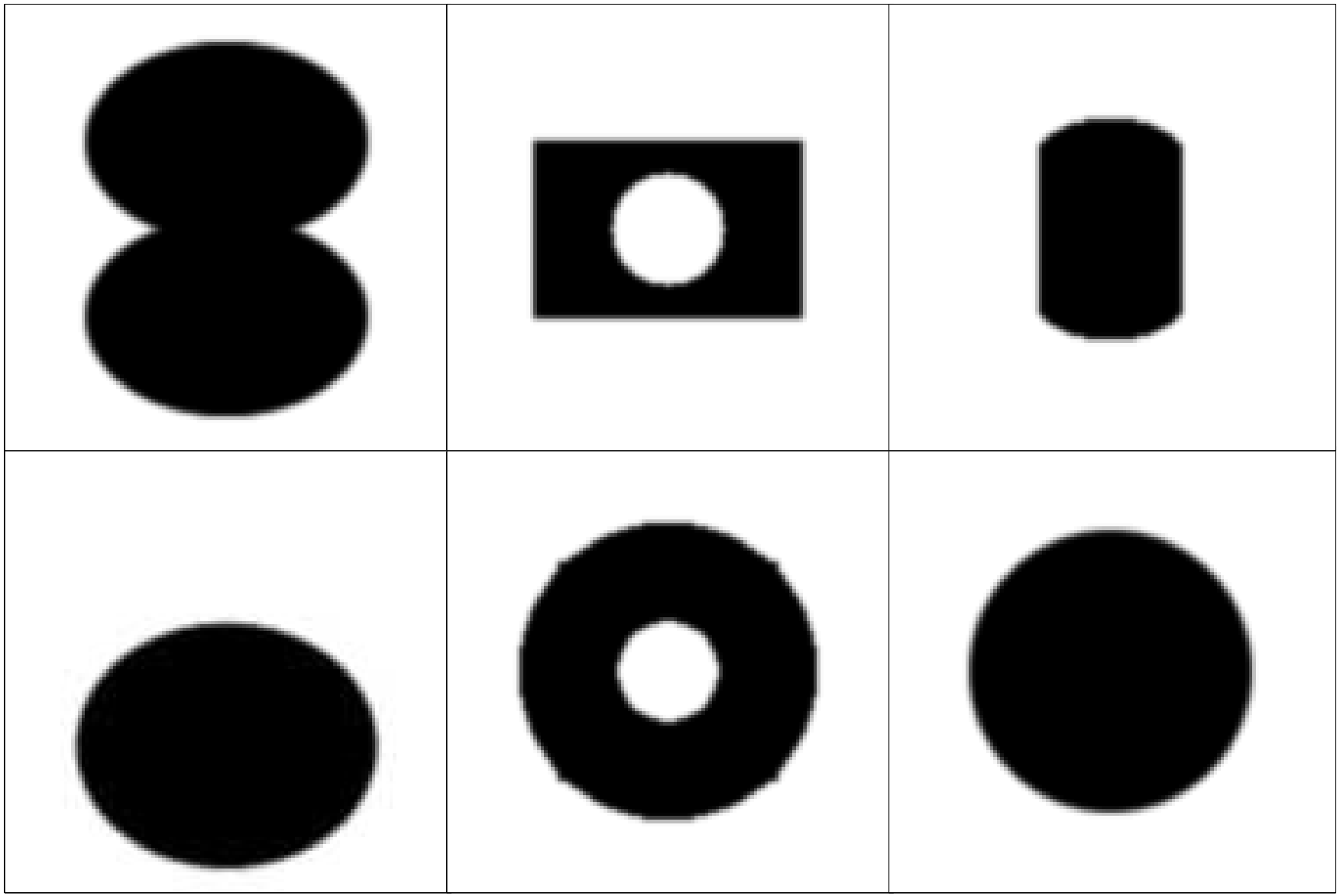
Biologically plausible measures of anatomical similarity.

Nonlinear distance measures

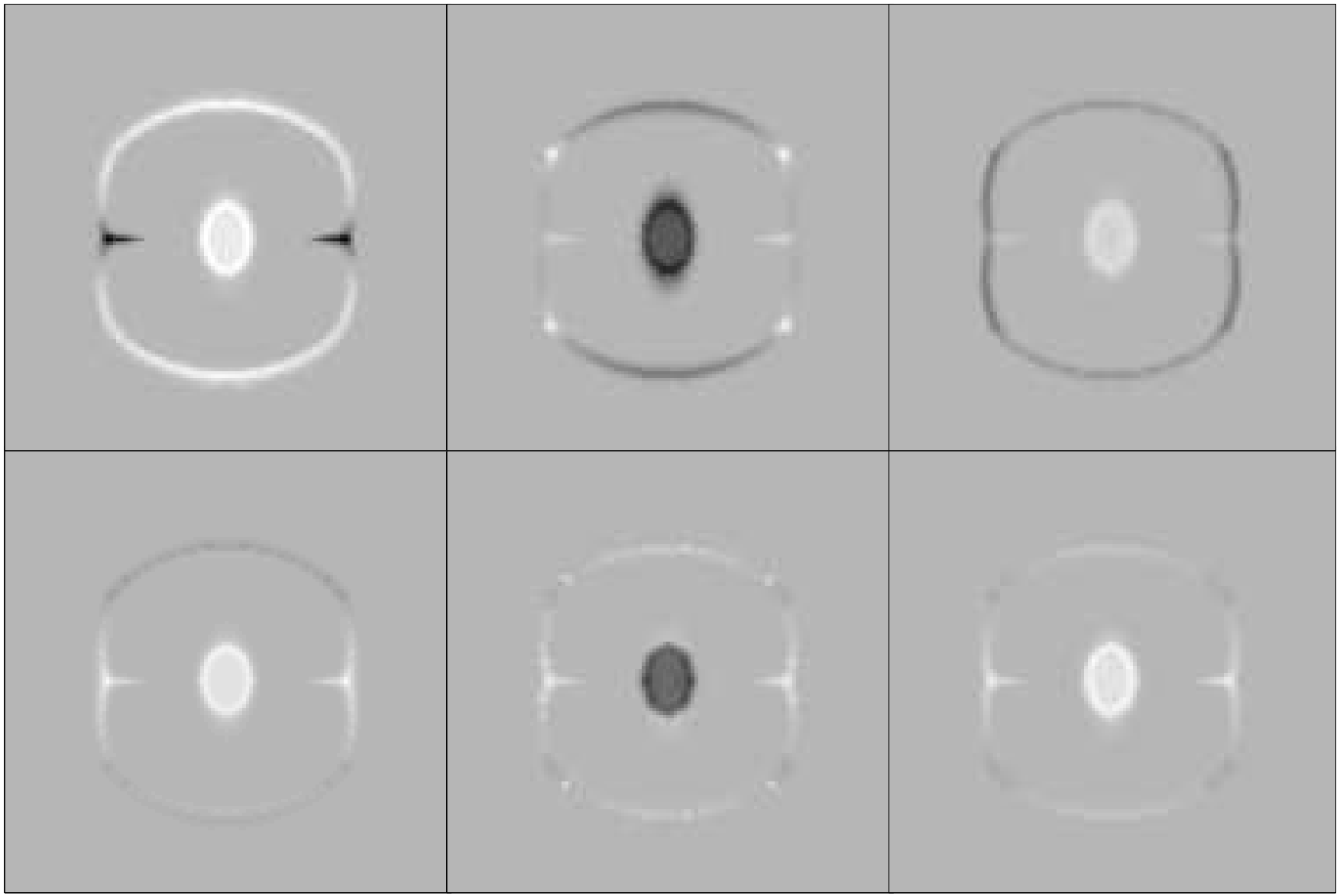




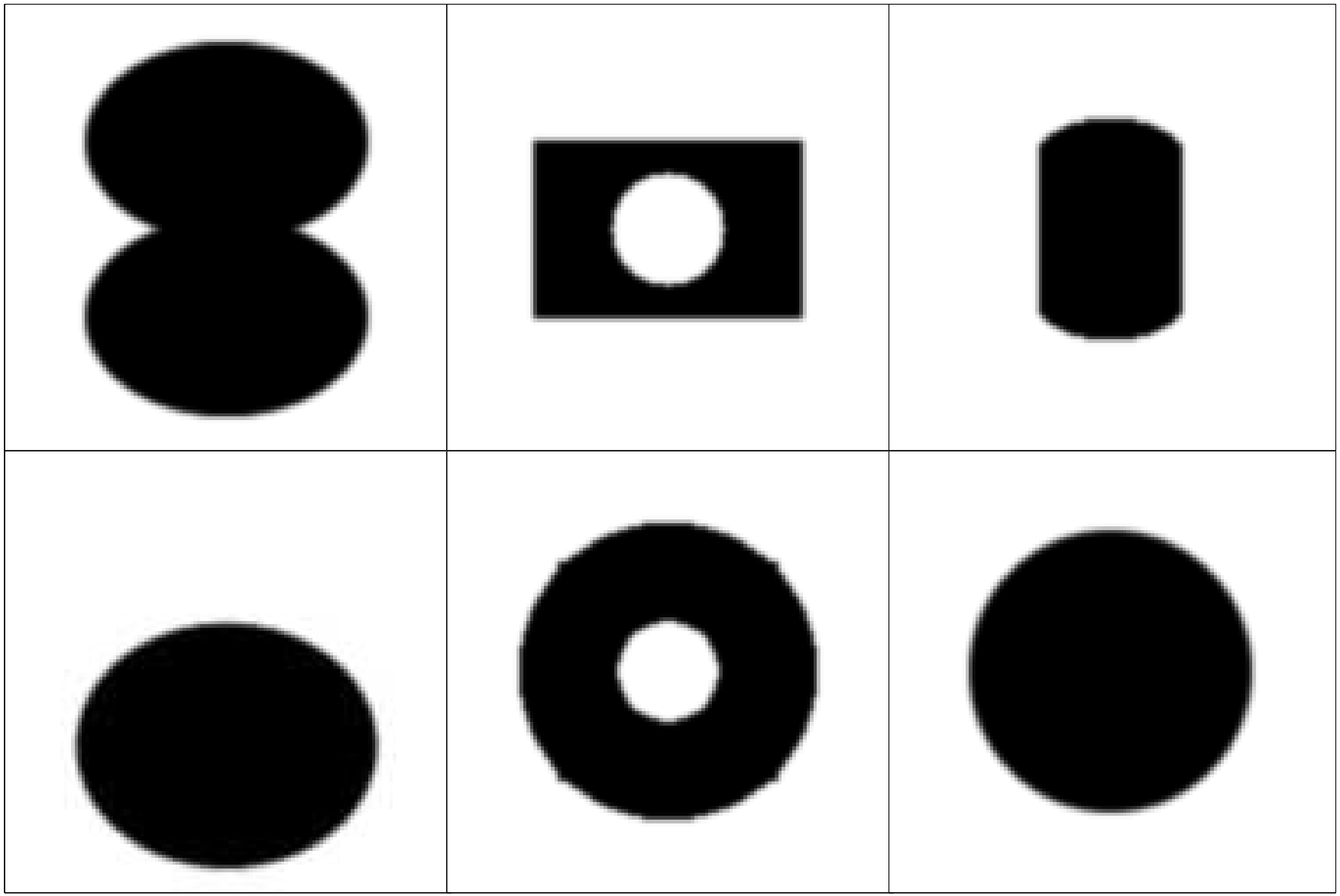
The 2D shapes (again)



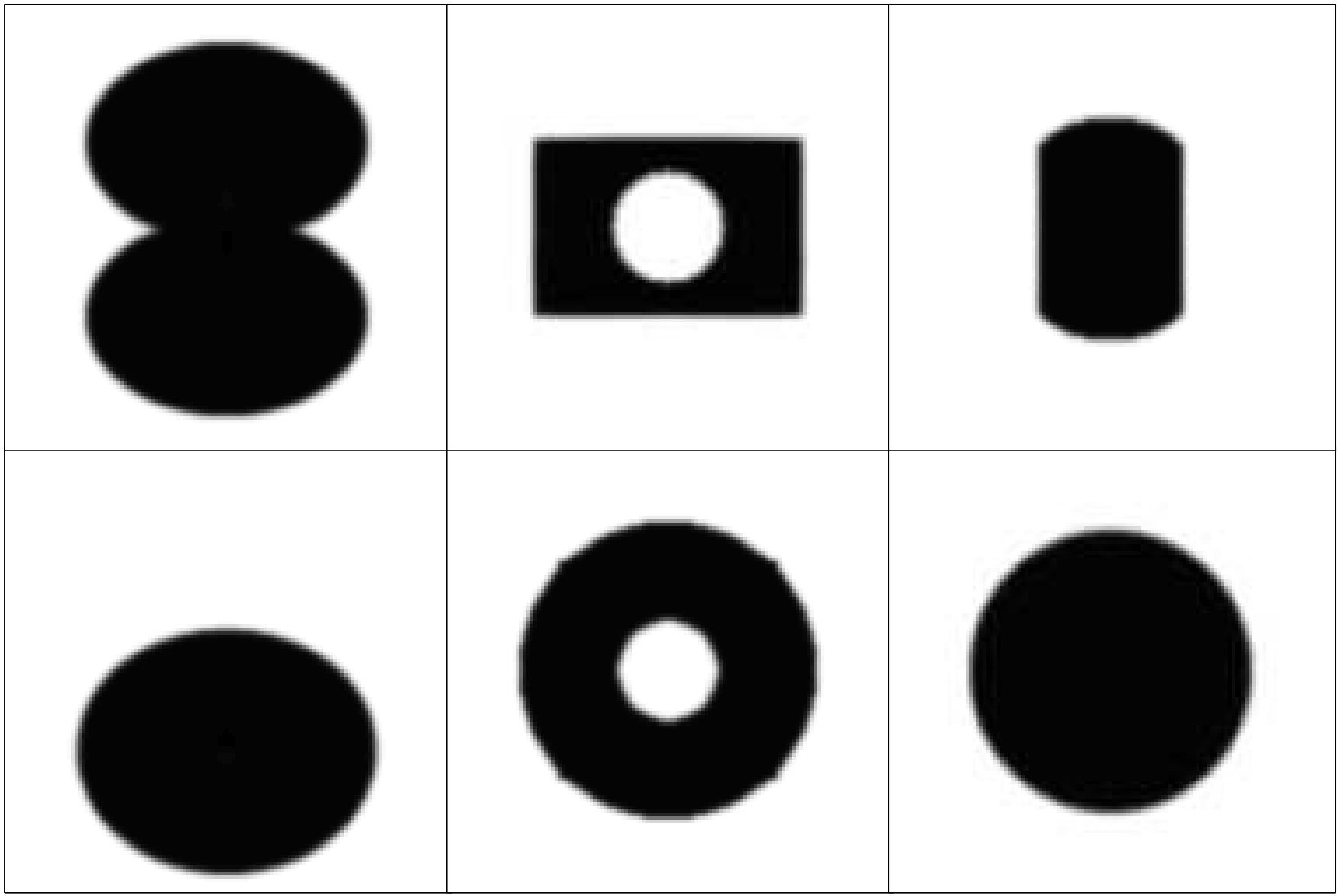
“Scalar momentum” – encodes the original shapes



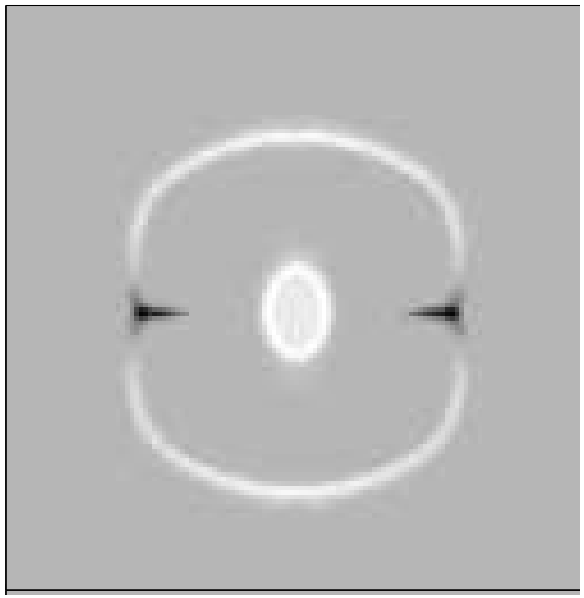
The 2D shapes (yet again)



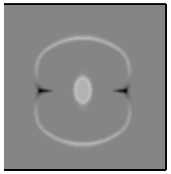
Reconstructed from scalar momentum and template.



“Scalar momentum” – encodes the original shapes



Residuals



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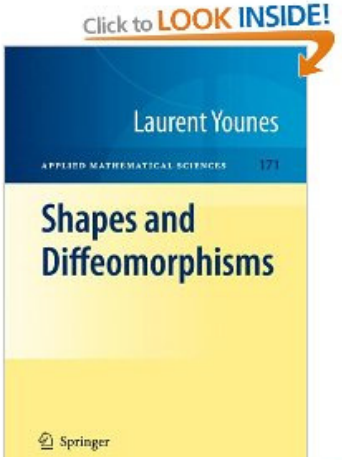
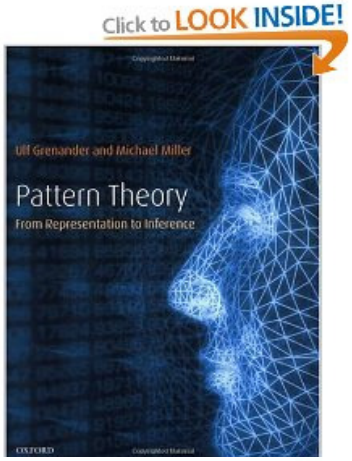
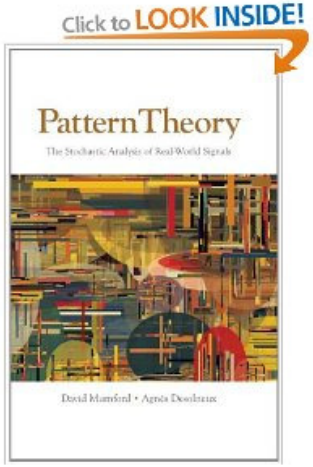
- Younes, Arrate & Miller. "*Evolutions equations in computational anatomy*". NeuroImage 45(1):S40-S50, 2009.

- Singh, Fletcher, Preston, Ha, King, Marron, Wiener & Joshi (2010). *Multivariate Statistical Analysis of Deformation Momenta Relating Anatomical Shape to Neuropsychological Measures*. T. Jiang et al. (Eds.): MICCAI 2010, Part III, LNCS 6363, pp. 529–537, 2010.

- Various textbooks







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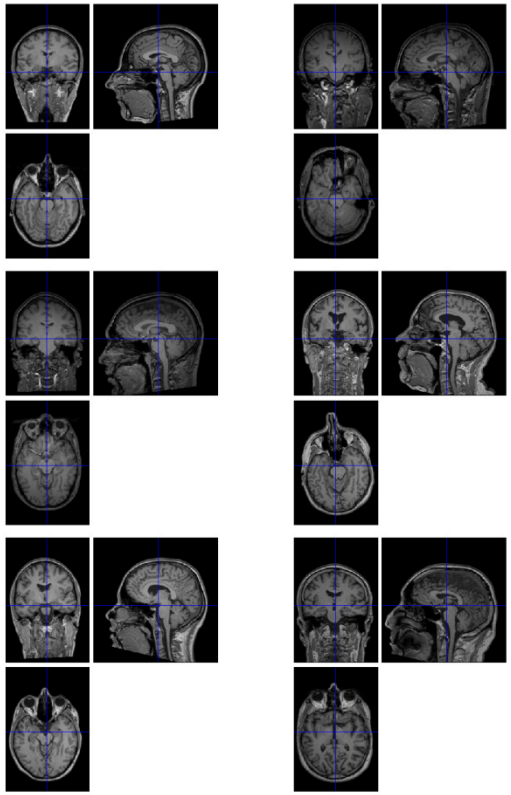
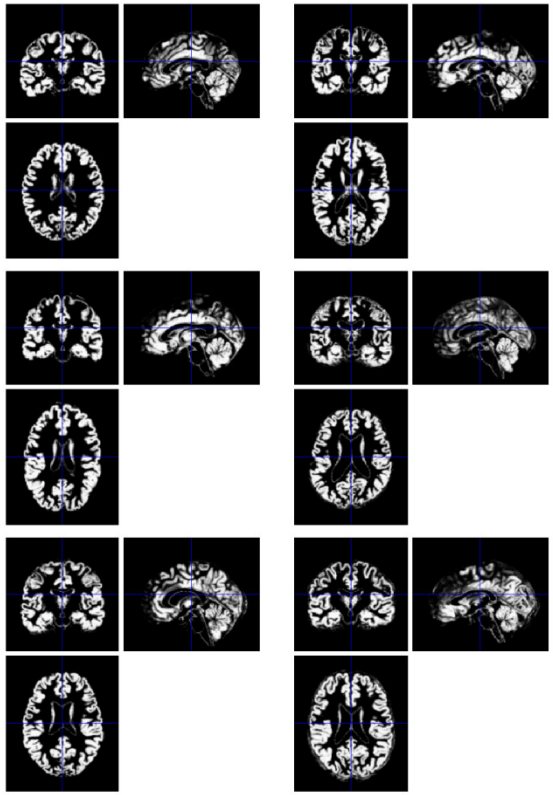
IXI Data

Original Images

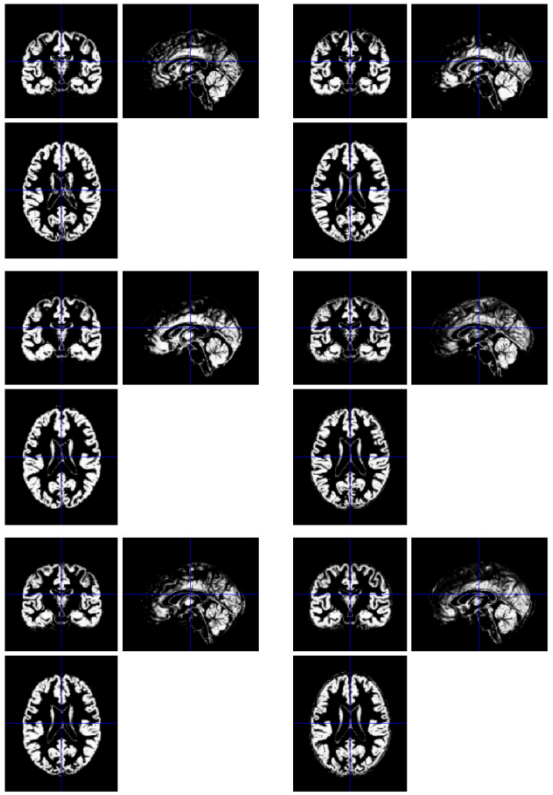


Rigidly Aligned Grey Matter

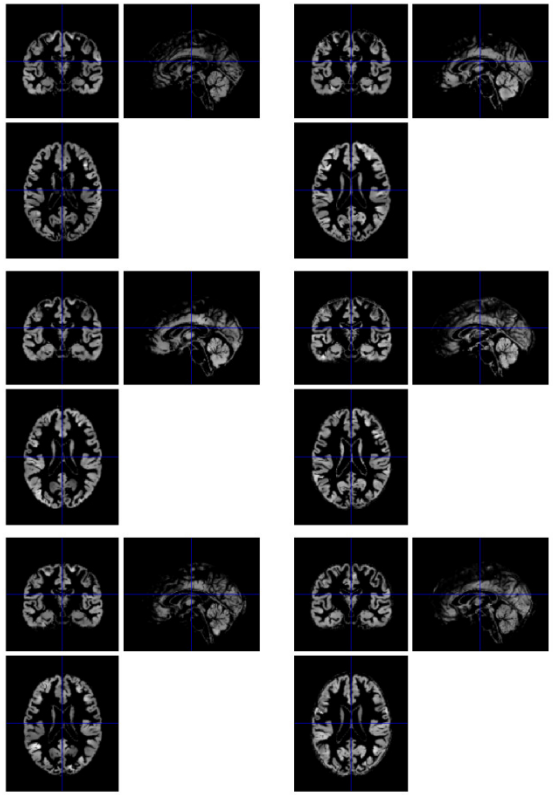


VBM-type Features

Warped Grey Matter

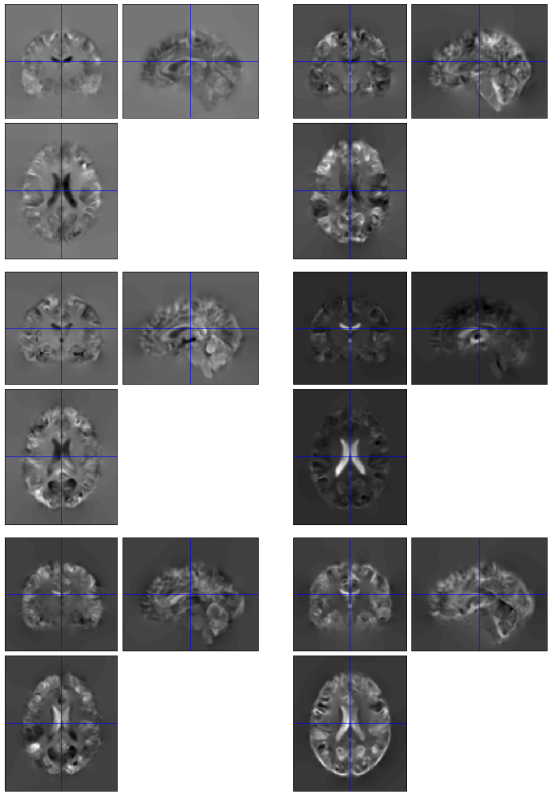


“Modulated” Warped GM

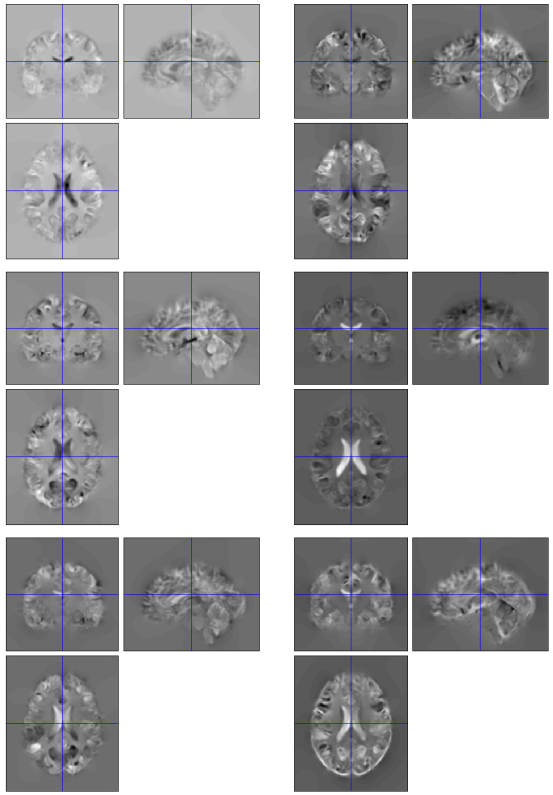


Volumetric Measures from Deformation Fields

Jacobian determinants

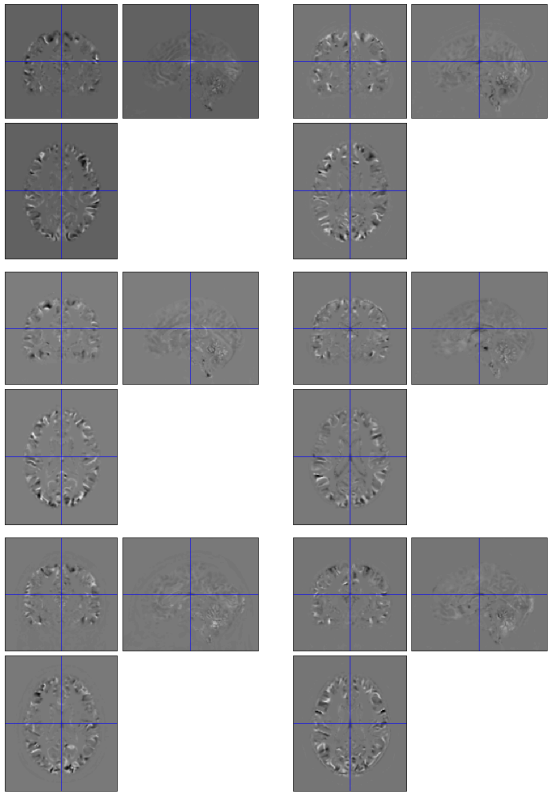


Initial Velocity Divergence

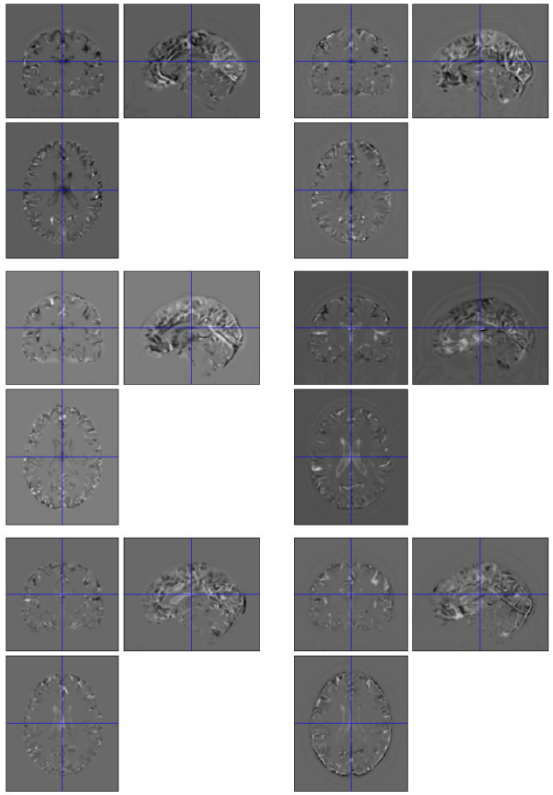


Scalar Momentum

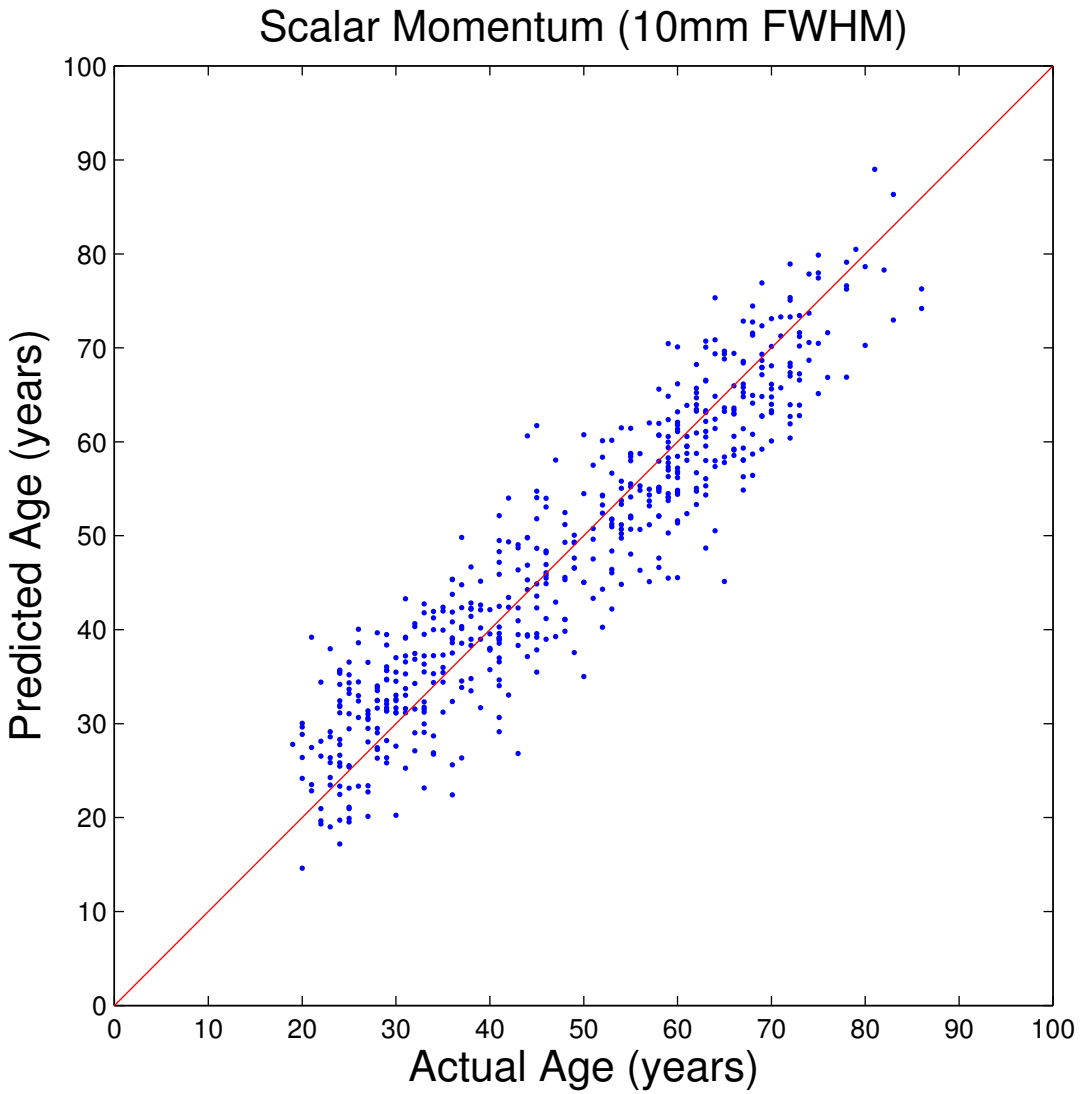
1st Component



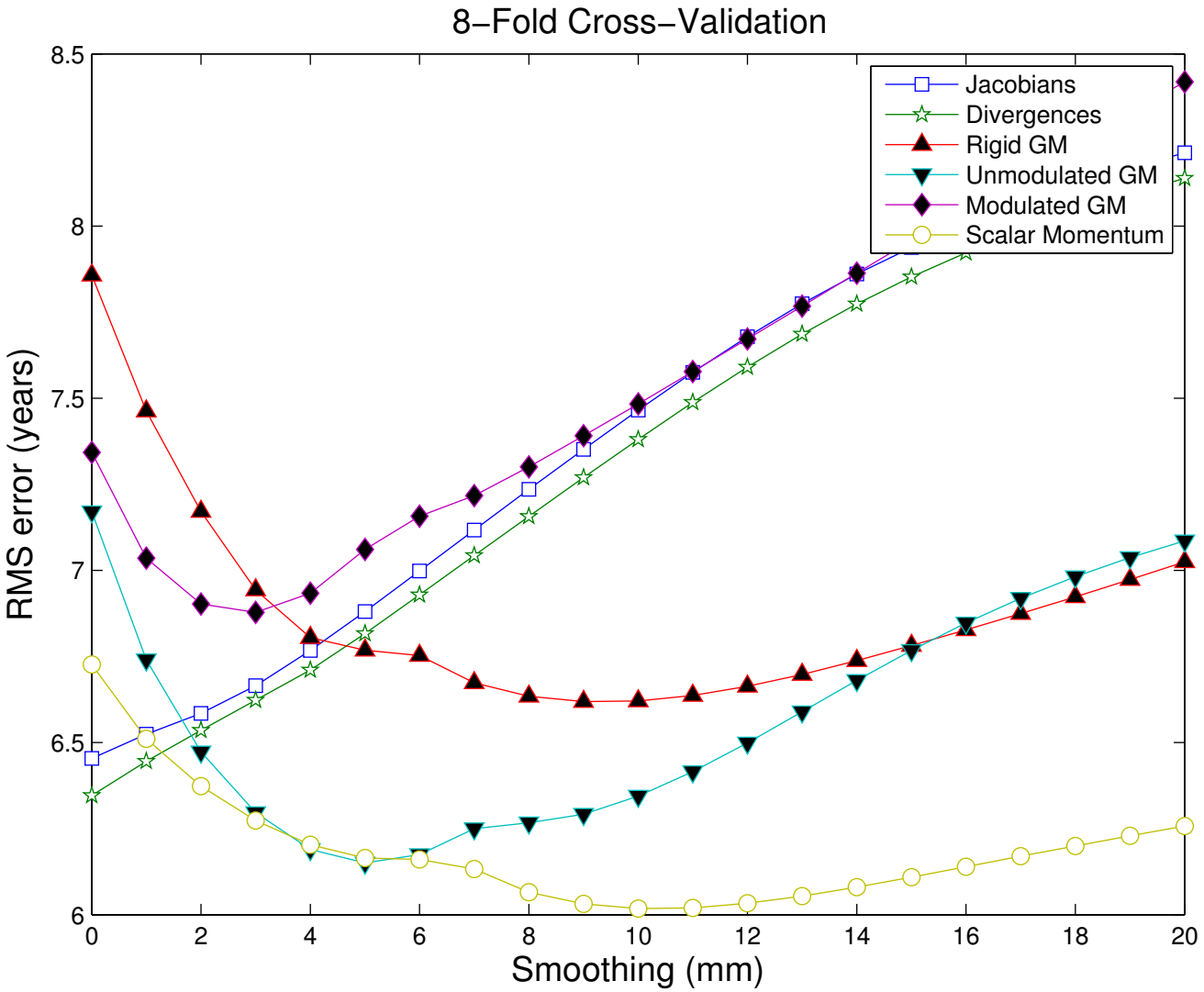
2nd Component



Age Prediction - Best Result

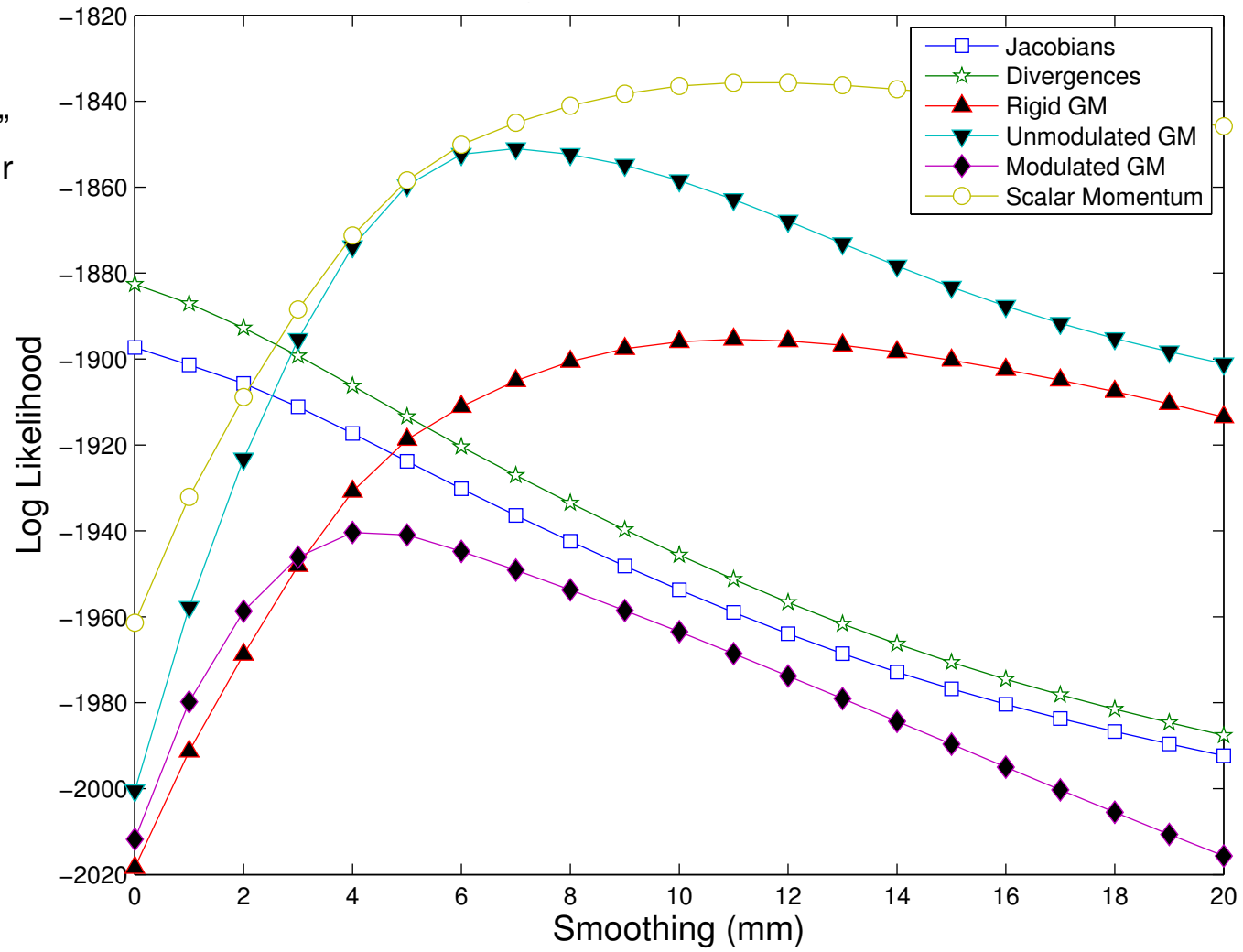


Age Prediction – Comparison Among Features

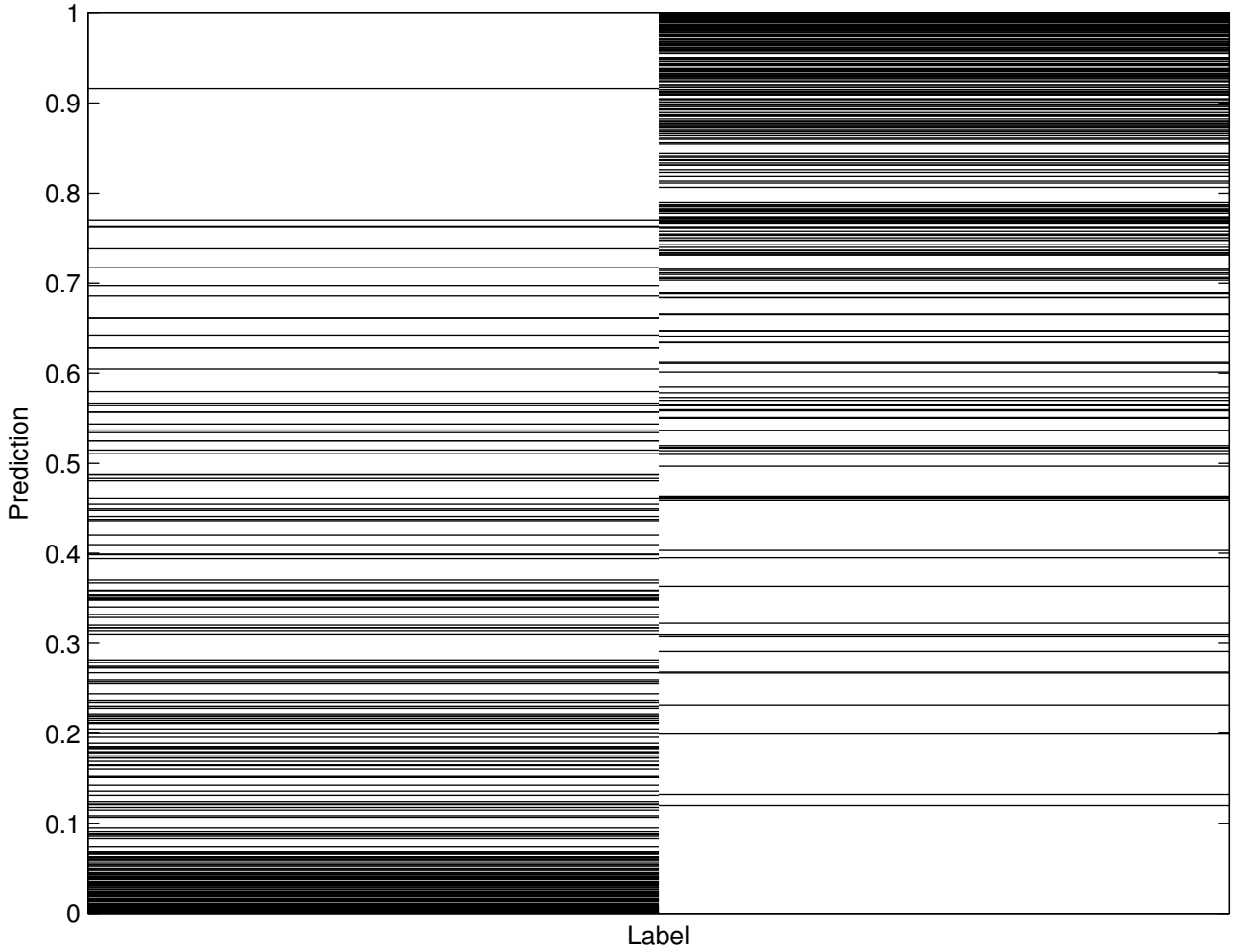


Age Prediction – Model Log Likelihoods

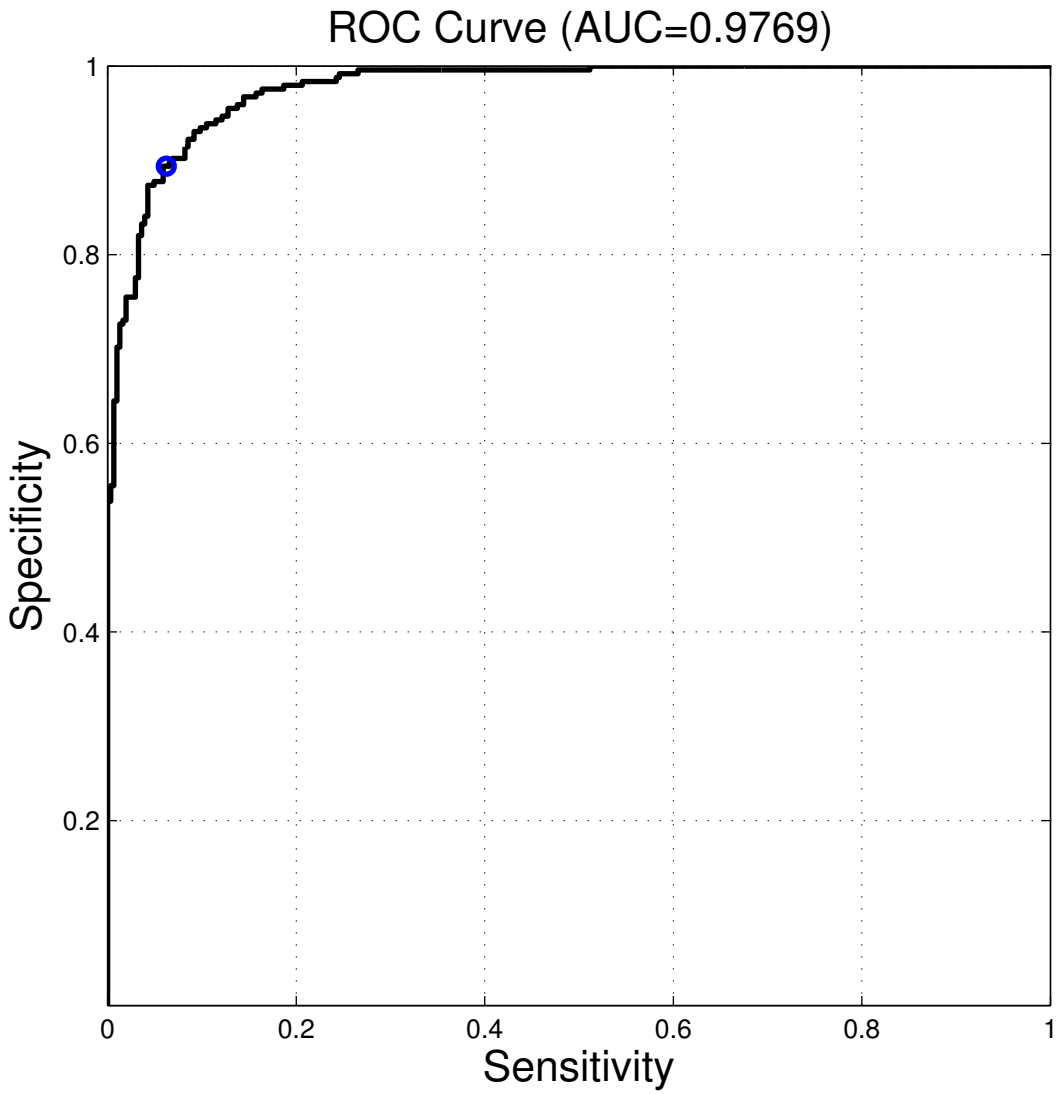
Differences > 4.6 indicate “decisive” evidence in favour of one approach over another.



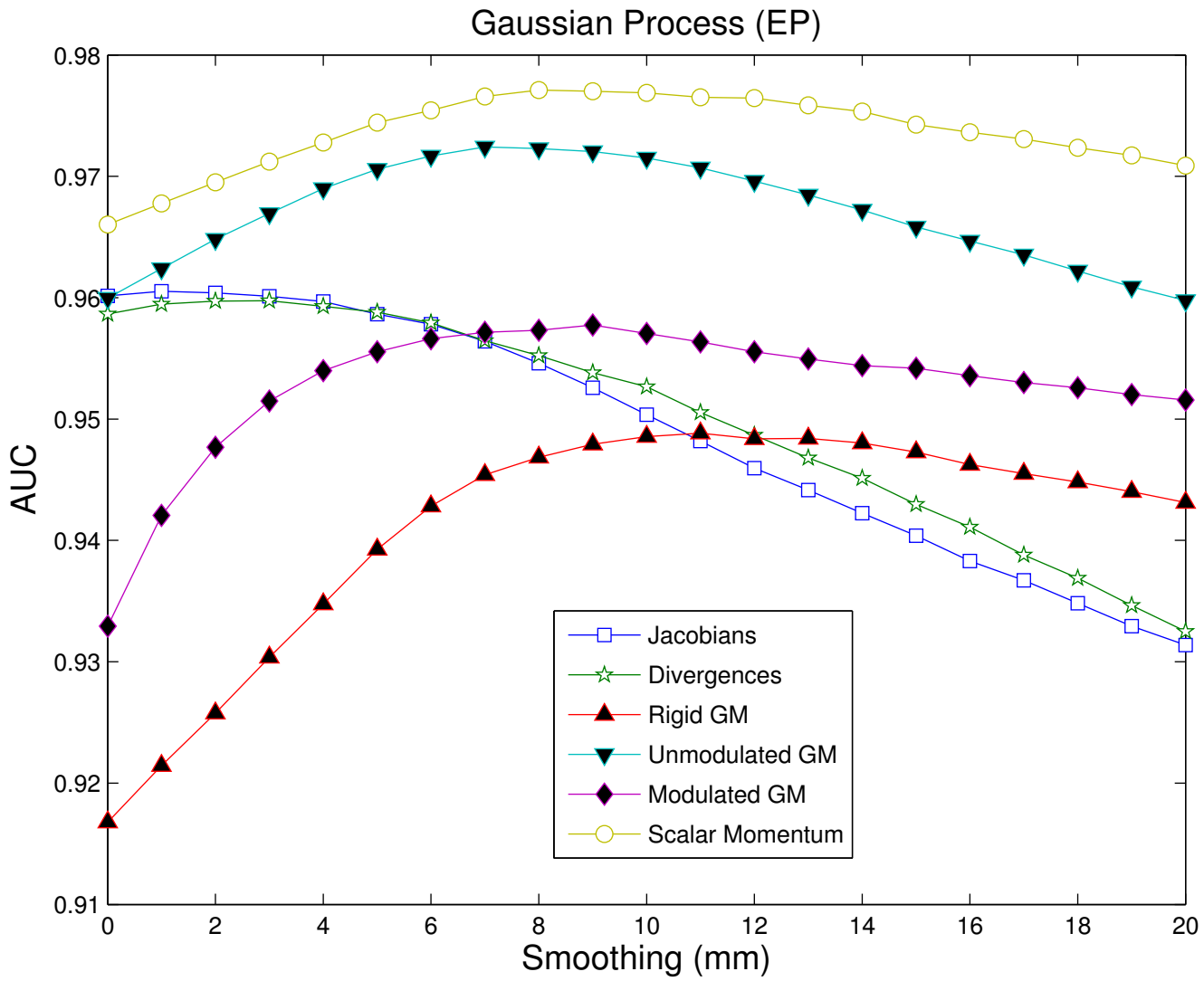
Sex Prediction – Best Result



Sex Prediction – Best Result

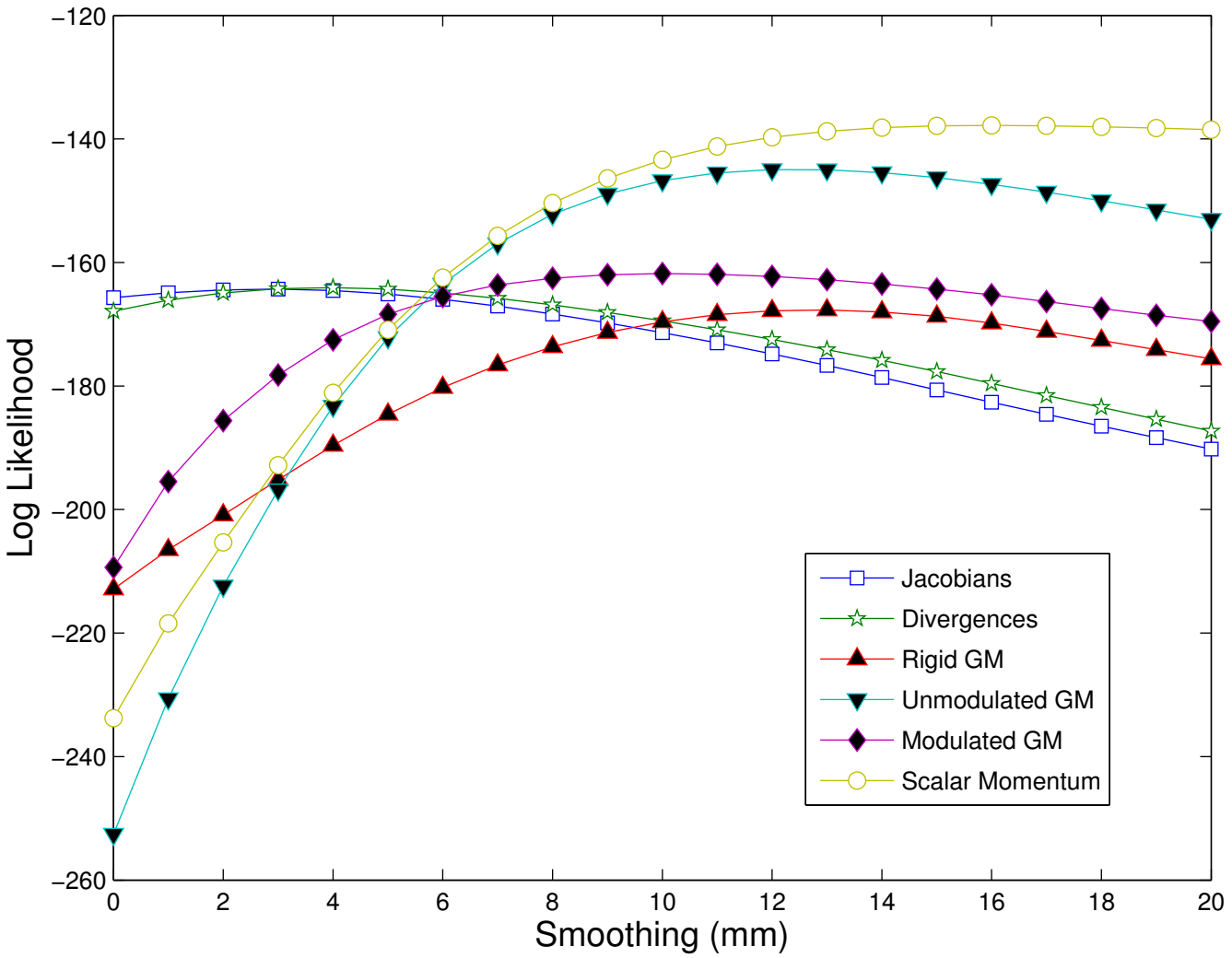


Sex Prediction – Comparison Among Features



Sex Prediction – Model Log Likelihoods

Differences > 4.6 indicate “decisive” evidence in favour of one approach over another.



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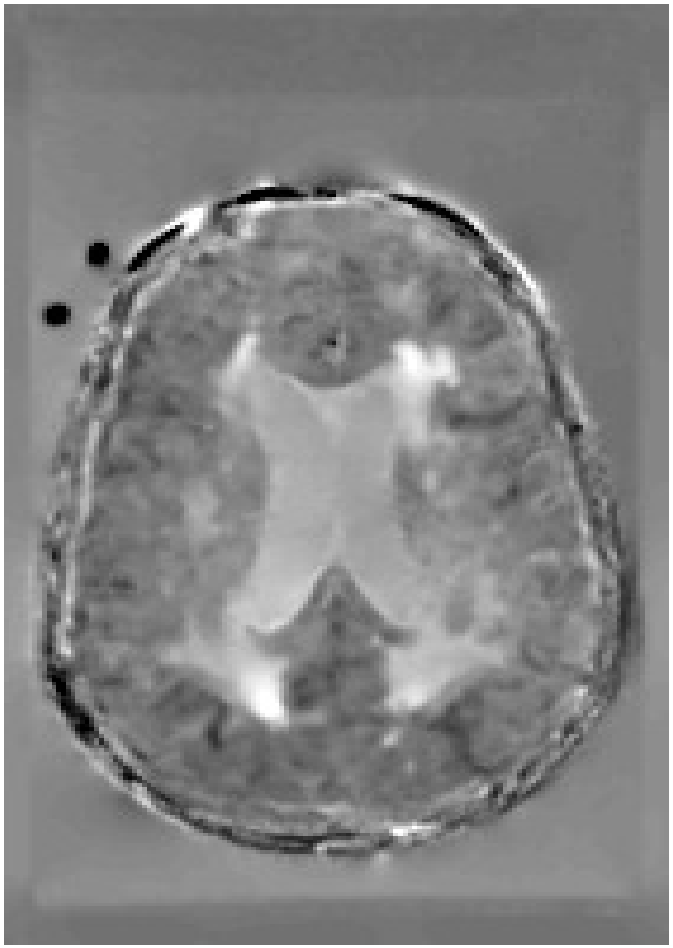
Overview

- Voxel-Based Morphometry
- Tensor-Based Morphometry
- Multivariate Approaches
- Scalar Momentum
- Some Evaluations
- **Longitudinal Registration**

Longitudinal Registration

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

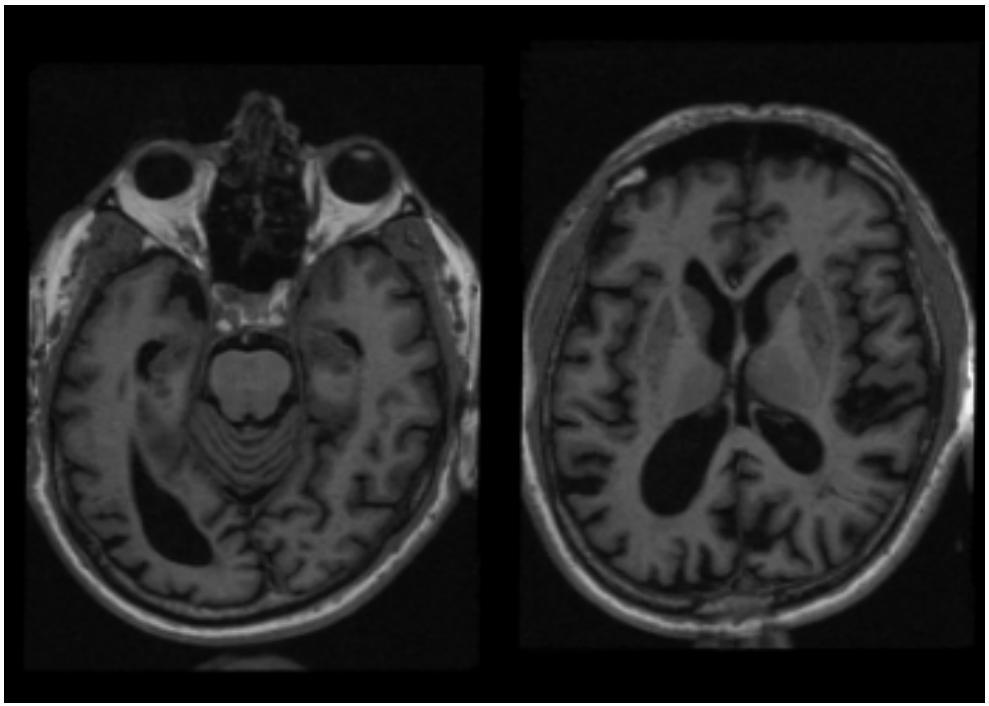


OASIS Data

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

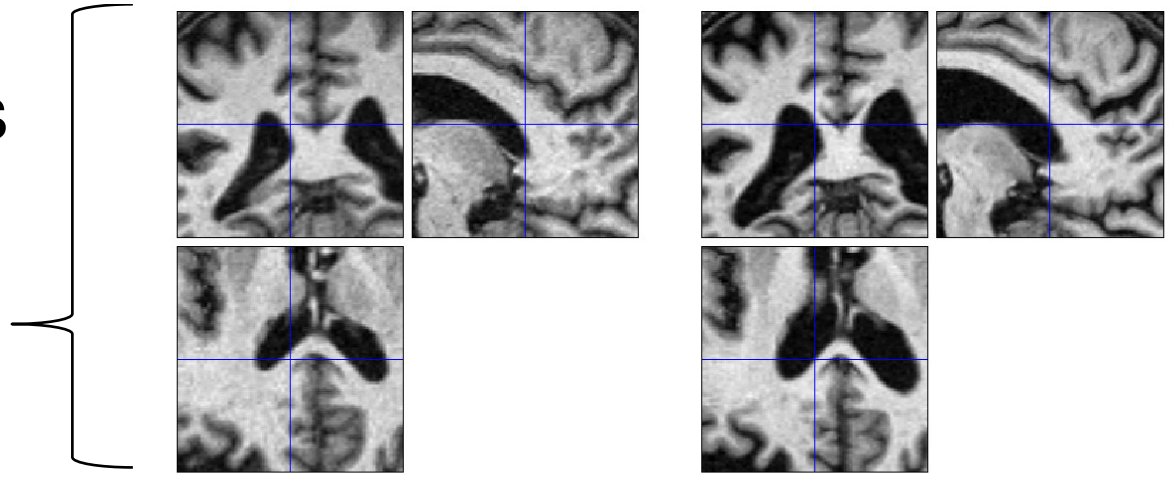
66 year old male with dementia (MMSE=19, CDR=1).

Five scans collected over 40 months.

Expansion/contraction.

Two Longitudinal Scans

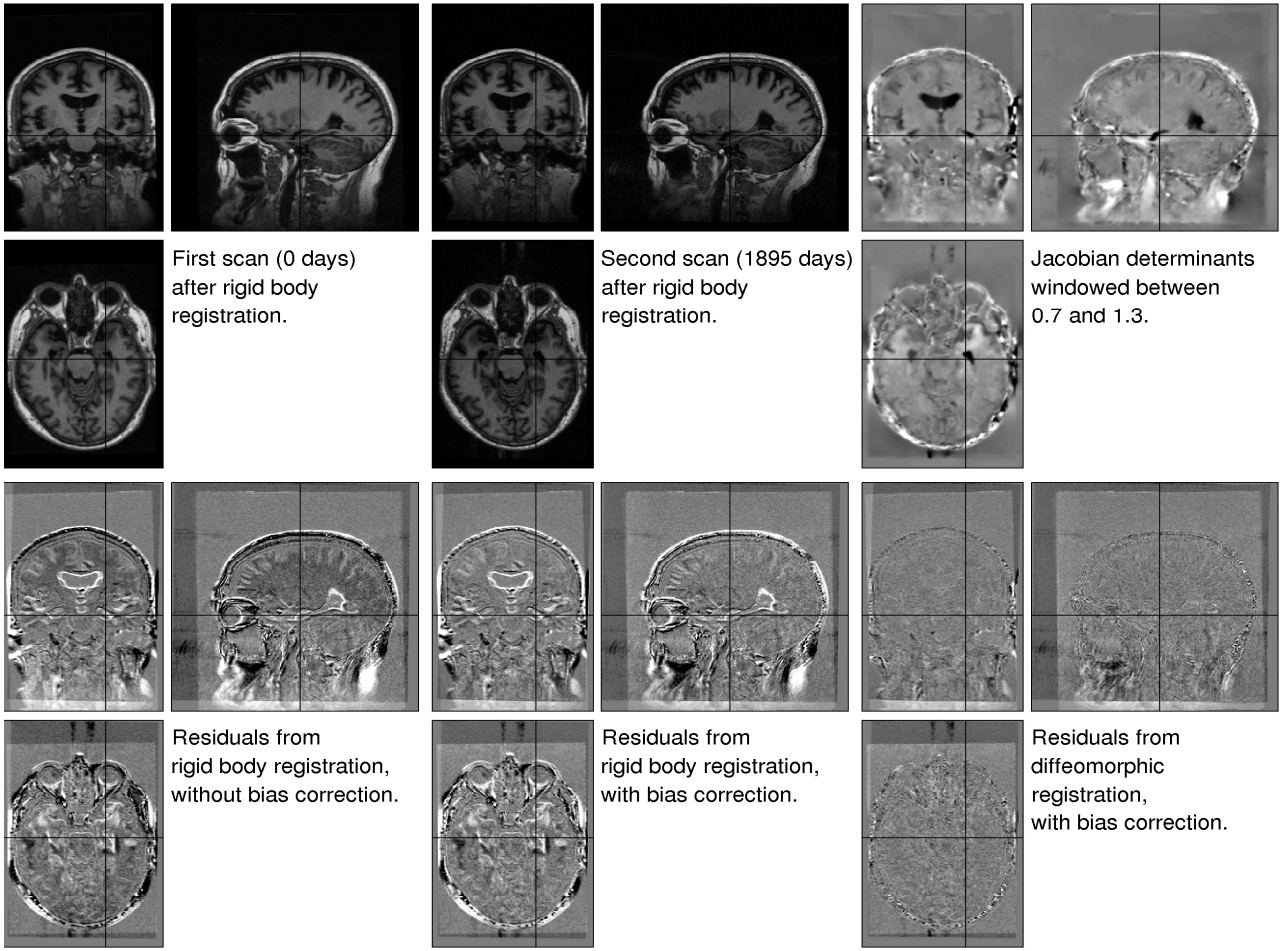
Two scans taken 6 years apart
(after rigid registration).



Oasis Data

OAS2 0002

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



First scan (0 days) after rigid body registration.

Second scan (1895 days) after rigid body registration.

Jacobian determinants windowed between 0.7 and 1.3.

Residuals from rigid body registration, without bias correction.

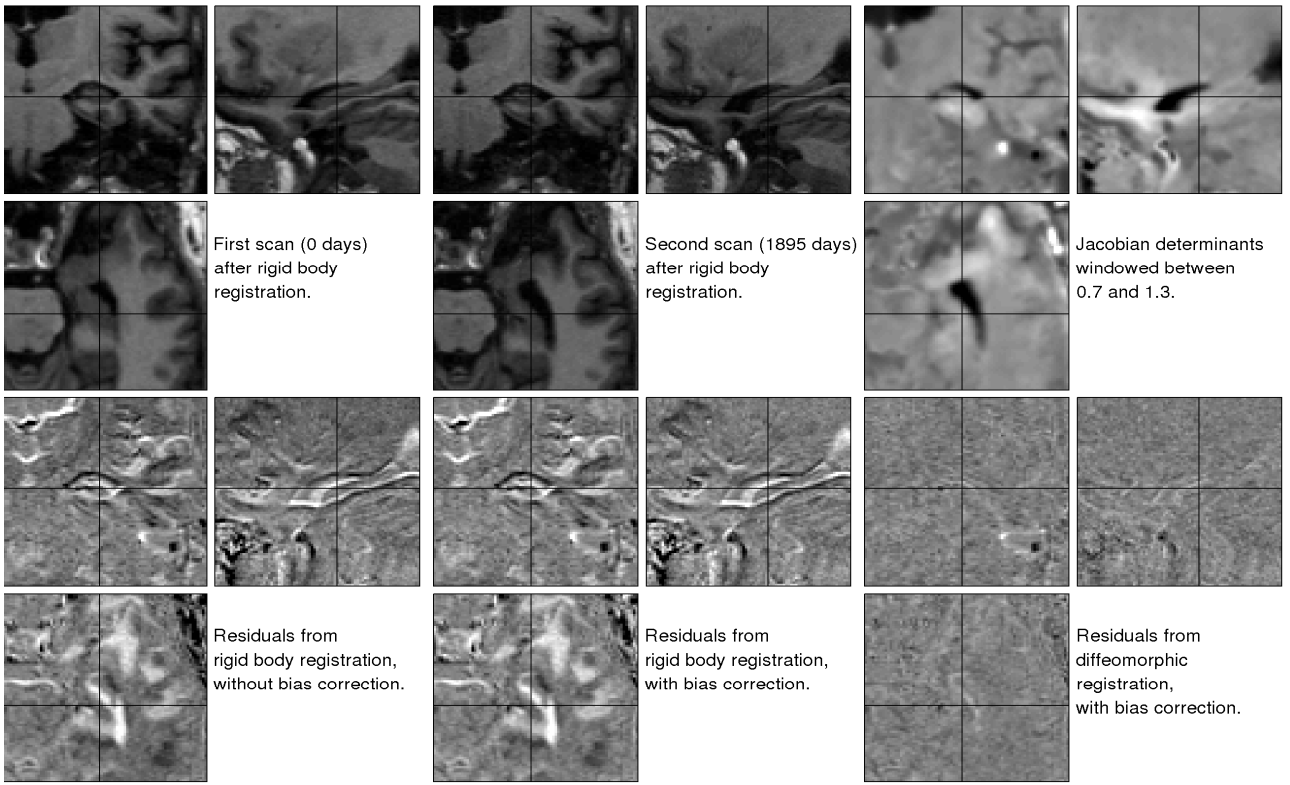
Residuals from rigid body registration, with bias correction.

Residuals from diffeomorphic registration, with bias correction.

Oasis Data

OAS2 0002

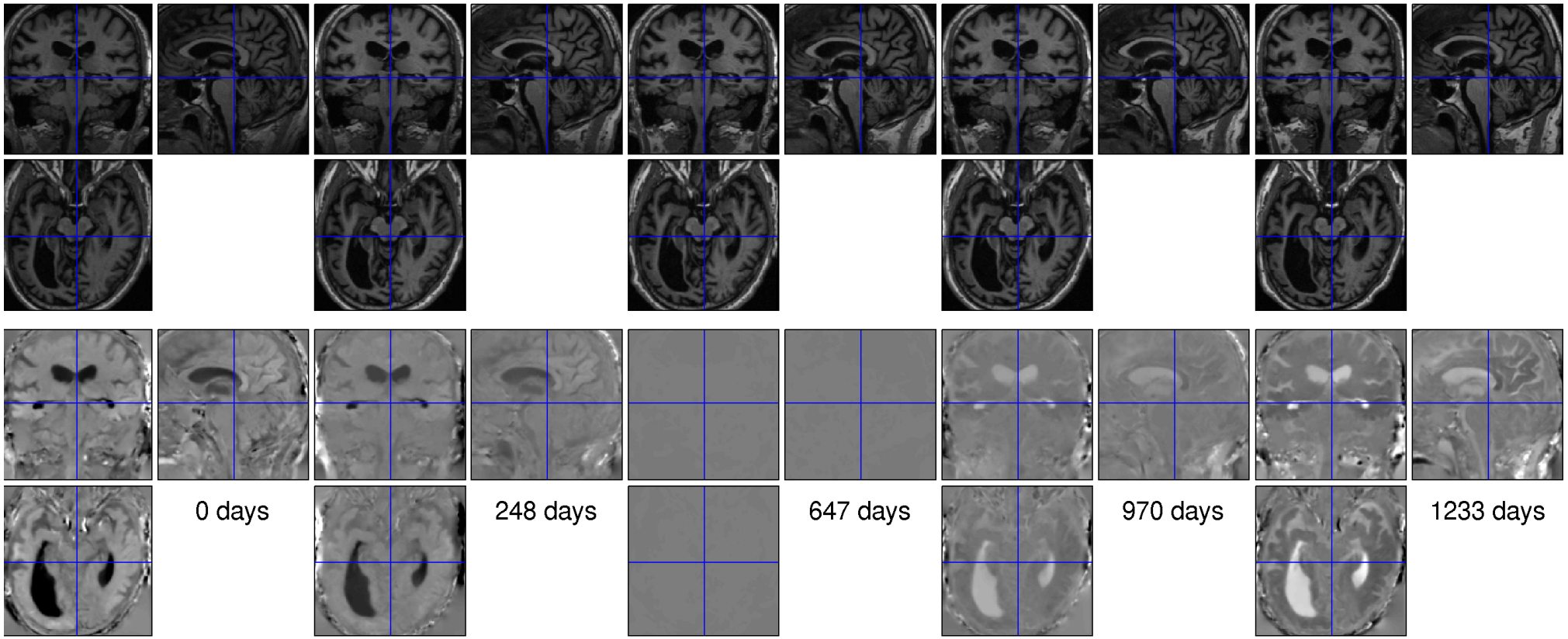
75 year old male, with MCI (MMSE=22, CDR=0.5).



Oasis Data

OAS2 0048

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



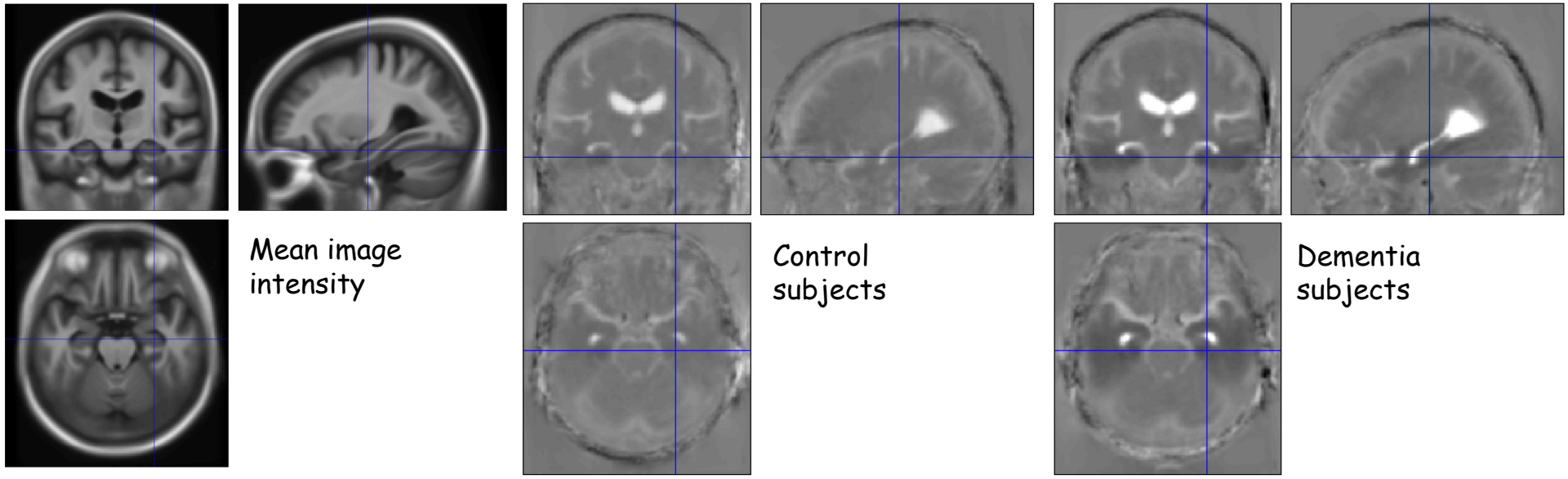
Oasis Data

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.



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