Computational Brain Anatomy

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Overview

- **Voxel-Based Morphometry**
  - **Morphometry in general**
  - **Volumetrics**
  - **VBM preprocessing followed by SPM**
- Tissue Segmentation
- Diffeomorphic Registration
- Longitudinal Registration
- Multivariate Shape Models

Measuring differences with MRI

- What are the significant differences between populations of subjects?
- What effects do various genes have on the brain?
- What changes occur in the brain through development or aging?

- A significant amount of the difference (measured with MRI) is anatomical.

There are many ways to model differences.

- Usually, we try to localise regions of difference.
  - **Univariate models**.
  - Using methods similar to SPM
  - Typically localising volumetric differences

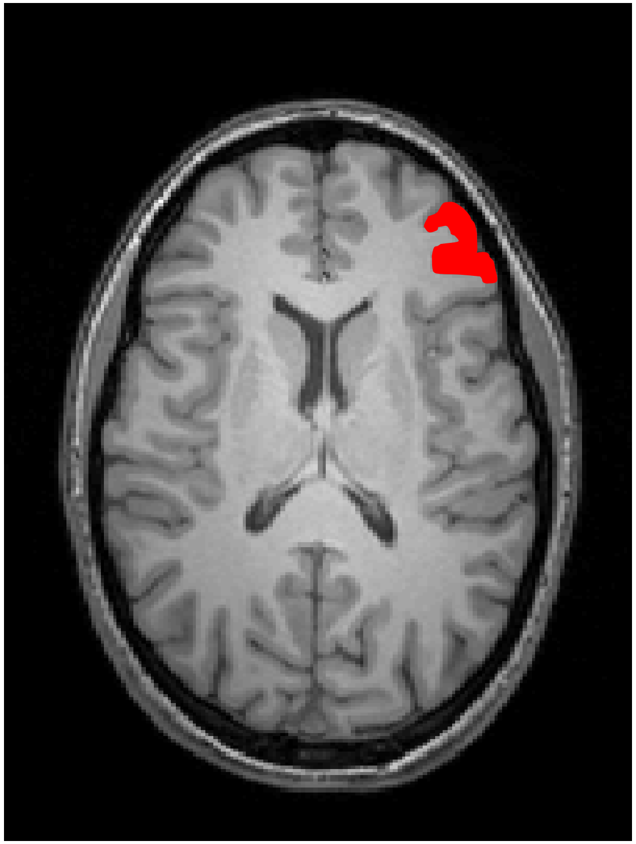
- Some anatomical differences can not be localised.
  - Need **multivariate models**.
  - Differences in terms of proportions among measurements.
  - Where would the difference between male and female faces be localised?

- Need to select the best model of difference to use, before trying to fill in the details.

Voxel-Based Morphometry

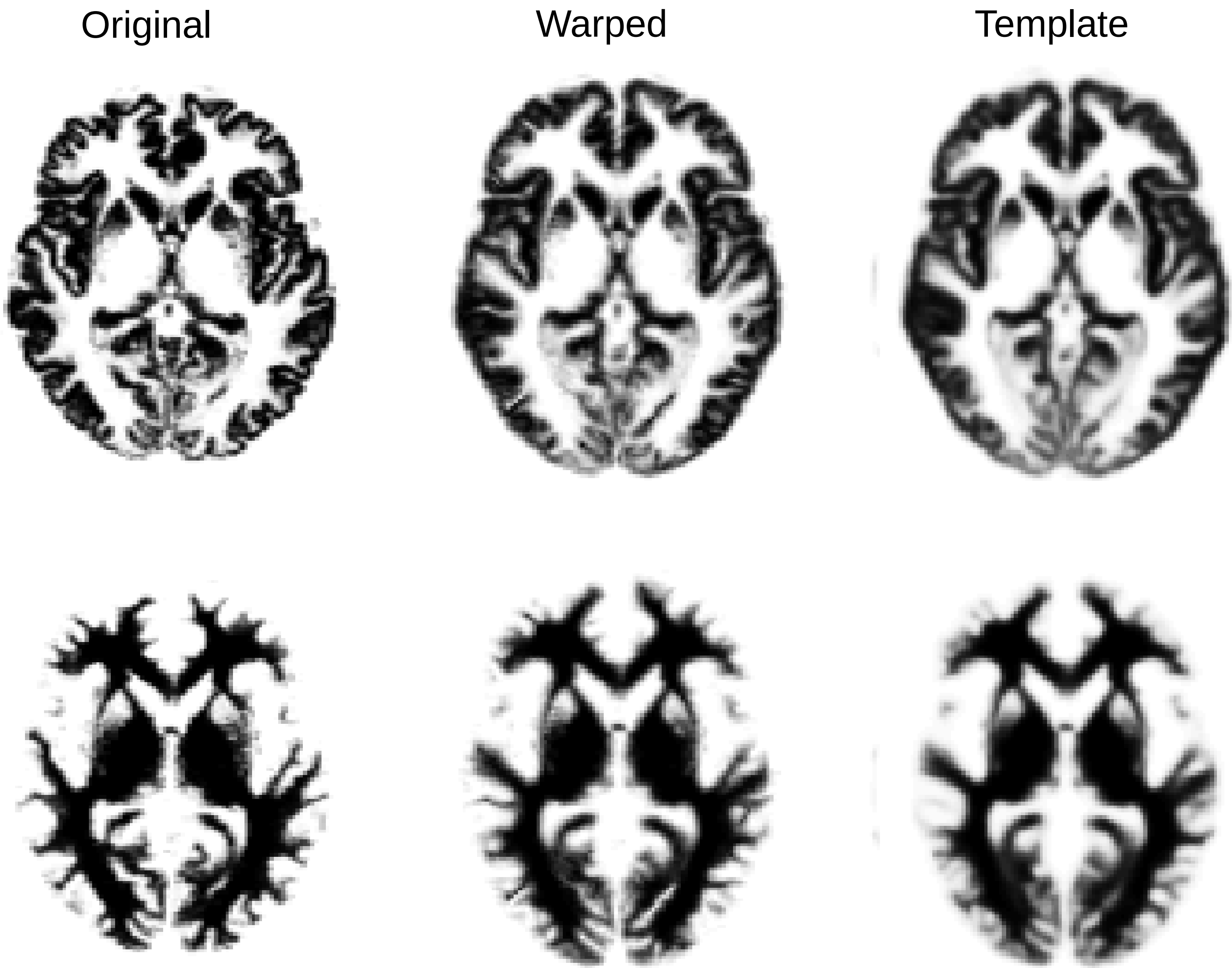
- Based on comparing **regional volumes of tissue**.
- Produce a map of statistically significant differences among populations of subjects.
  - e.g. compare a patient group with a control group.
  - or identify correlations with age, test-score etc.
- The data are pre-processed to sensitise the tests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

Volumetry

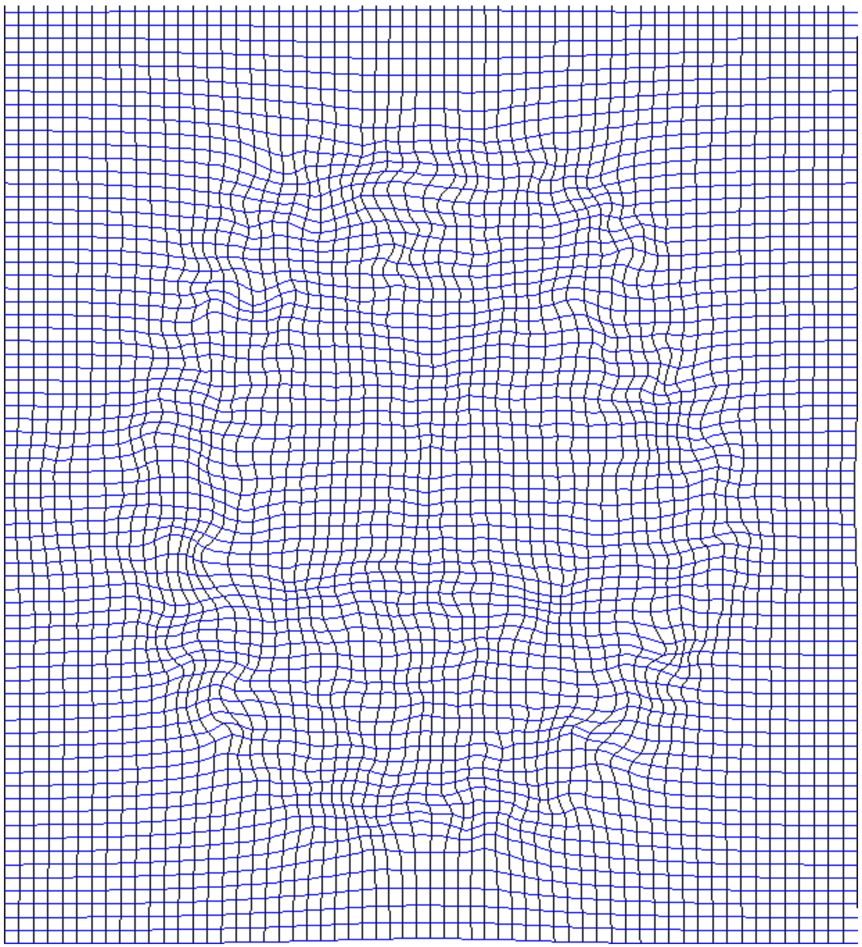


T1-Weighted MRI

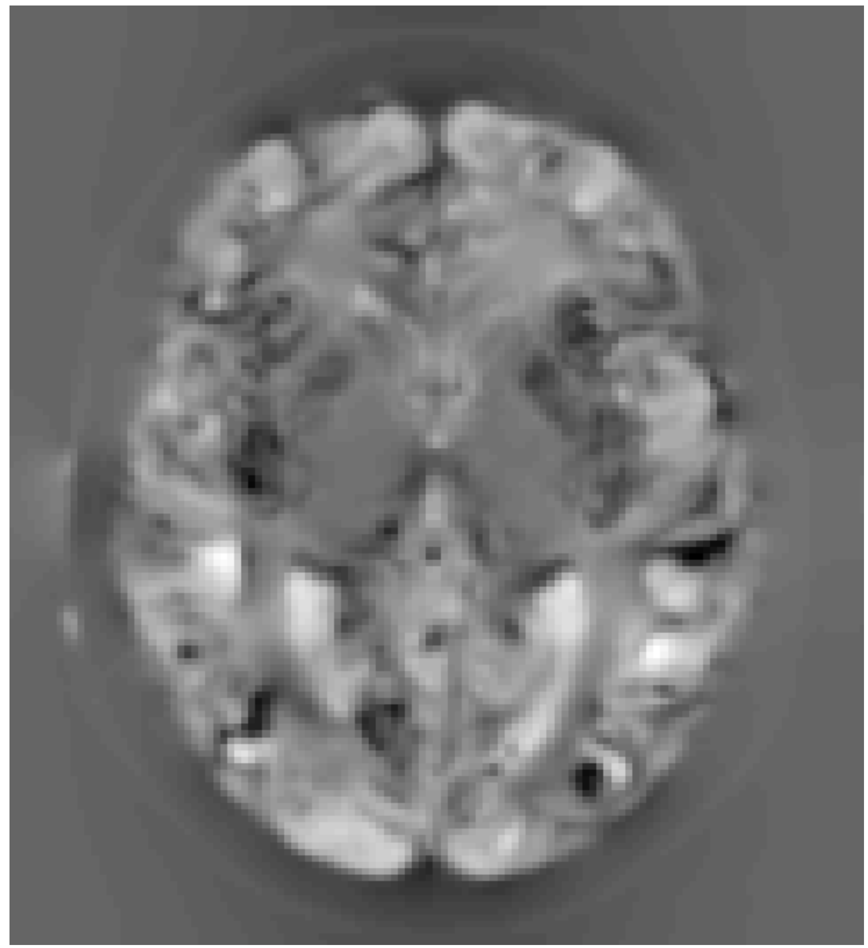
Grey Matter


Original
Warped
Template

“Modulation” – change of variables.



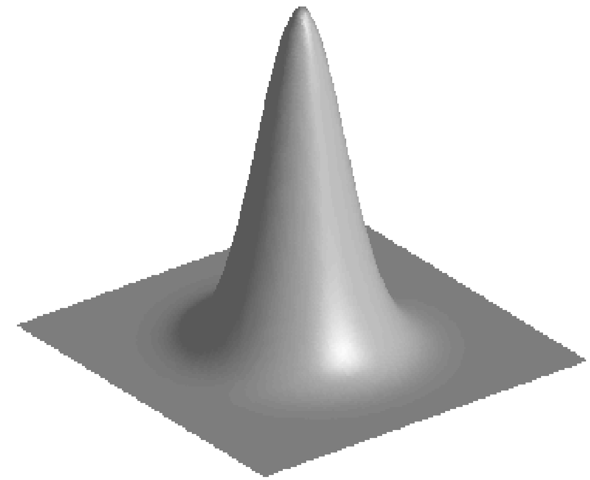
Deformation Field



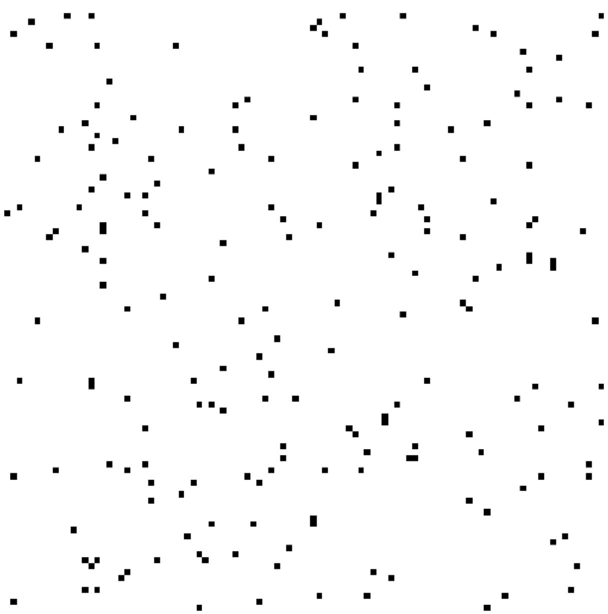
Jacobians determinants
Encode relative volumes.

Smoothing

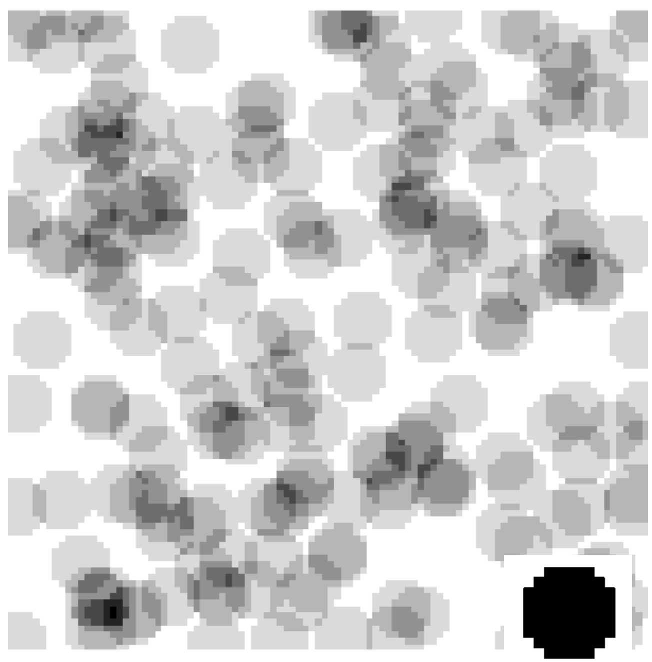
Each voxel after smoothing effectively becomes the result of applying a weighted region of interest (ROI).



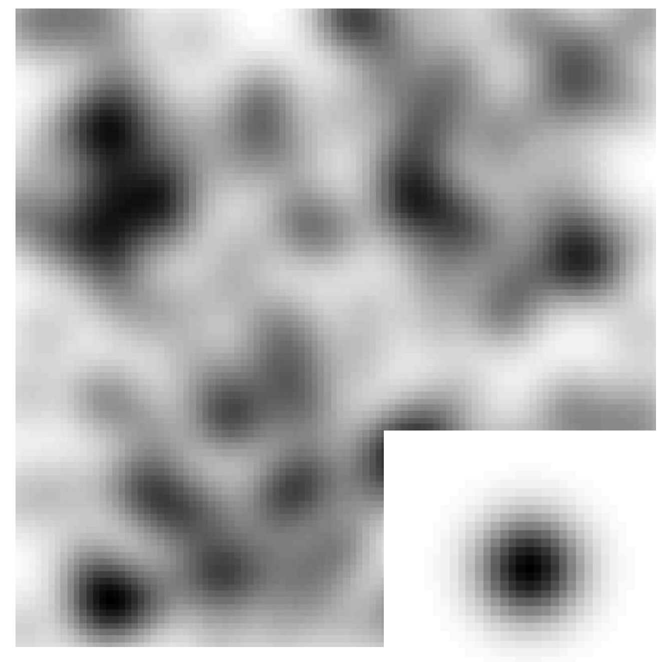
Before convolution



Convolved with a circle

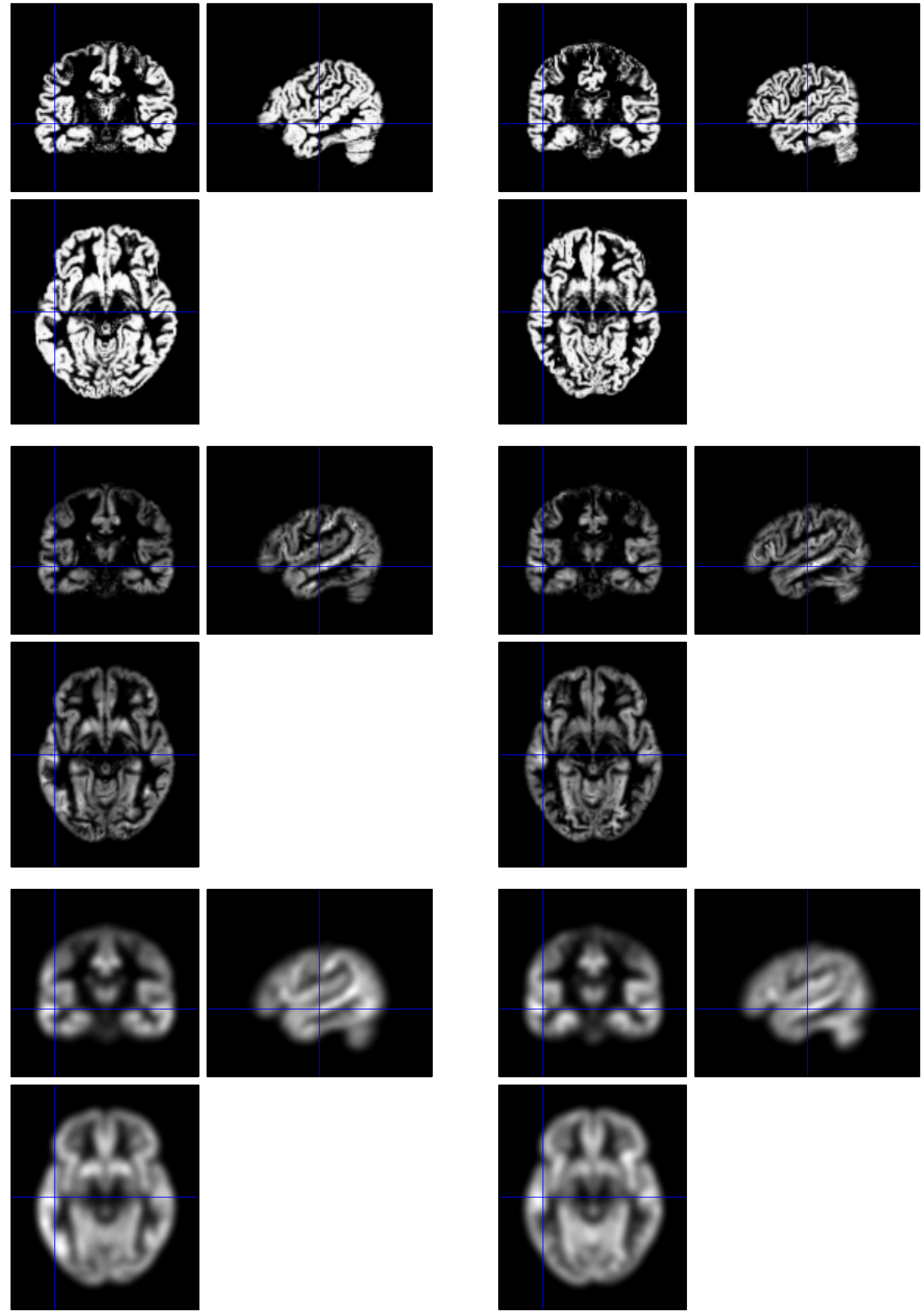


Convolved with a Gaussian

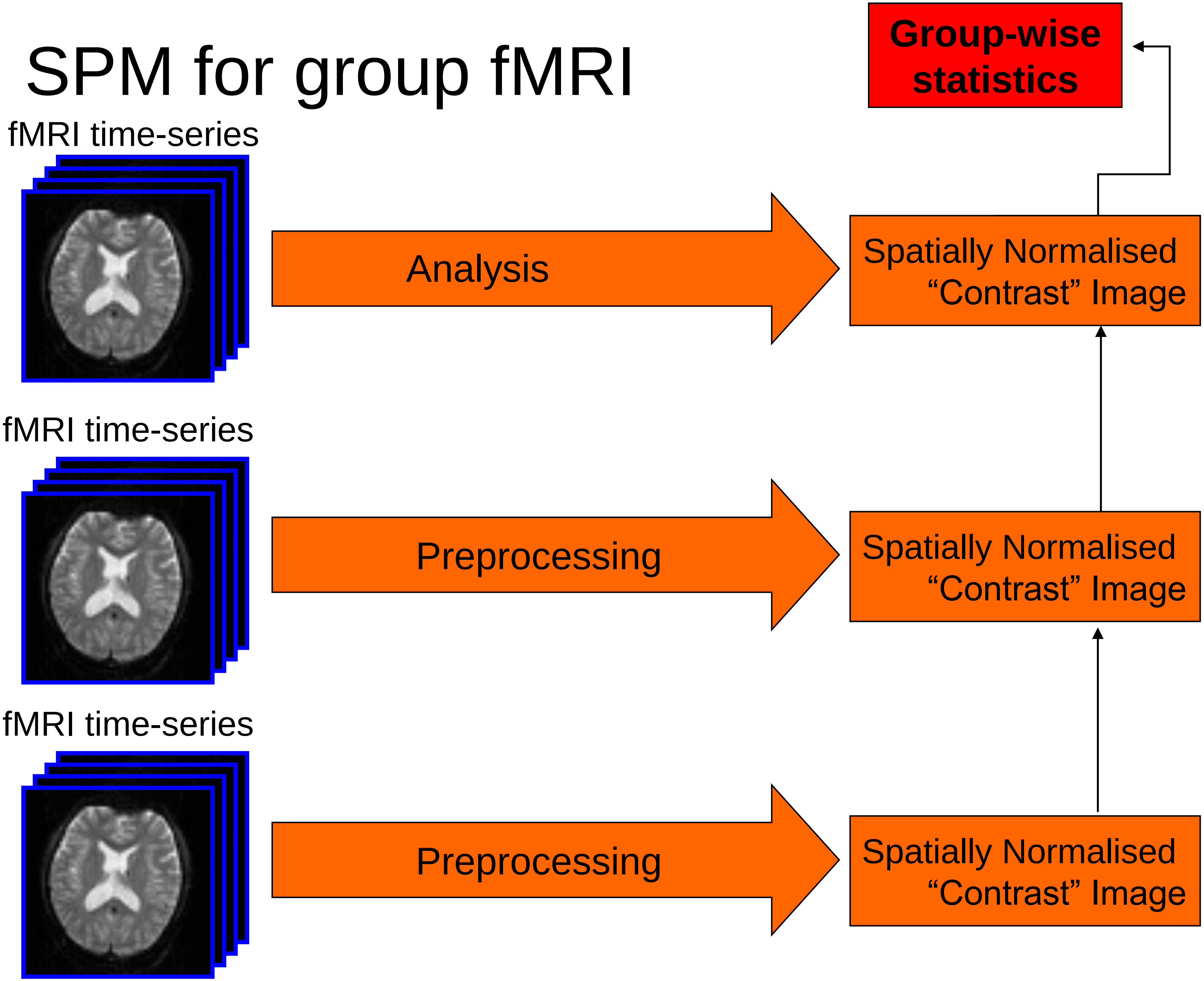


VBM Pre-processing in SPM12

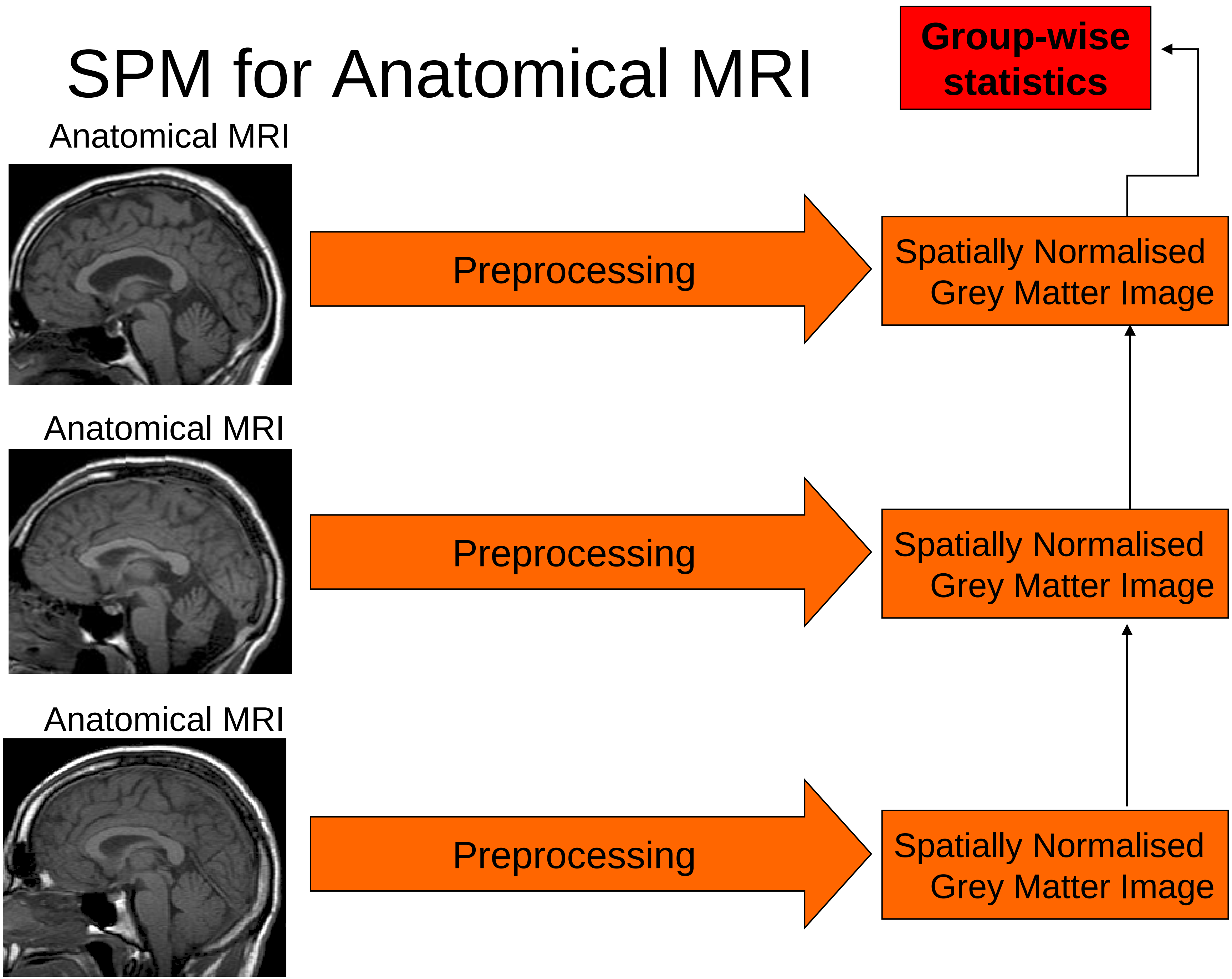
- Use Segment for characterising intensity distributions of tissue classes, and writing out “imported” images that Dartel can use.
- Run Dartel to estimate all the deformations.
- Dartel warping to generate smoothed, “modulated”, warped grey matter.
- Statistics.



SPM for group fMRI

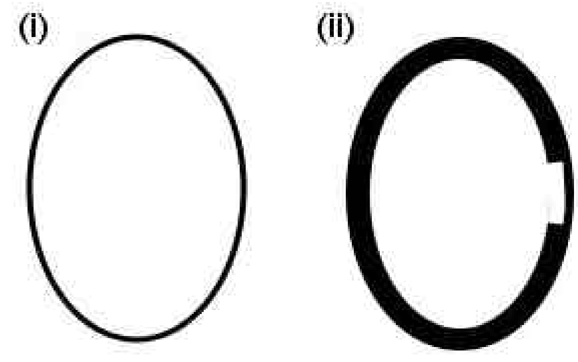


SPM for Anatomical MRI



“Globals” for VBM

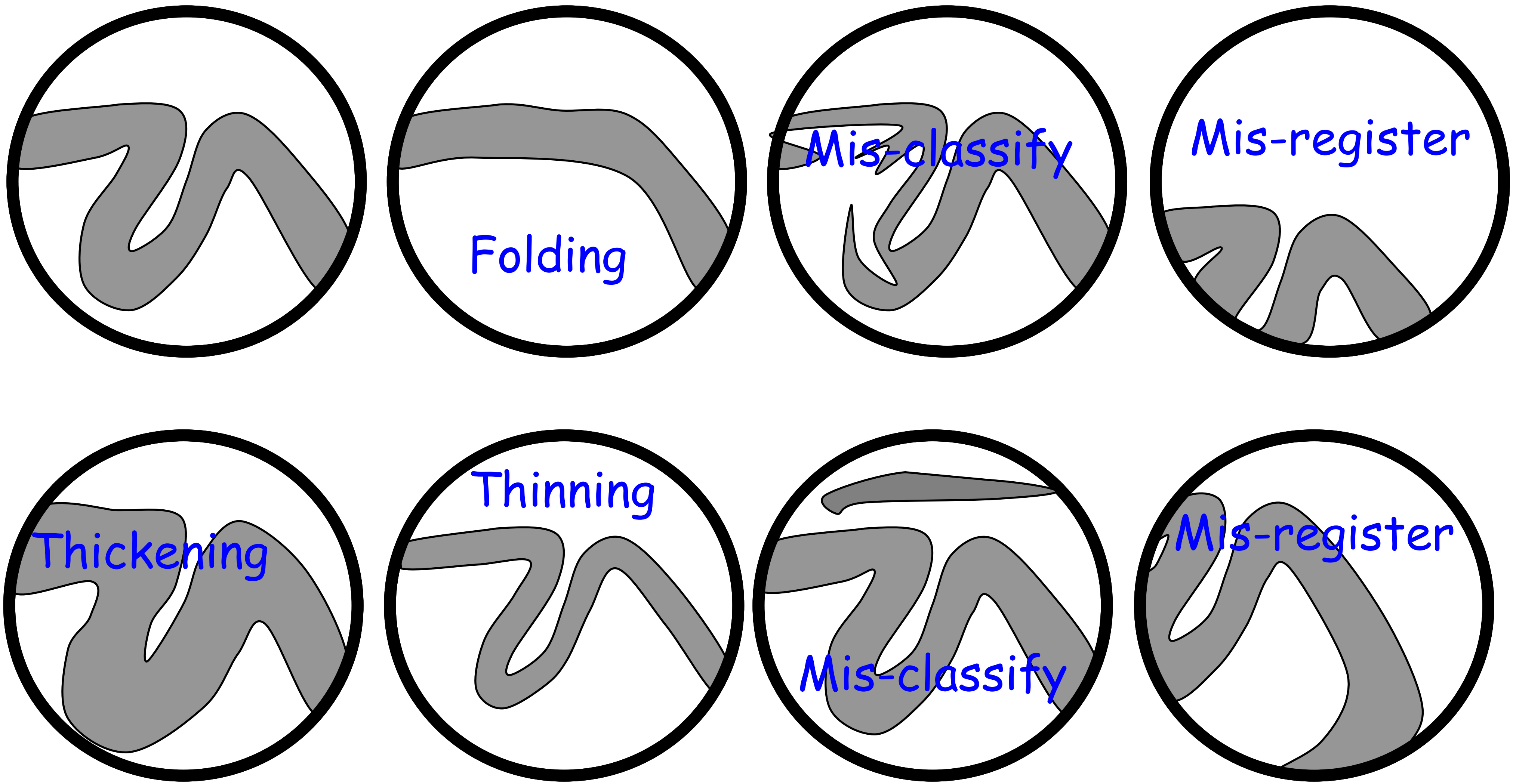
- Shape is really a multivariate concept
  - Dependencies among different regions
- SPM is mass univariate
  - Combining voxel-wise information with “global” integrated tissue volume provides a compromise
  - Either ANCOVA or proportional scaling.



(ii) is globally thicker, but locally thinner than (i) – either of these effects may be of interest to us.

- Total intracranial volume (TIV) integrates GM, WM and CSF, or attempts to measure the skull-volume directly
  - Can still identify global brain shrinkage (skull is fixed!)
  - Can give more powerful and/or more interpretable results
  - See also Pell et al (2009) doi:10.1016/j.neuroimage.2008.02.050

Some Explanations of the Differences



Selected References

- Wright, McGuire, Poline, Travere, Murray, Frith, Frackowiak & Friston (1995). "*A voxel-based method for the statistical analysis of gray and white matter density applied to schizophrenia*". Neuroimage 2(4):244-252.
- Ashburner & Friston (2000). "*Voxel-based morphometry-the methods*". Neuroimage 11(6):805-821.
- Mechelli et al. (2005) "*Voxel-based morphometry of the human brain: Methods and applications*". Current Medical Imaging Reviews 1(2):105-103.
- Ashburner (2009). "*Computational Anatomy with the SPM software*". Magnetic Resonance Imaging 27(8):1163-1174.

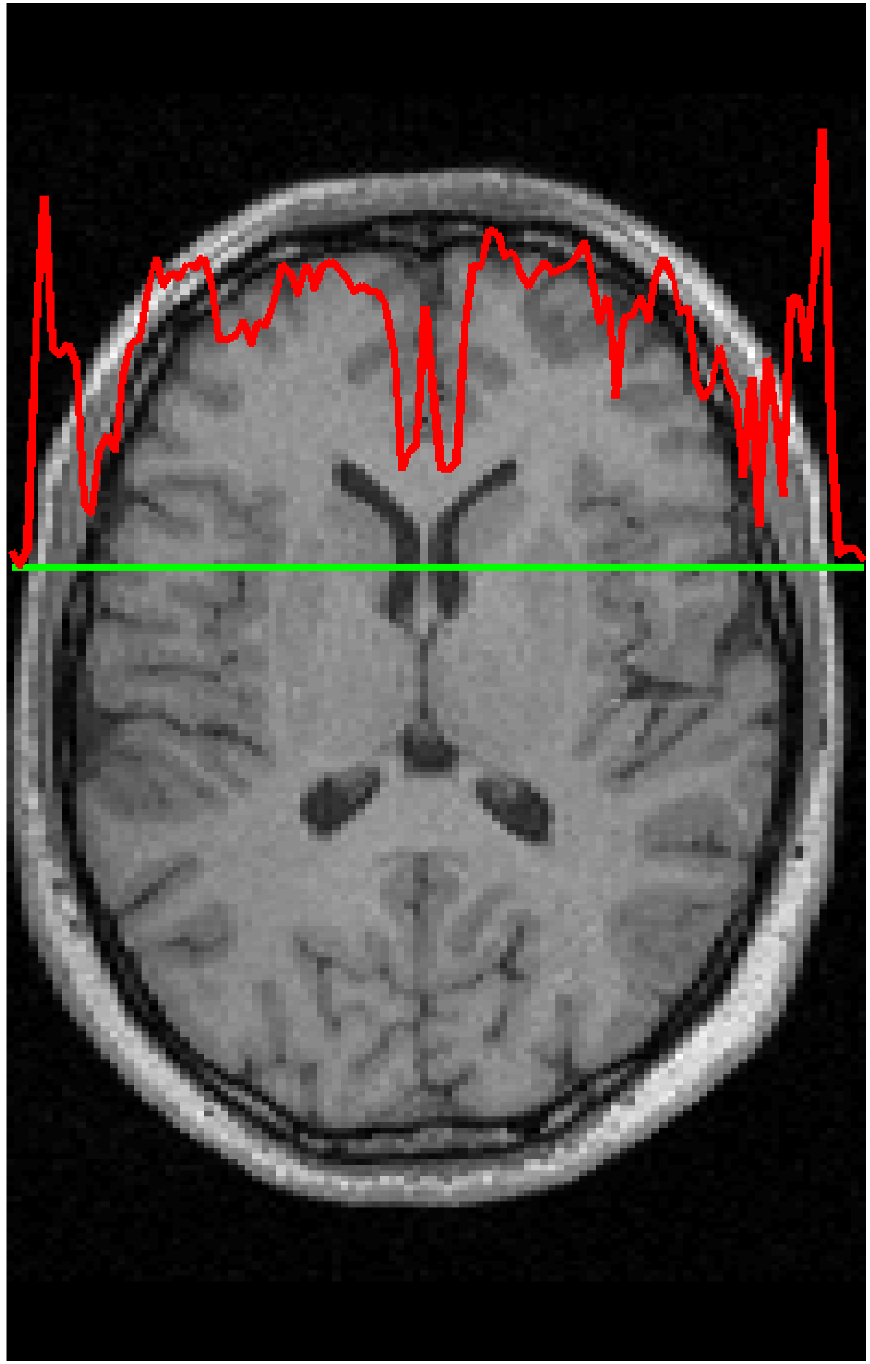
Overview

- Voxel-Based Morphometry
- **Tissue Segmentation**
  - **Gaussian mixture model**
  - **Intensity non-uniformity correction**
  - **Deformed tissue probability maps**
- Diffeomorphic Registration
- Longitudinal Registration
- Multivariate Shape Models

Segmentation

- Segmentation in SPM8 also estimates a spatial transformation that can be used for spatially normalising images.

- It uses a generative model, which involves:
  - Mixture of Gaussians (MOG)
  - Bias Correction Component
  - Warping (Non-linear Registration) Component



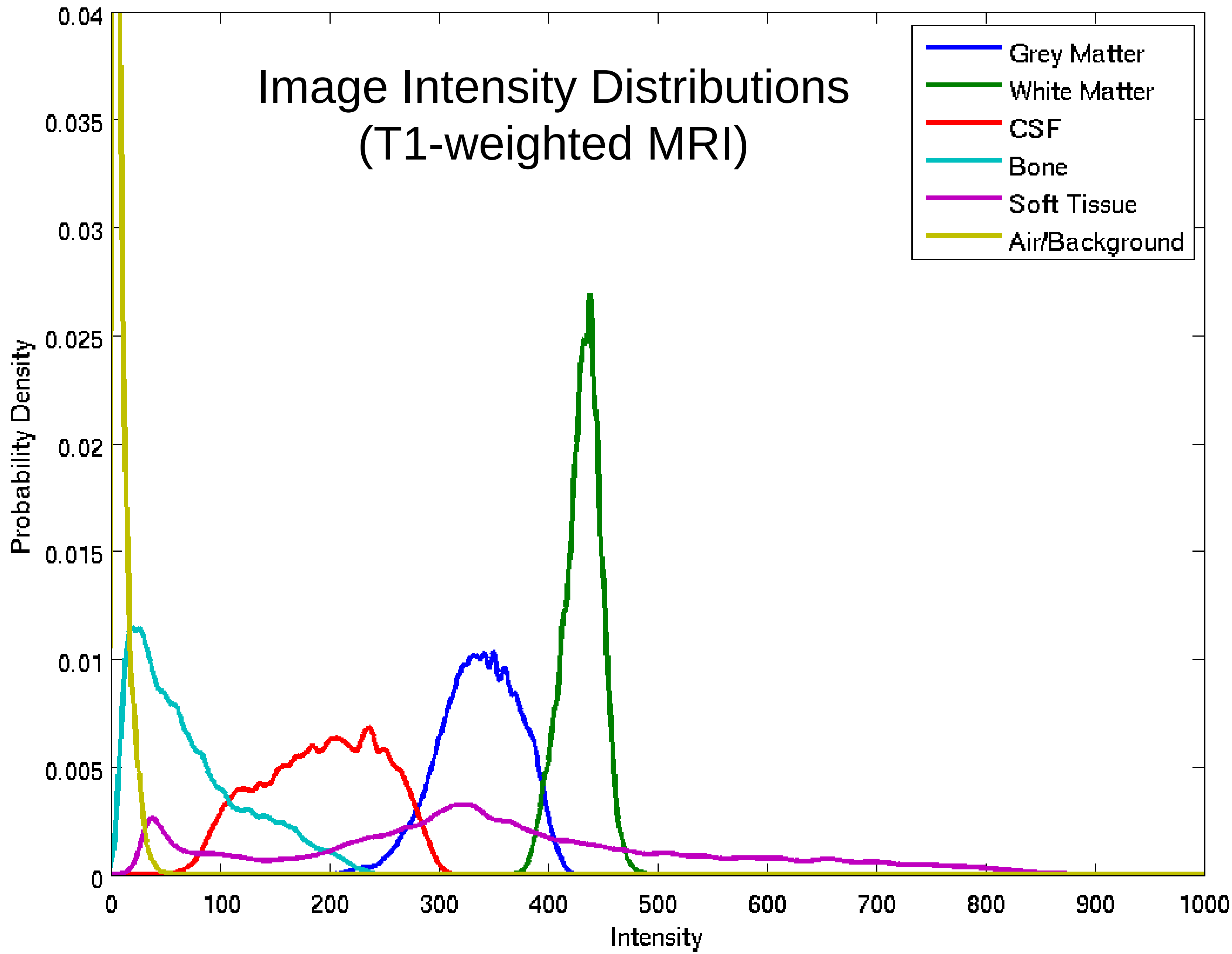
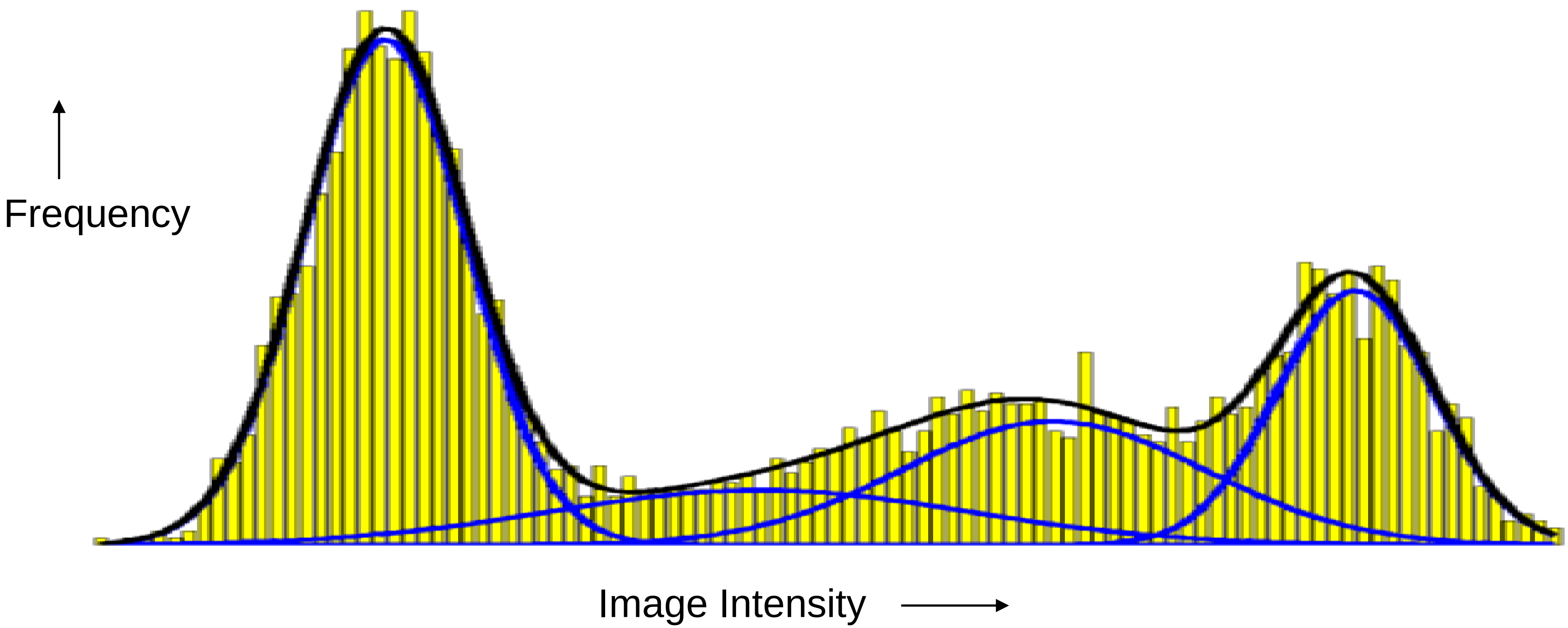


Image Intensity Distributions
(T1-weighted MRI)
Grey Matter
White Matter
CSF
Bone
Soft Tissue
Air/Background
Probability Density
Intensity
0
0.005
0.01
0.015
0.02
0.025
0.03
0.035
0.04
0
100
200
300
400
500
600
700
800
900
1000

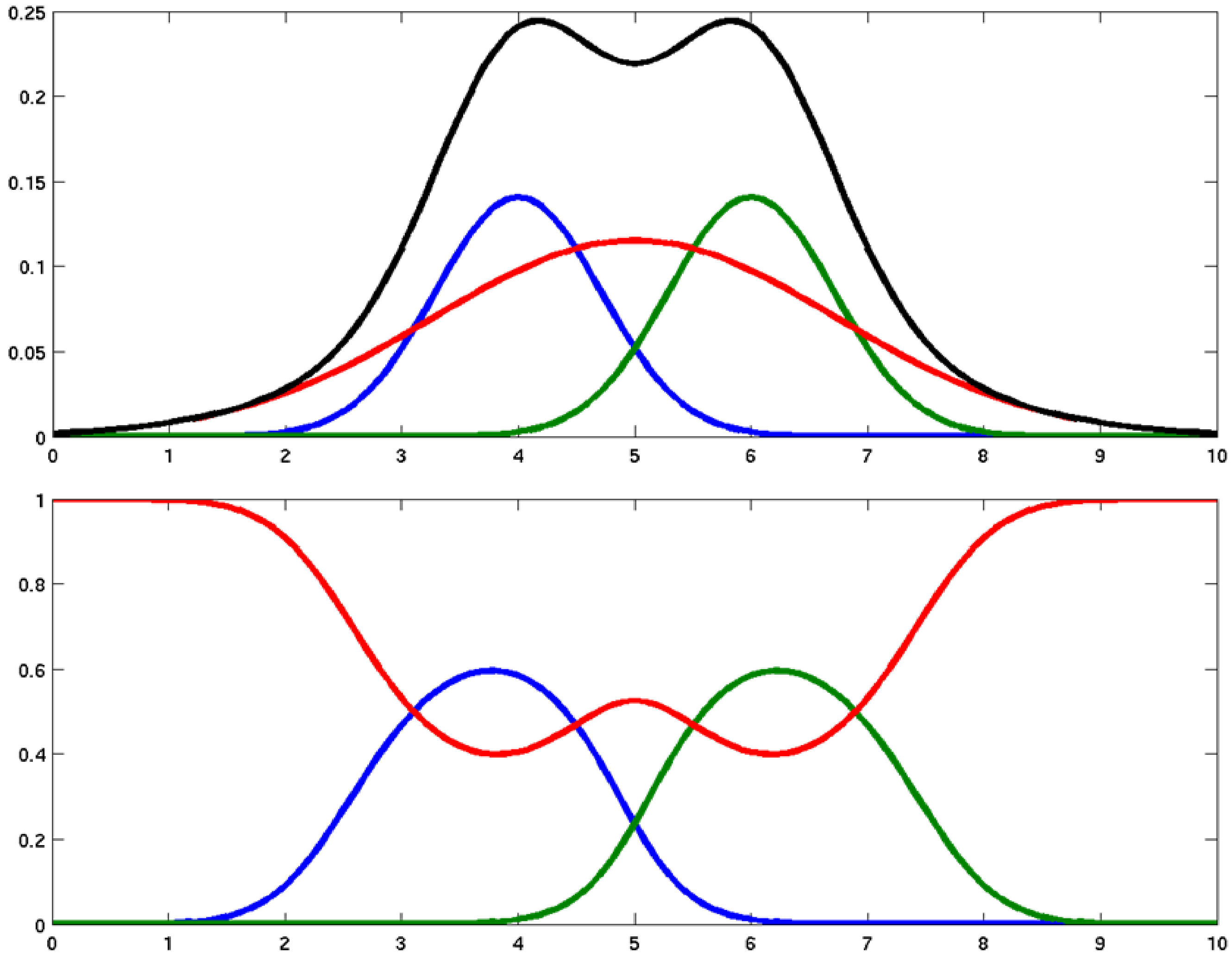
Mixture of Gaussians (MOG)

- Classification is based on a Mixture of Gaussians model (MOG), which represents the intensity probability density by a number of Gaussian distributions.

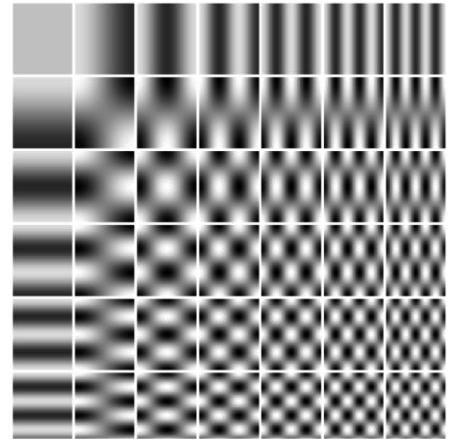


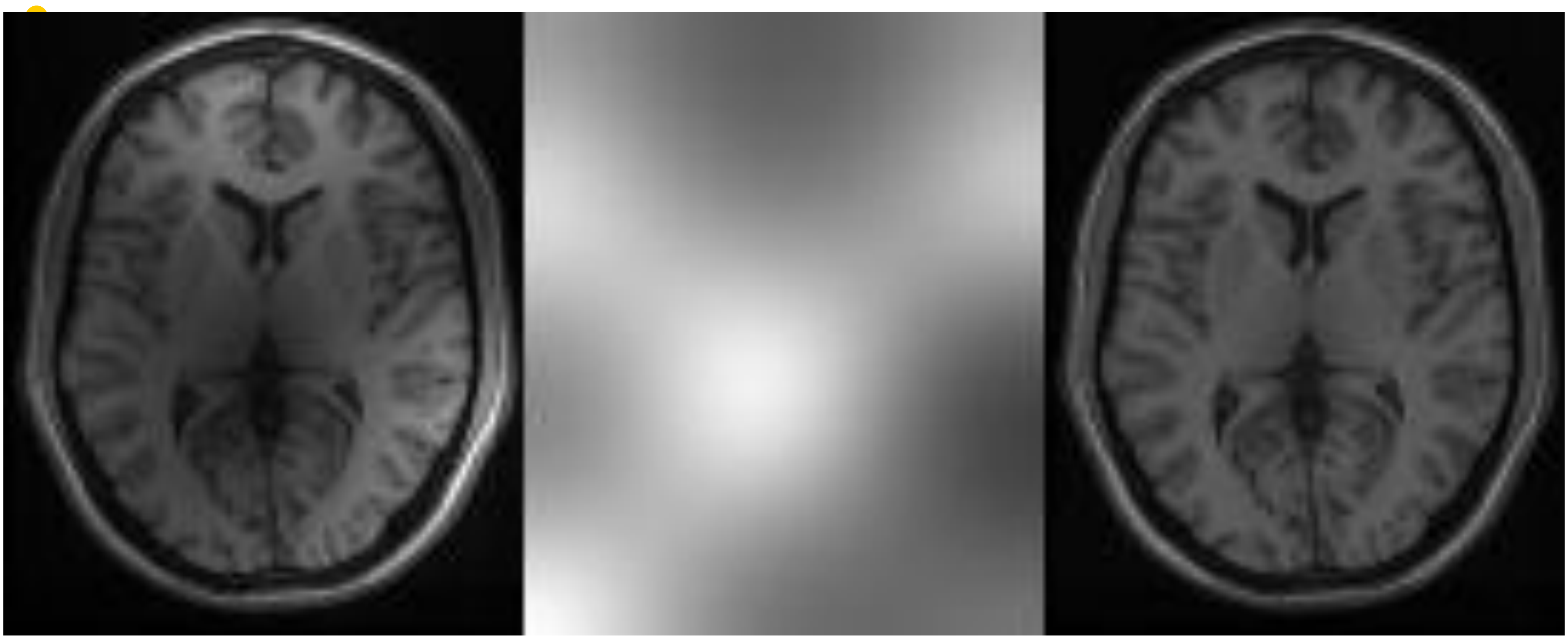
Belonging Probabilities

Belonging probabilities are assigned by normalising to one.



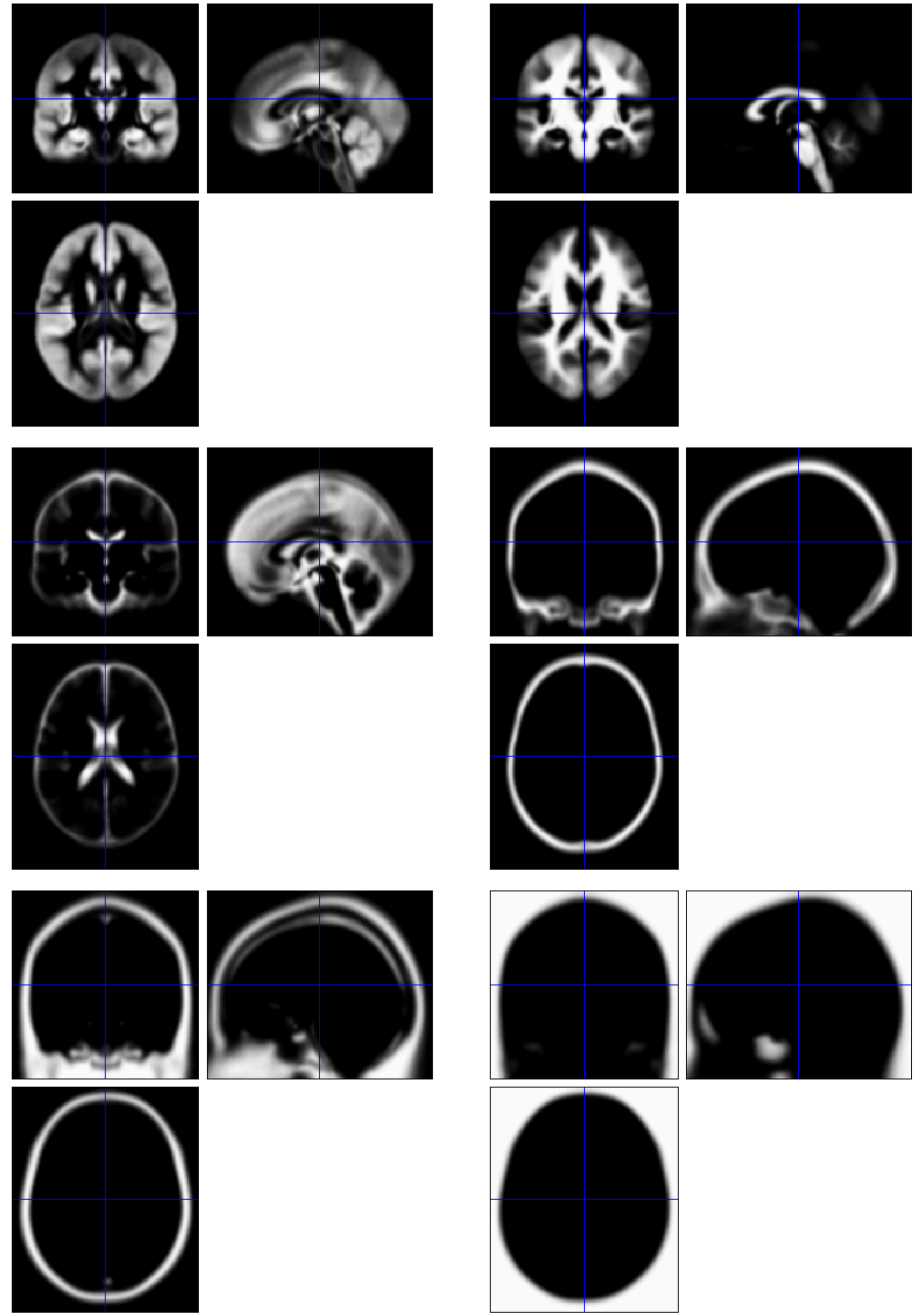
Modelling a Bias Field





Corrupted image **Bias Field** **Corrected image**

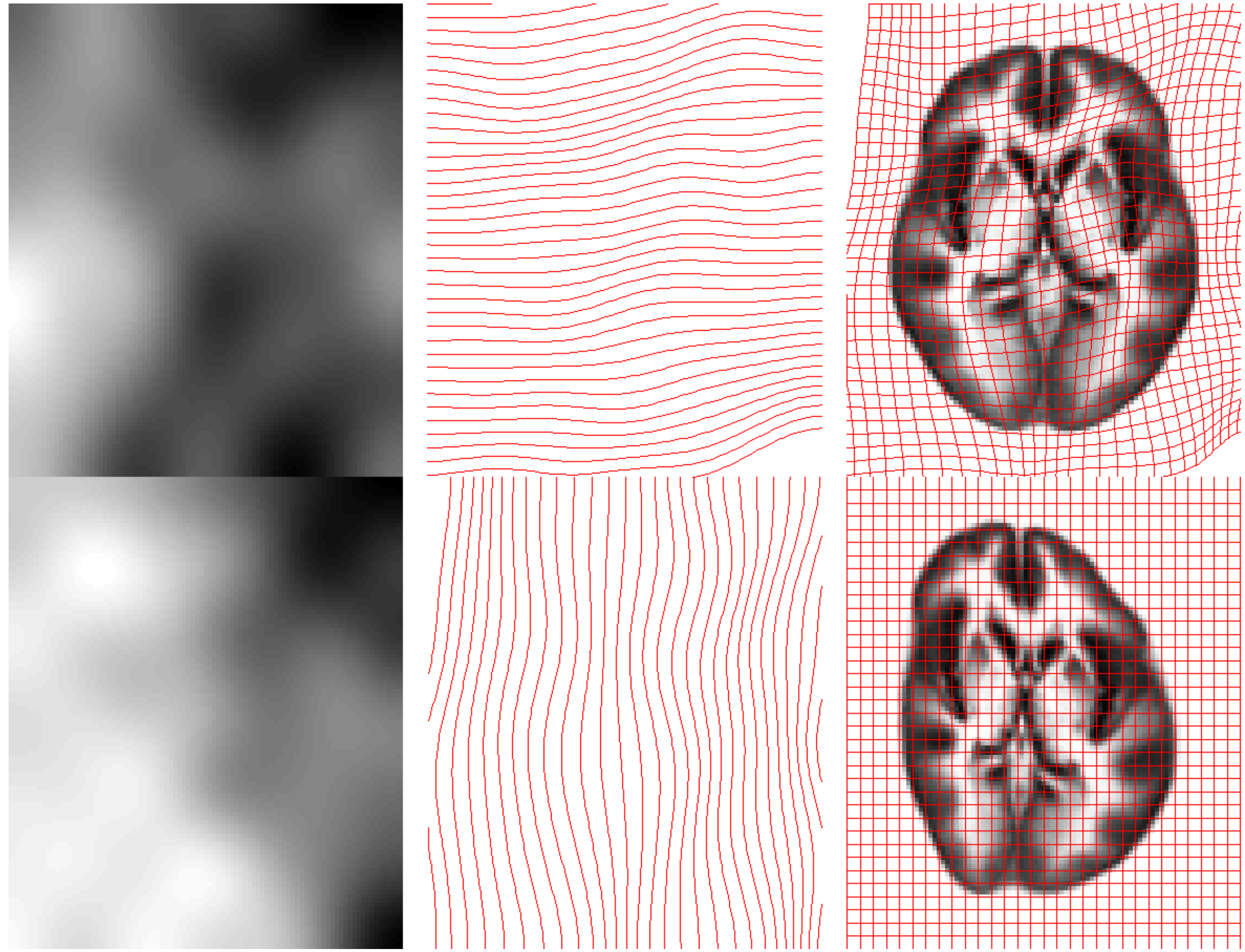
Tissue Probability Maps

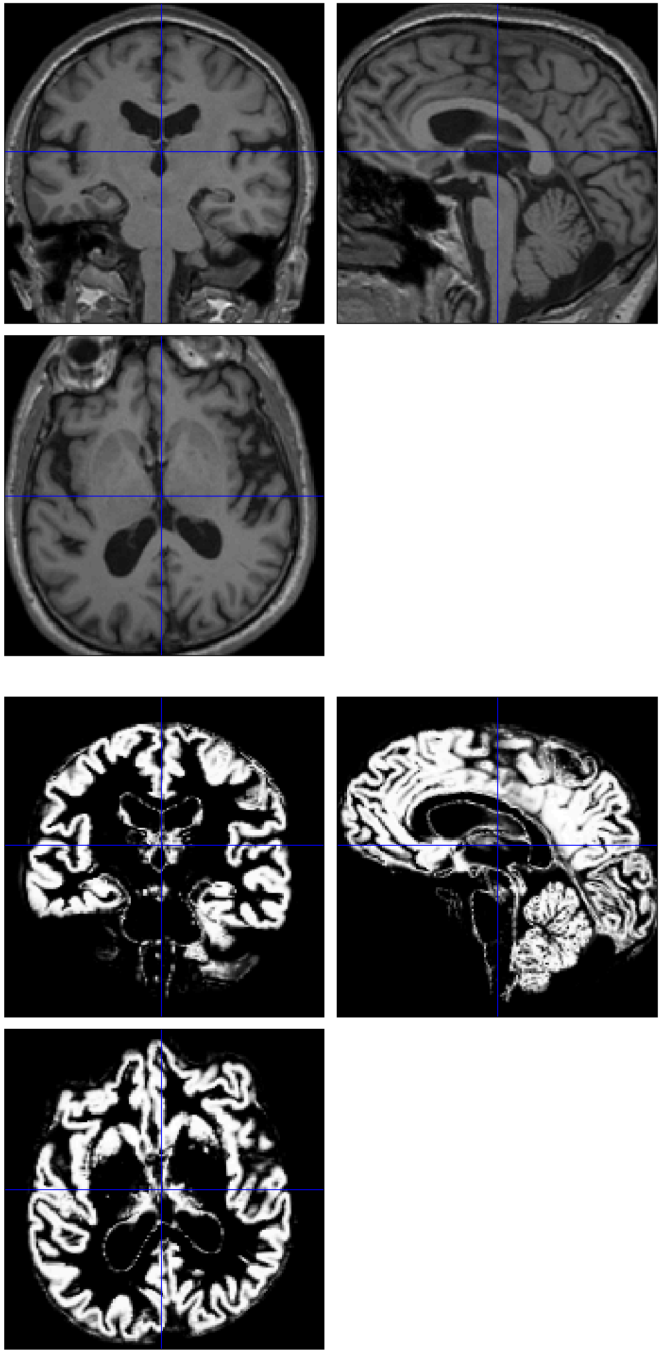


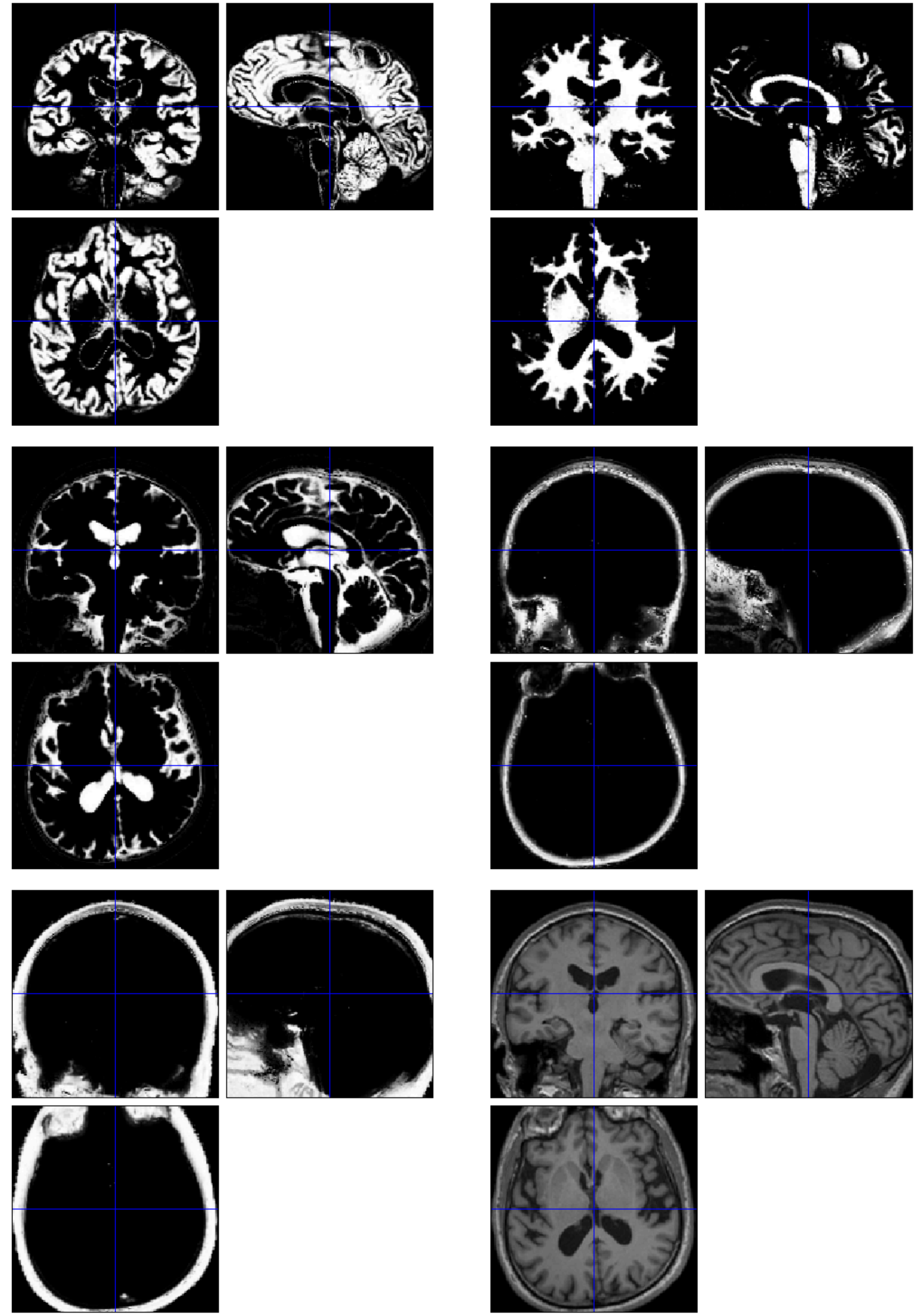
Includes additional non-brain tissue classes (bone, and soft tissue)

Deforming the Tissue Probability Maps

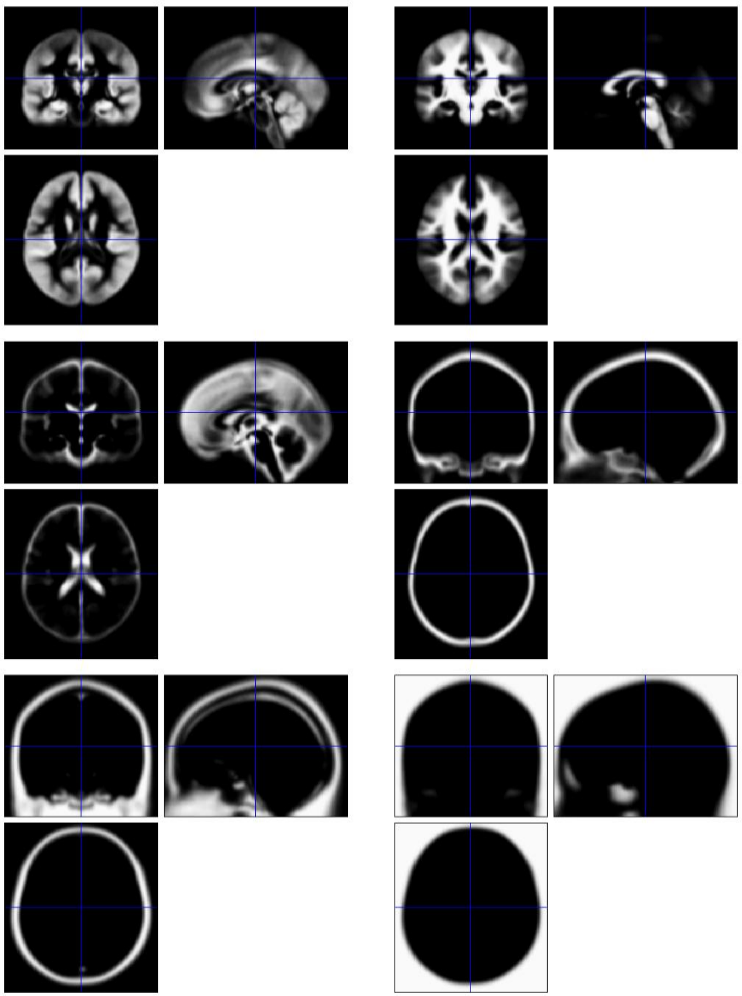
* Tissue probability images are deformed so that they can be overlaid on top of the image to segment.

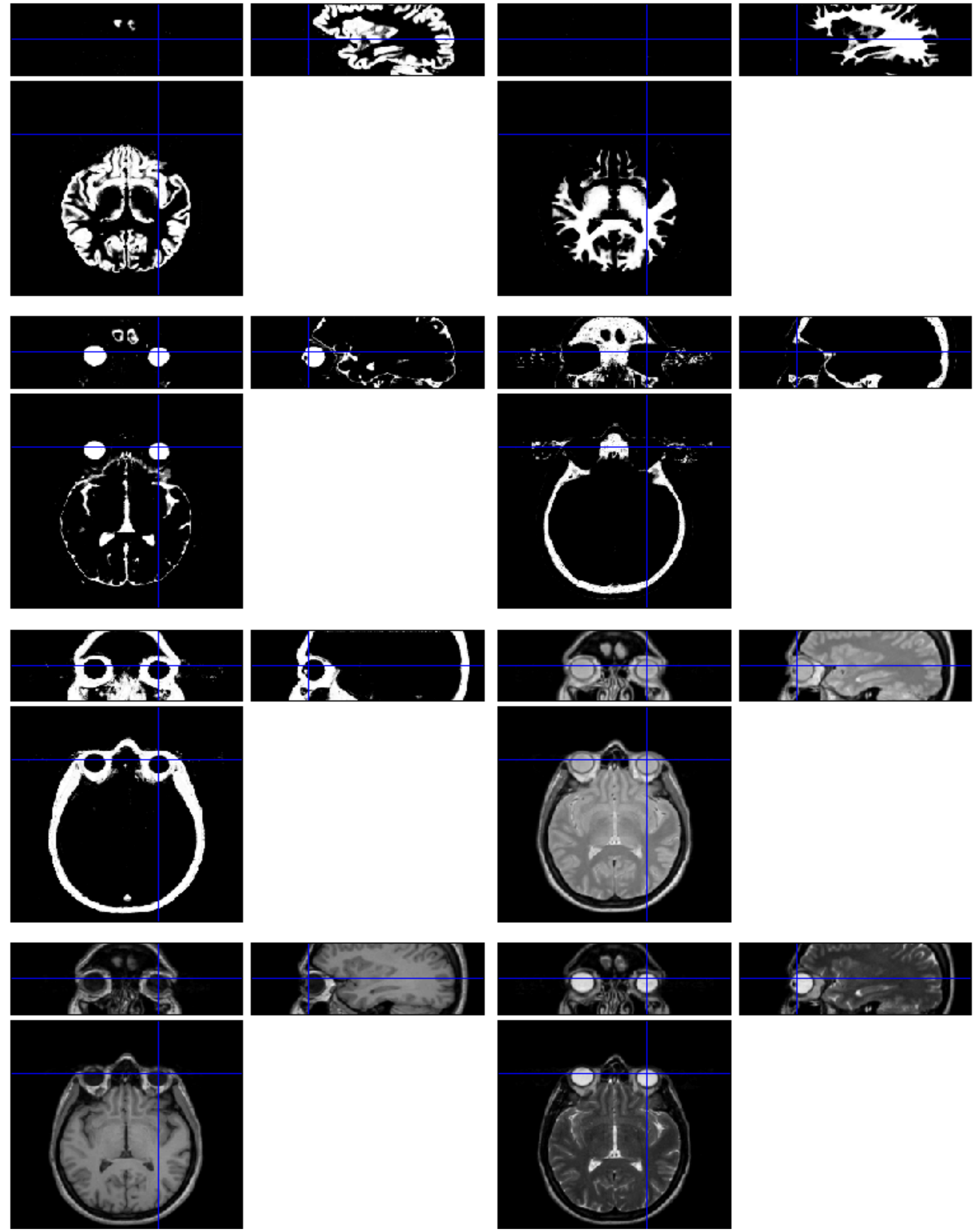






Multi-spectral





Limitations of the current model

- Assumes that the brain consists of only the tissues modelled by the TPMs
  - No spatial knowledge of lesions (stroke, tumours, etc)
- Prior probability model is based on healthy brains (IXI dataset from London).
  - Less accurate for subjects outside this population
- Needs reasonable quality images to work with
  - No severe artefacts
  - Good separation of intensities
  - Reasonable initial alignment with TPMs.

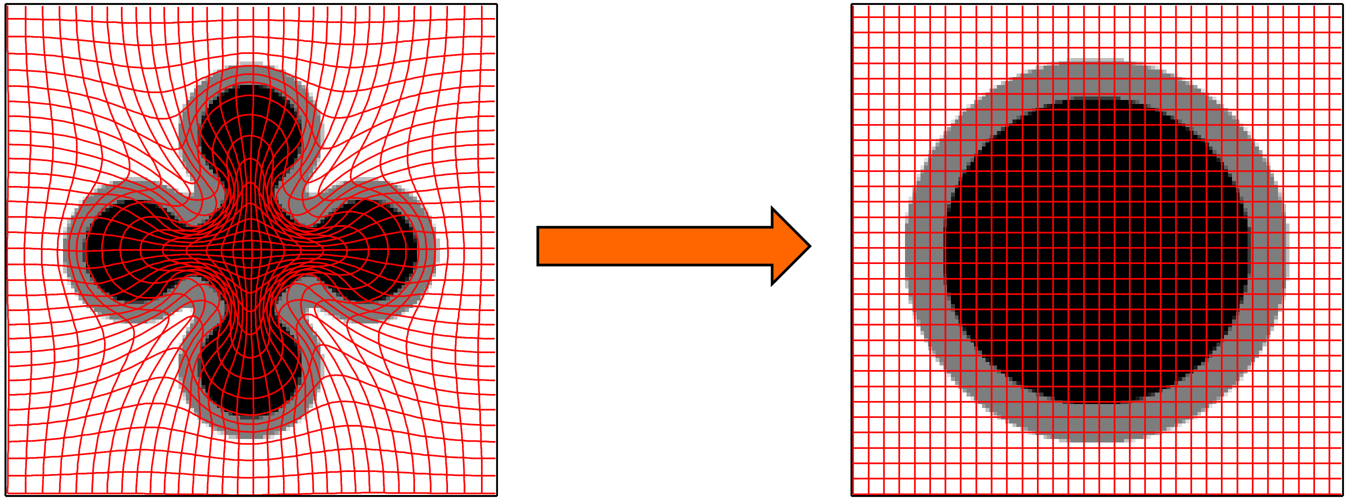
Selected References

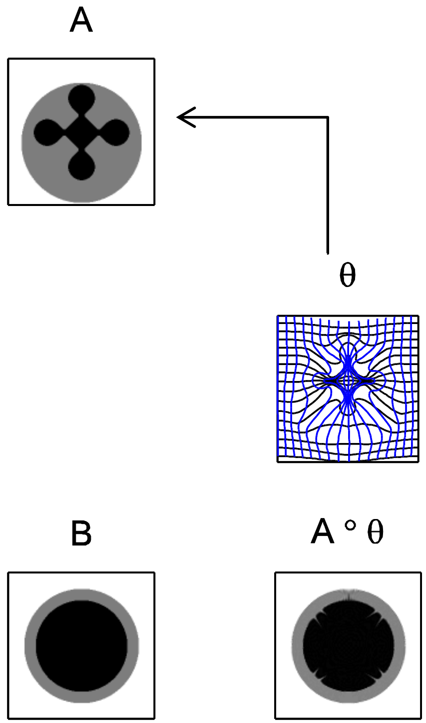
- Ashburner & Friston (2005). "*Unified Segmentation*". NeuroImage **26**:839-851.

Overview

- Morphometry
- Voxel-Based Morphometry
- Tissue Segmentation
- **Diffeomorphic Registration**
  - **Compositions**
  - **Objective function**
  - **Template creation**
- Longitudinal Registration
- Multivariate Shape Models

Diffeomorphic Deformations





Composition

Small Deformation Approximation

The composition:

$$\vartheta \circ \varphi$$

Would be approximated with:

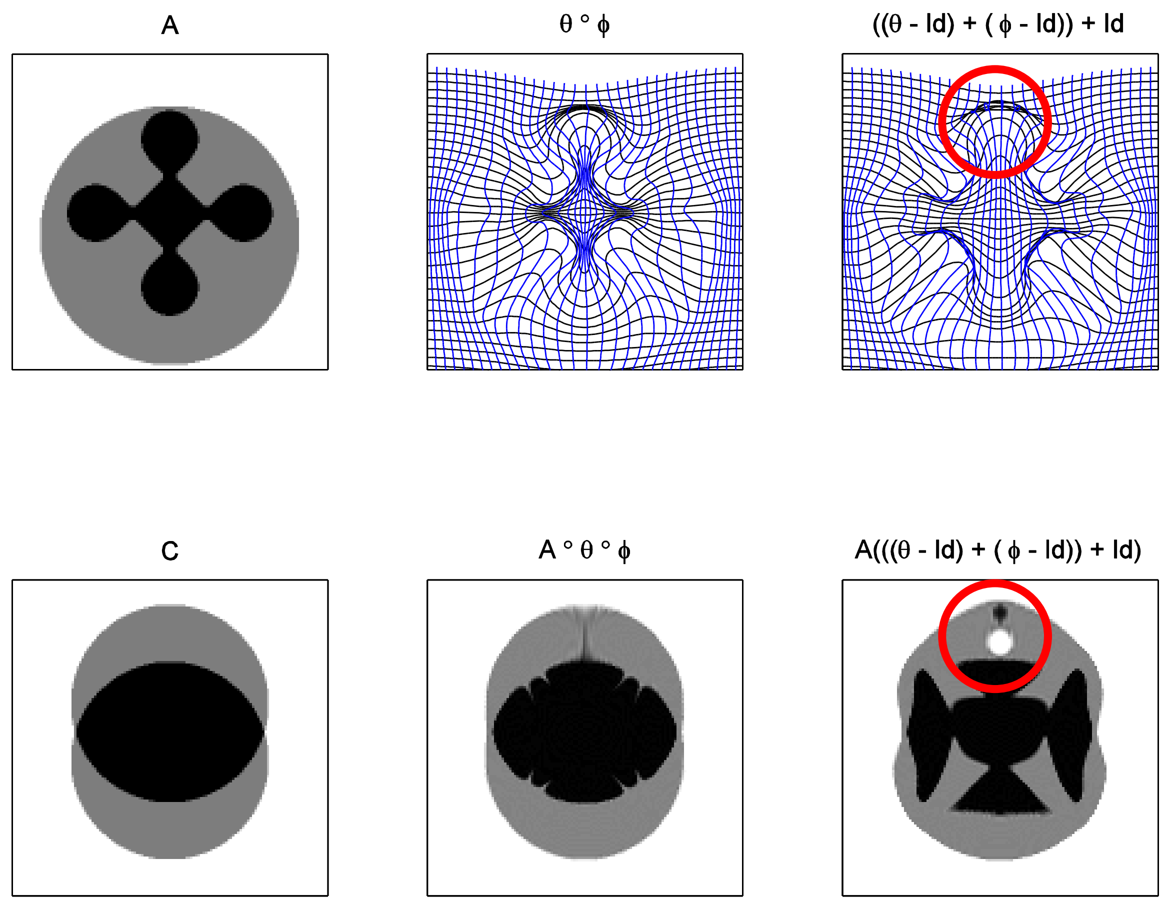
$$Id + ((\vartheta - Id) + (\varphi - Id))$$

The inversion:

$$\varphi^{-1}$$

Would be approximated with:

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



Not good approximations for large deformations.

Diffeomorphic Image Registration

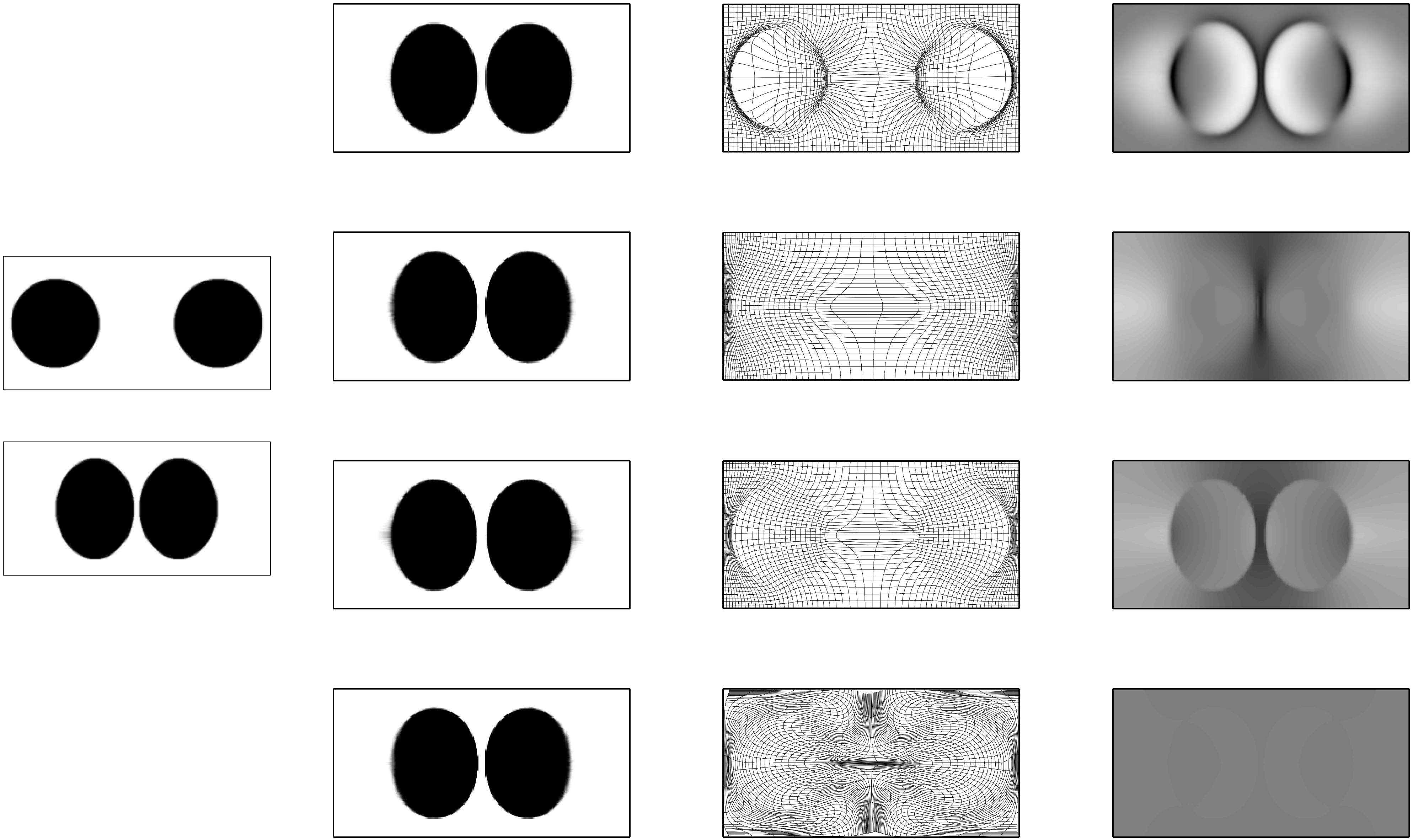
- Minimises two terms:

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.

In case anyone asks for equations

Dartel

$$E = \frac{1}{2} \| Lv \|^2 \, dt + \frac{1}{2\sigma^2} \| I_0 \circ \varphi_1^{-1} - I_1 \|^2$$

$$\varphi_0 = id$$

$$\dot{\varphi} = v \circ \varphi_t$$

Geodesic Shooting

$$E = \frac{1}{2} \| Lv_0 \|^2 \, dt + \frac{1}{2\sigma^2} \| I_0 \circ \varphi_1^{-1} - I_1 \|^2$$

$$\varphi_0 = id$$

$$\dot{\varphi} = v_t \circ \varphi_t$$

$$v_t = K(| d\varphi_t^{-1} | (d\varphi_t^{-1})^T ((L^* L v_0) \circ \varphi_t^{-1}))$$

equivalent solution to this variational problem:

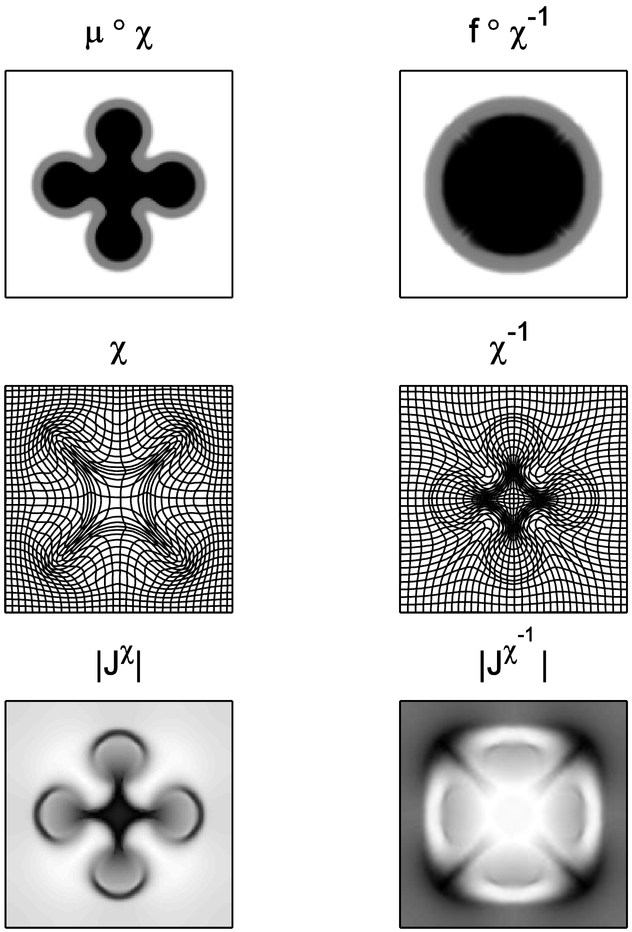
$$E = \frac{1}{2} \int_{t=0}^{1} \| Lv_t \|^2 \, dt + \frac{1}{2\sigma^2} \| I_0 \circ \varphi_1^{-1} - I_1 \|^2$$

$$\varphi_0 = id$$

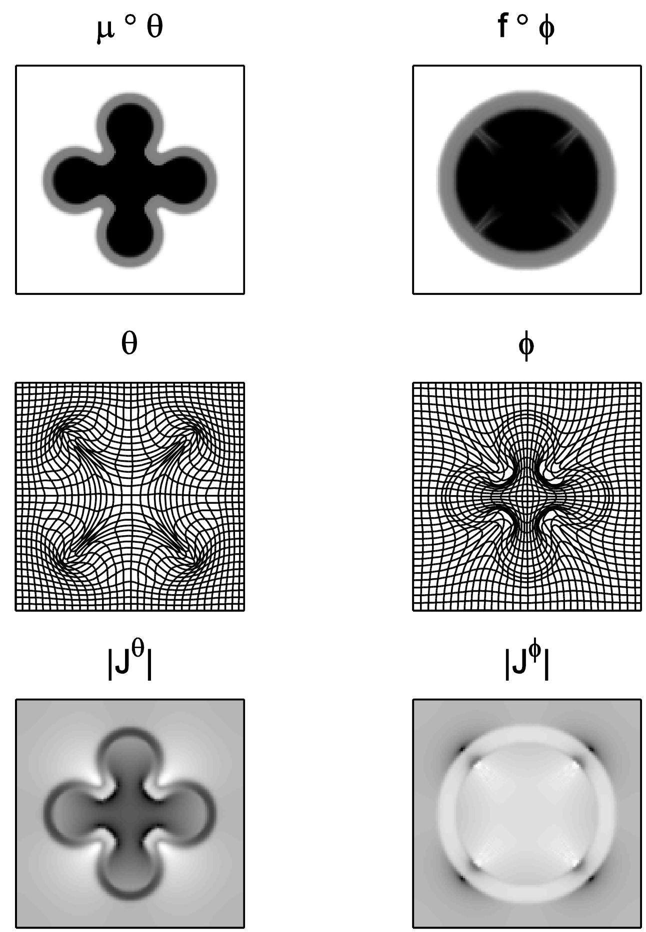
$$\dot{\varphi} = v_t \circ \varphi_t$$

Dartel & GS Compared

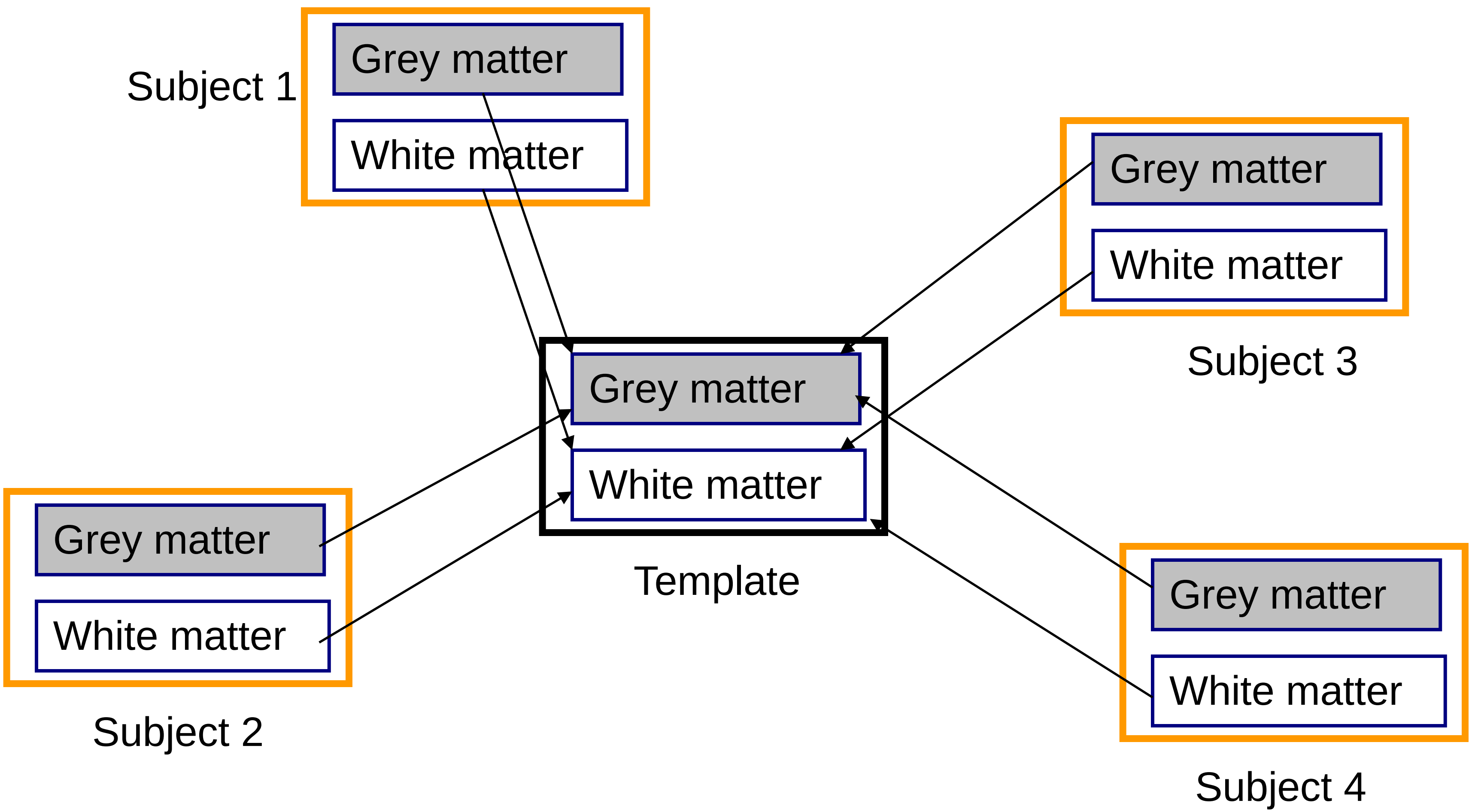
Dartel



Geodesic Shooting



Simultaneous registration of GM to GM and WM to WM

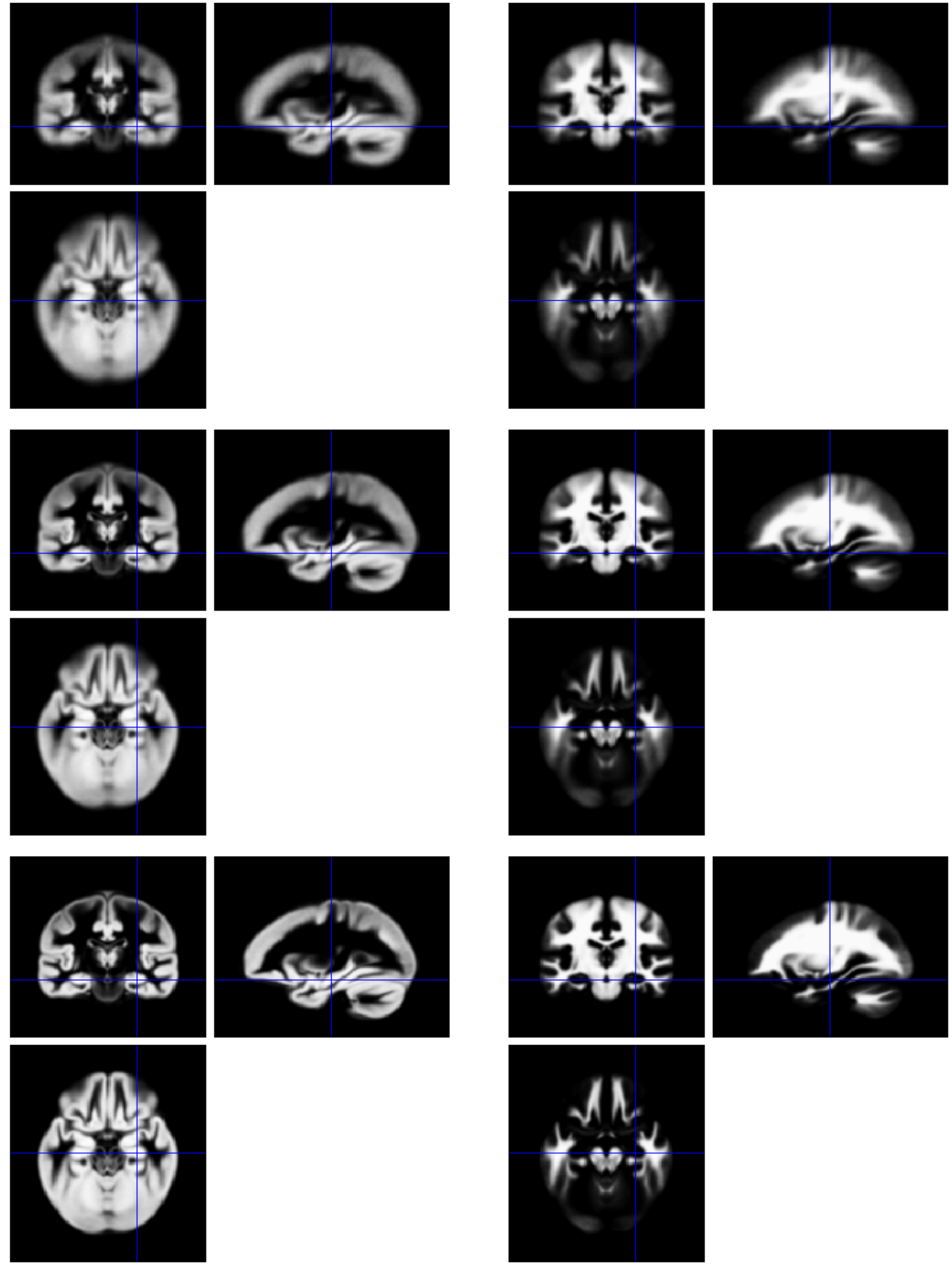


Template

Iteratively generated from 471 subjects

Began with rigidly aligned tissue probability maps

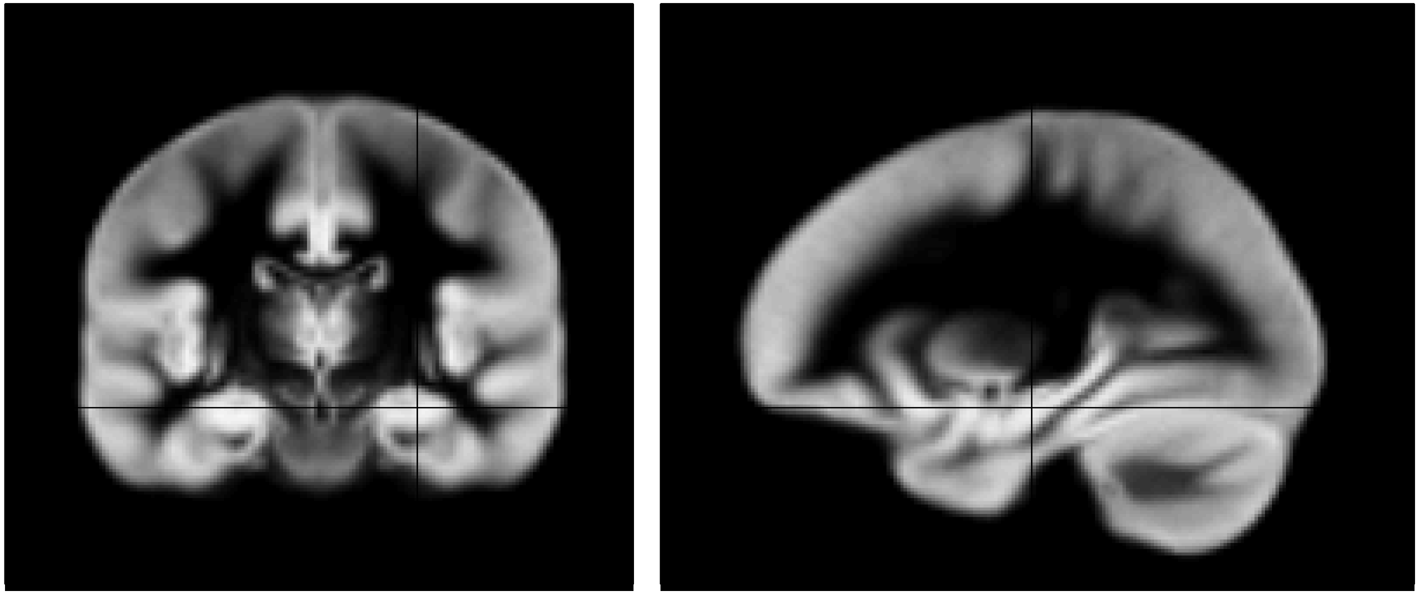
Used an inverse consistent formulation

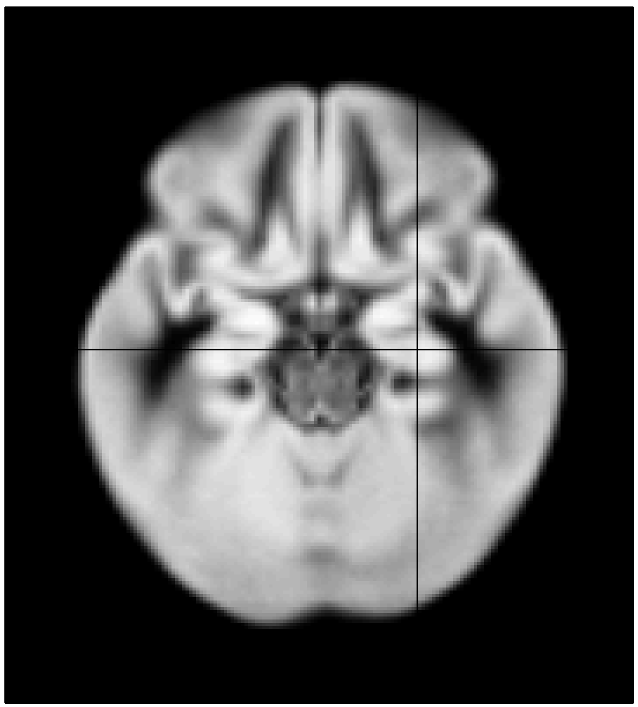


Initial Average

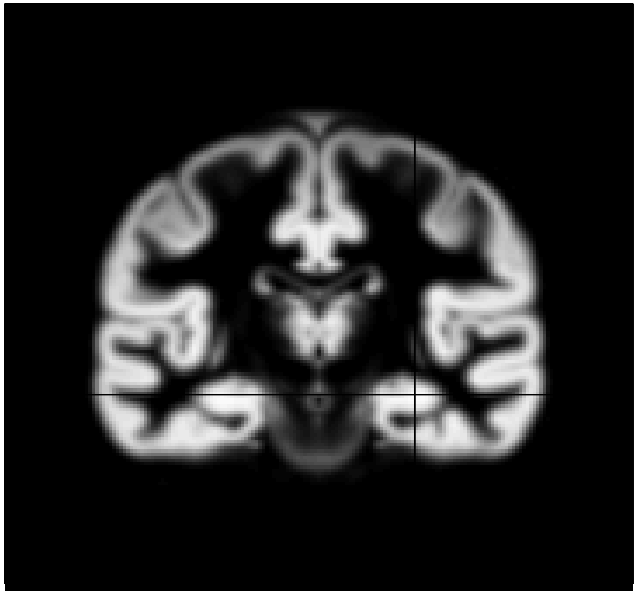
After a few iterations

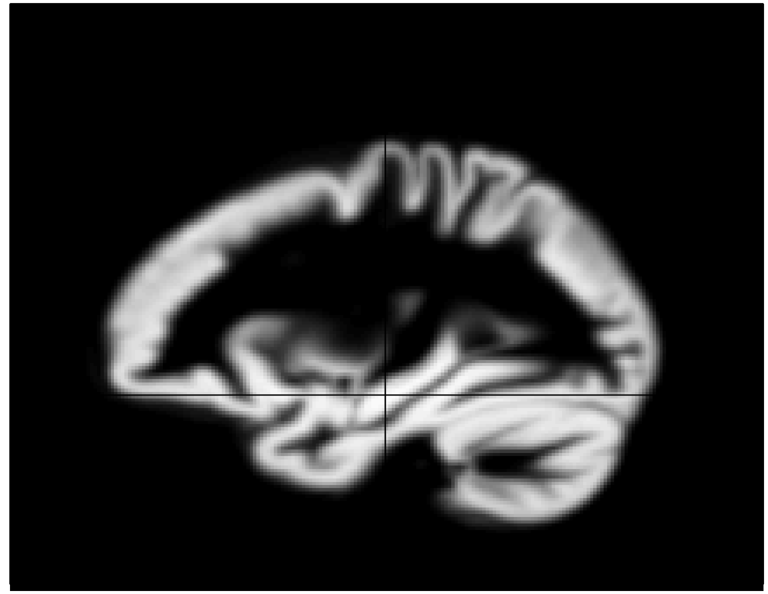
Final template

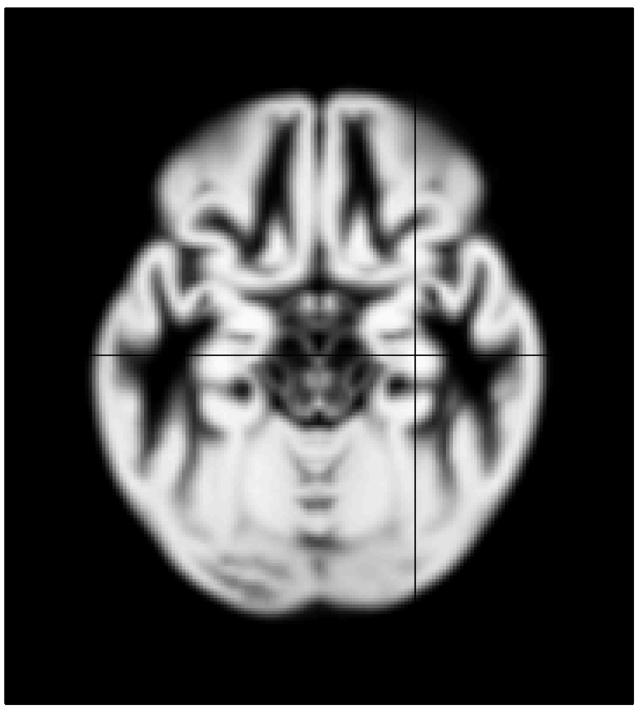




Grey matter average of 452 subjects – affine

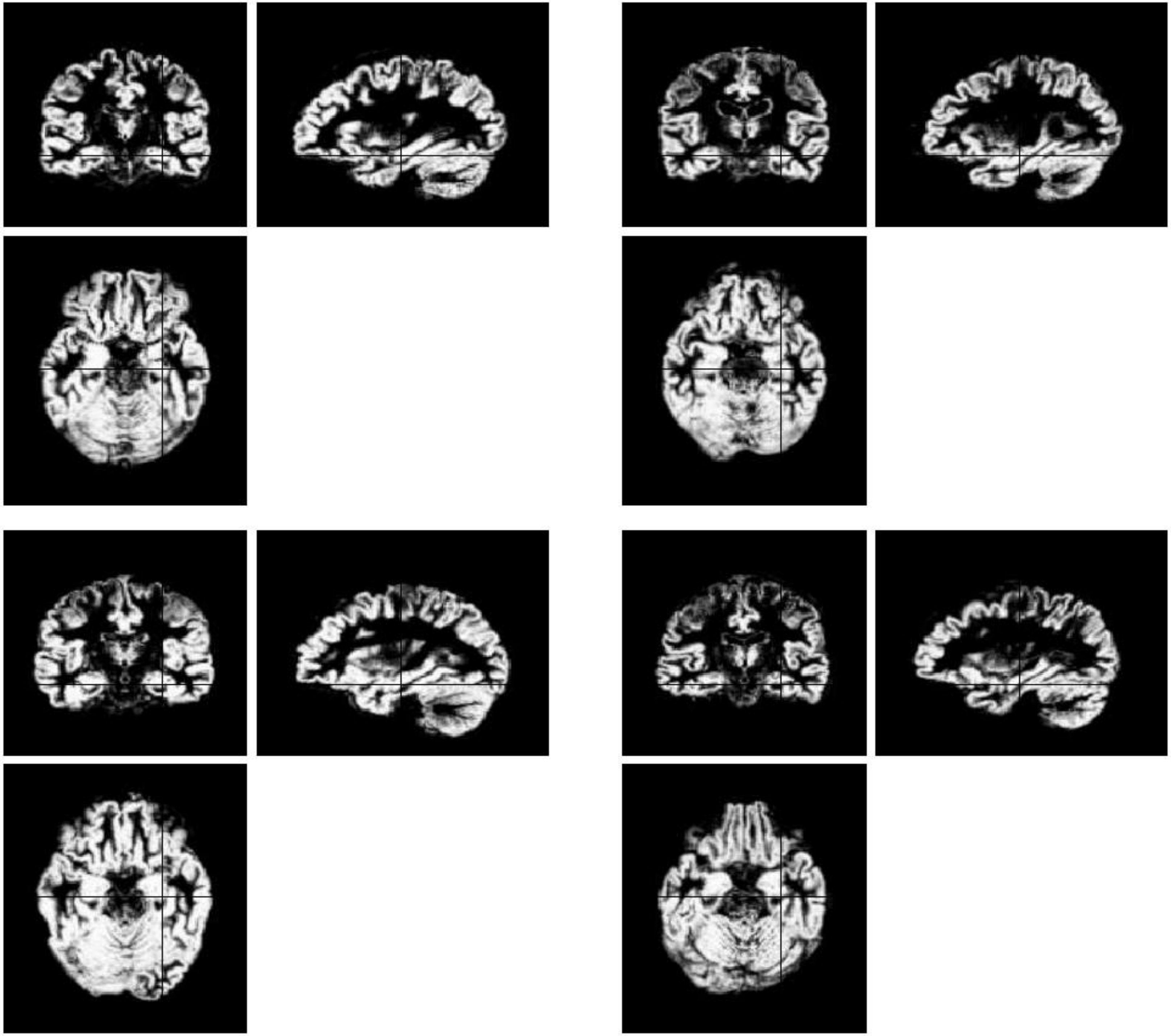




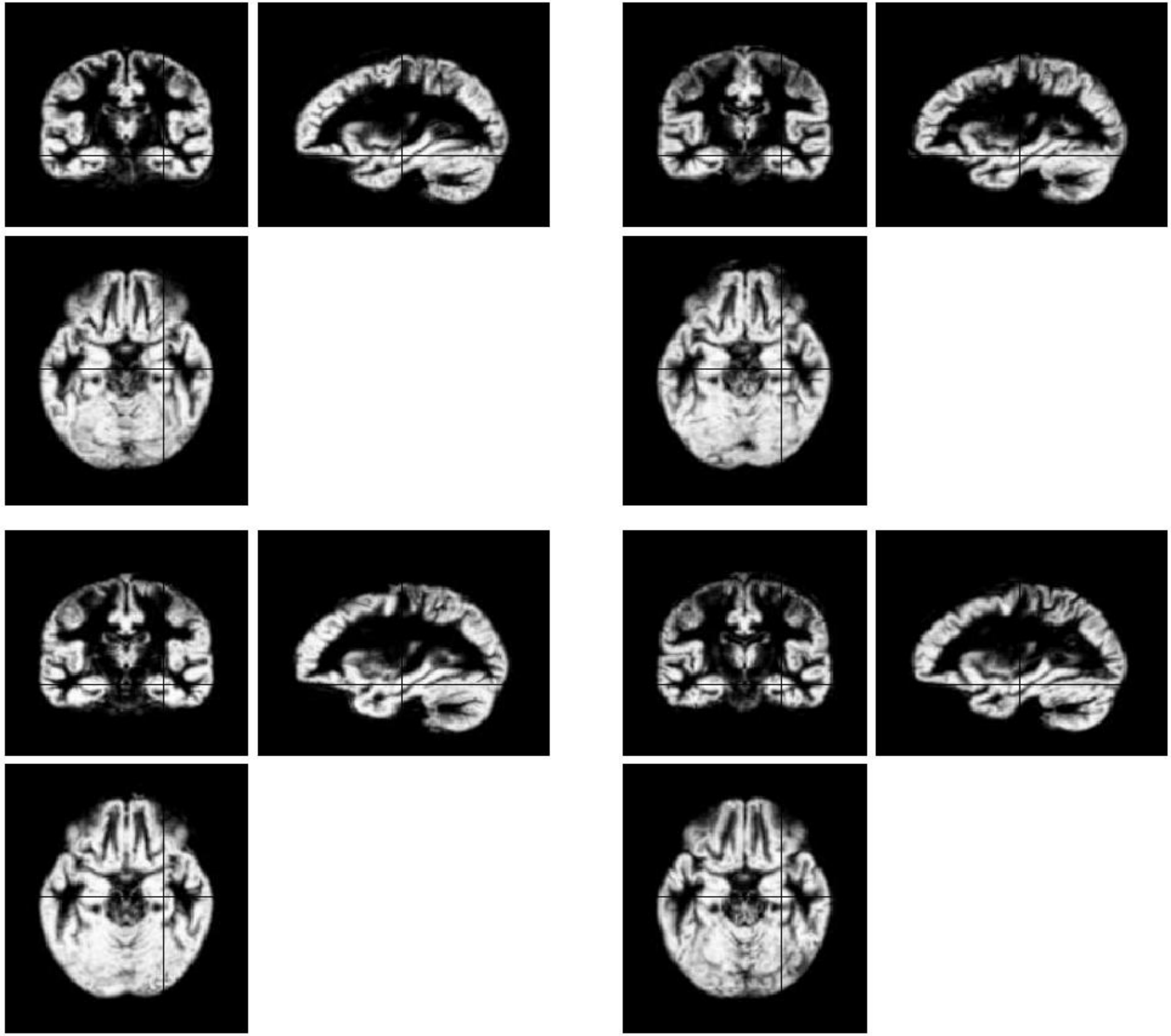


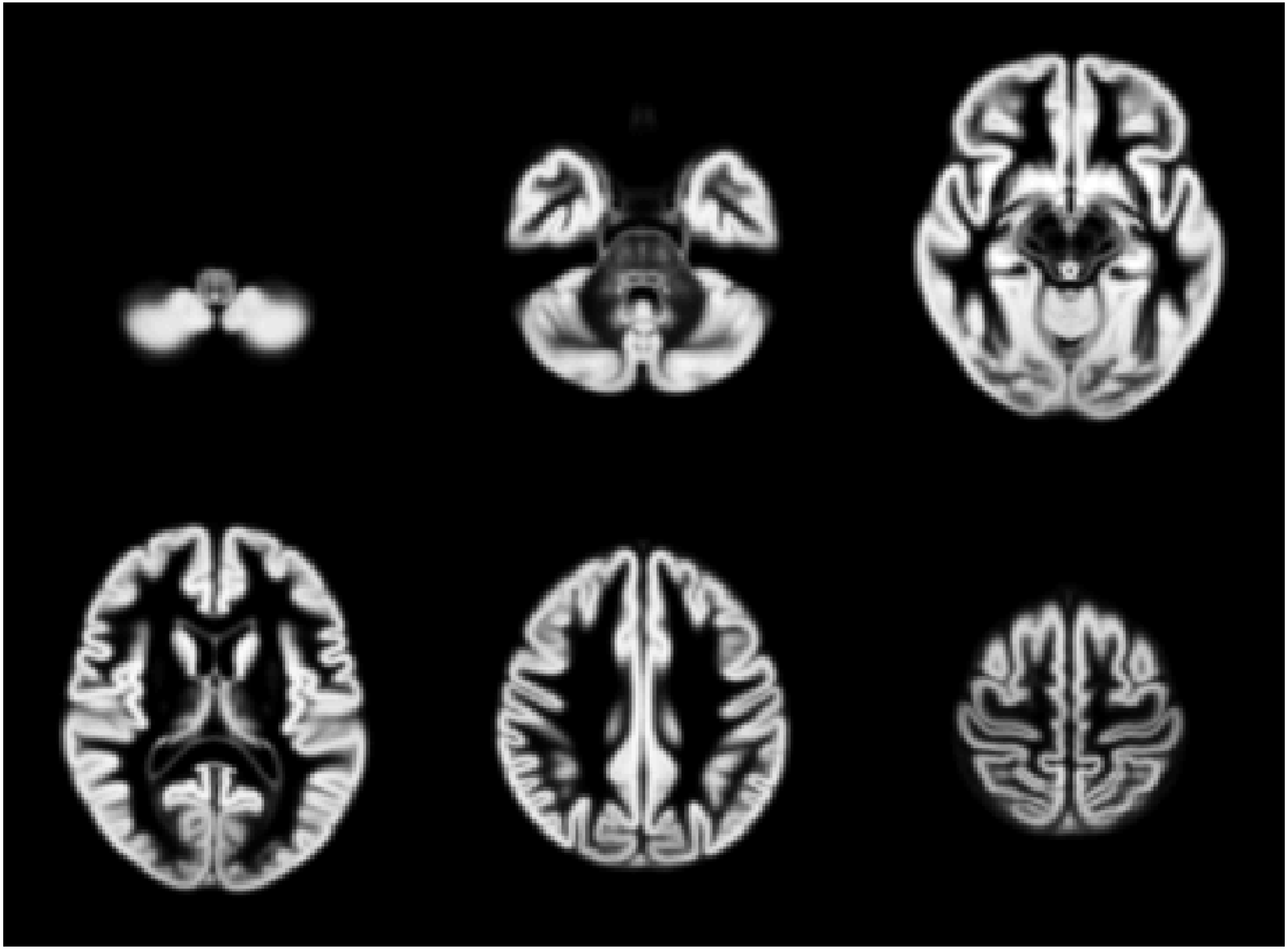
Grey matter average of 471 subjects - nonlinear

Initial
GM images

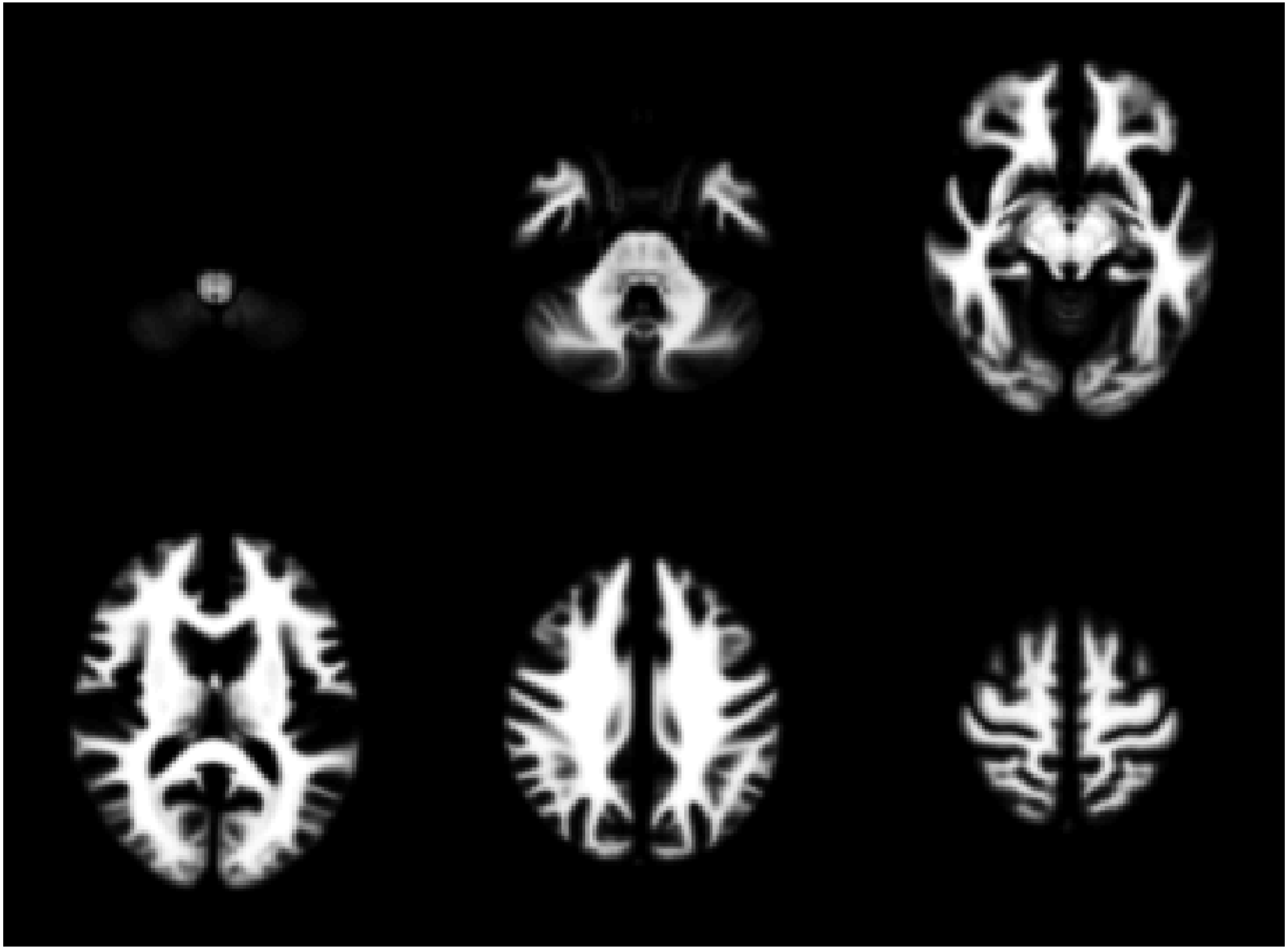


Warped GM images

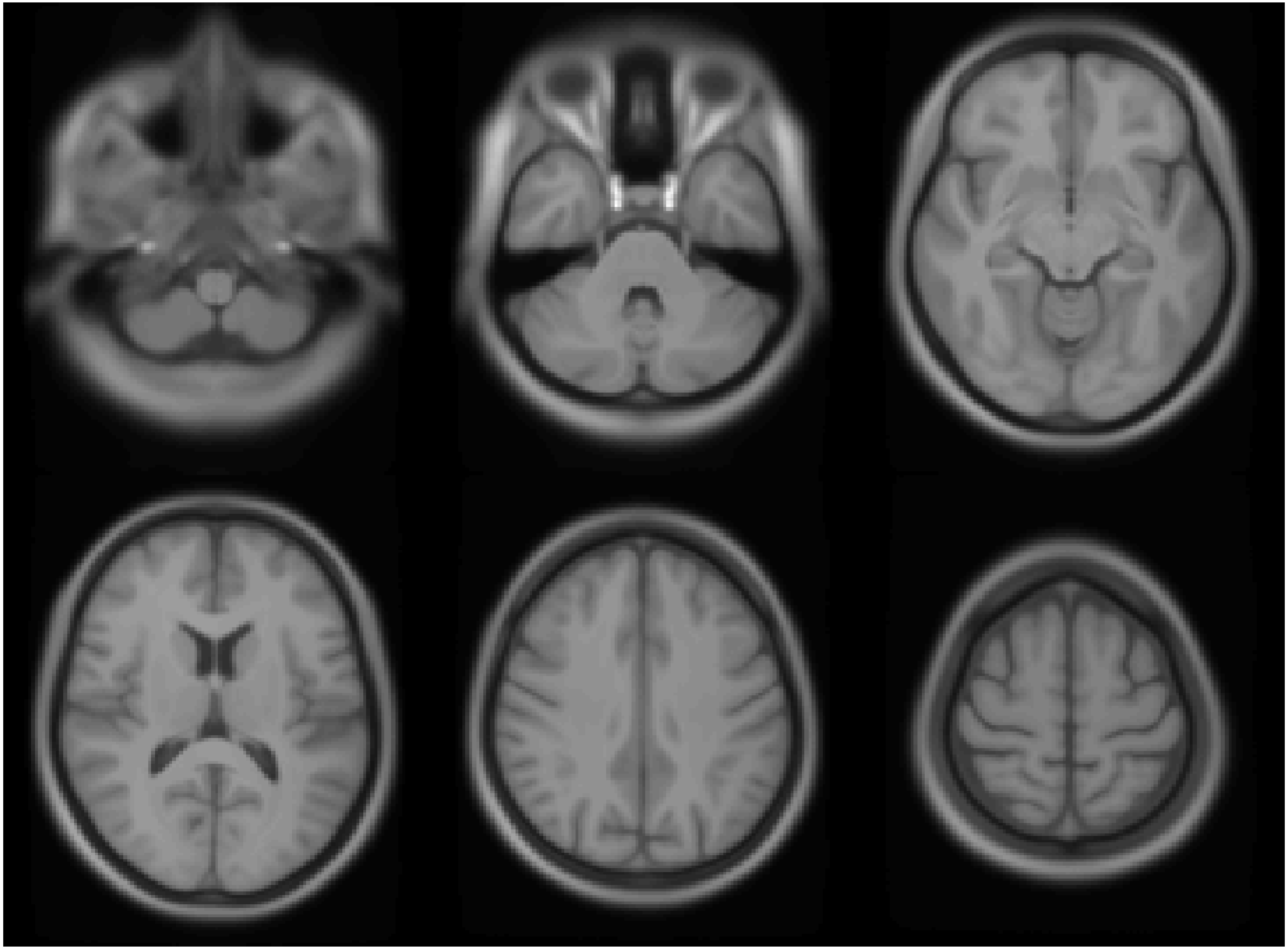




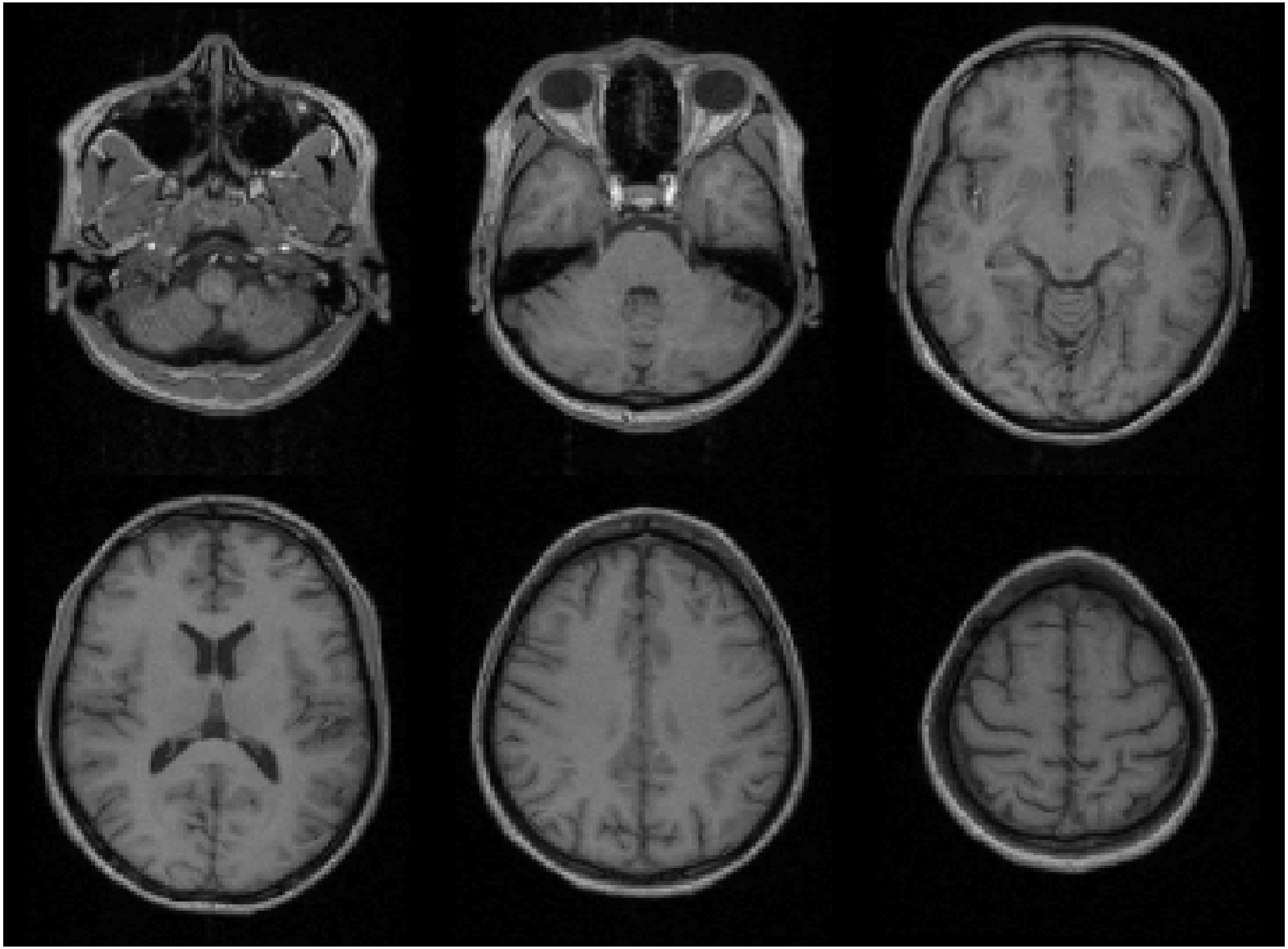
471 Subject Average



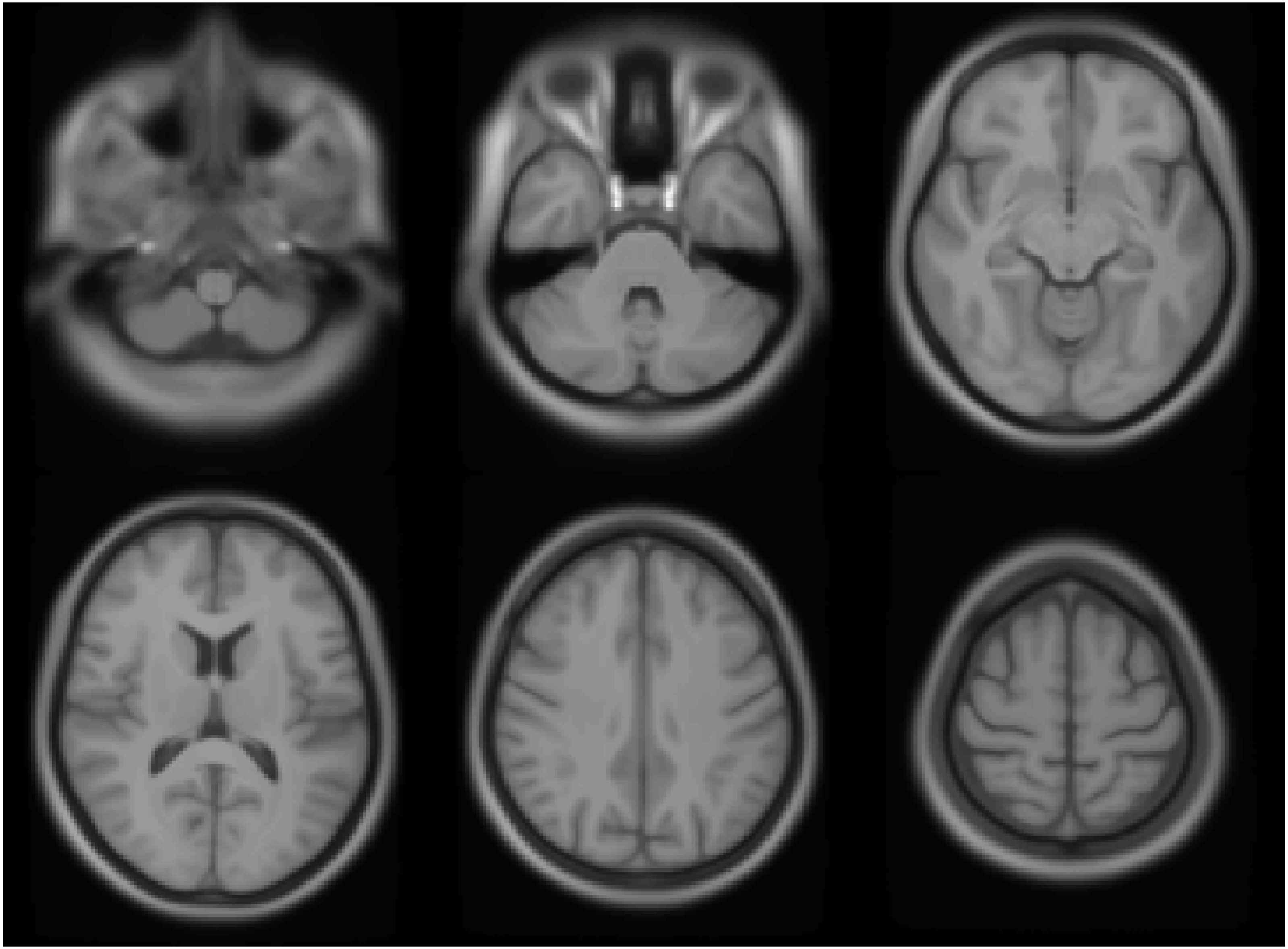
471 Subject Average



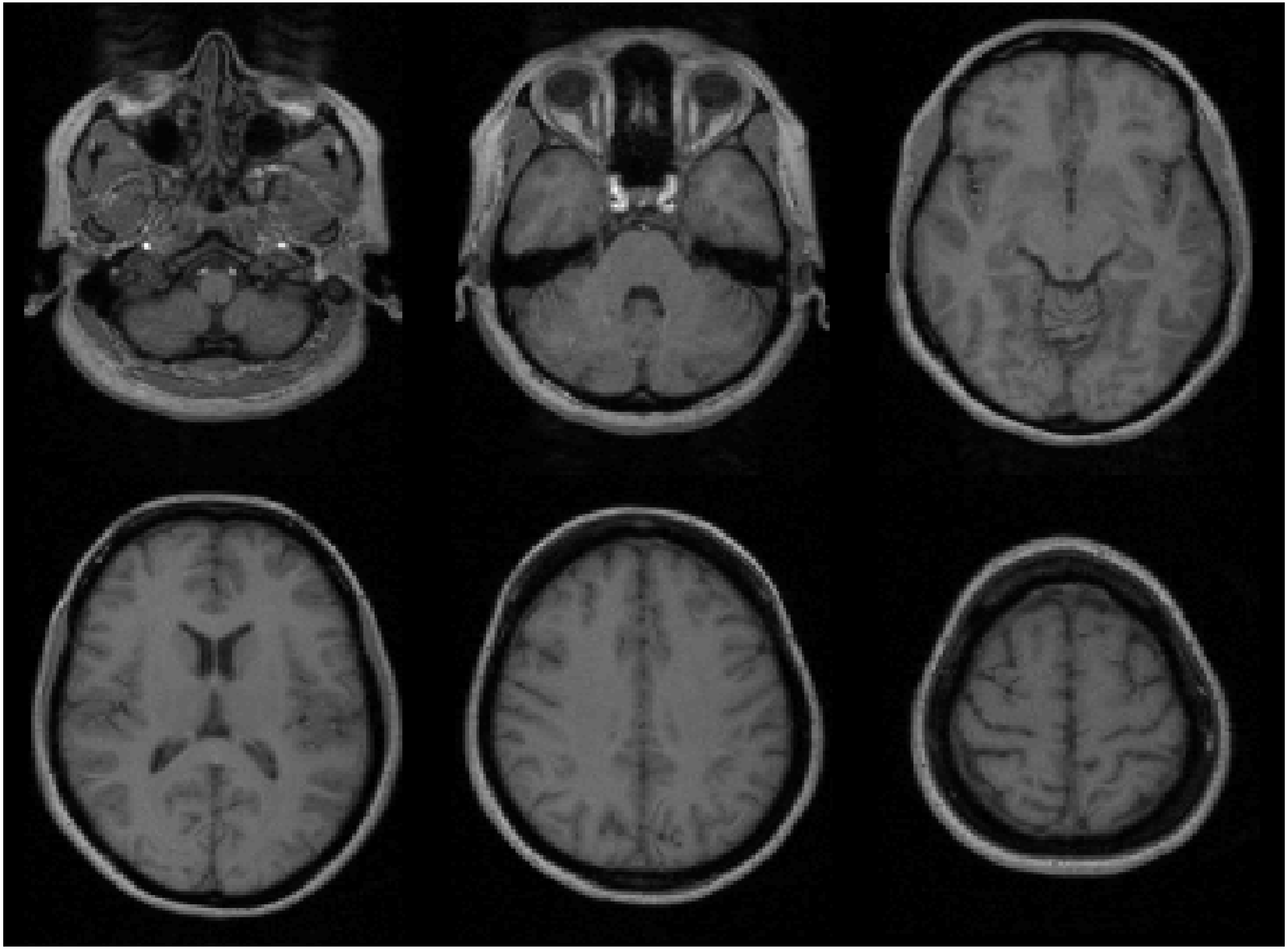
471 Subject Average



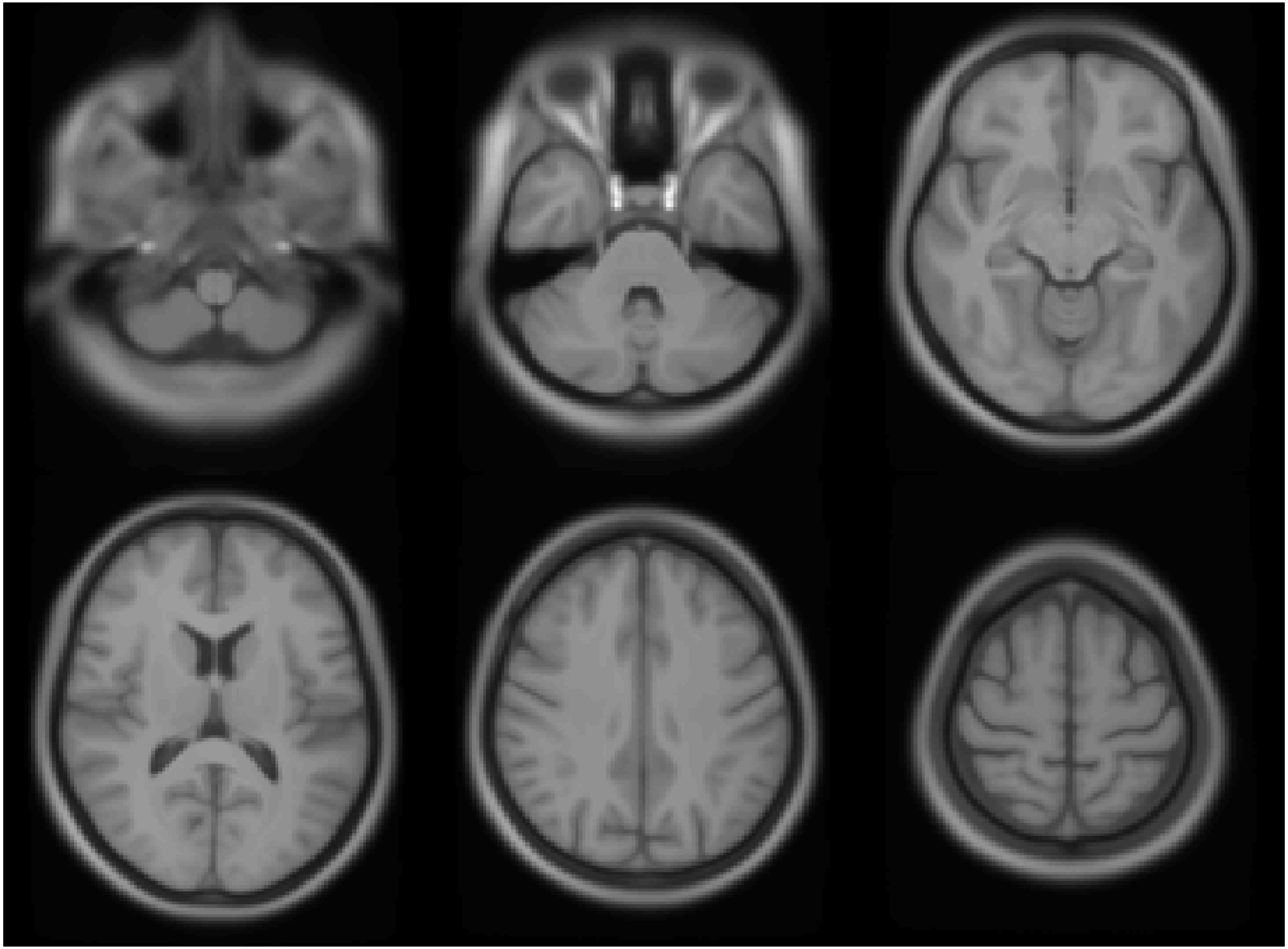
Subject 1



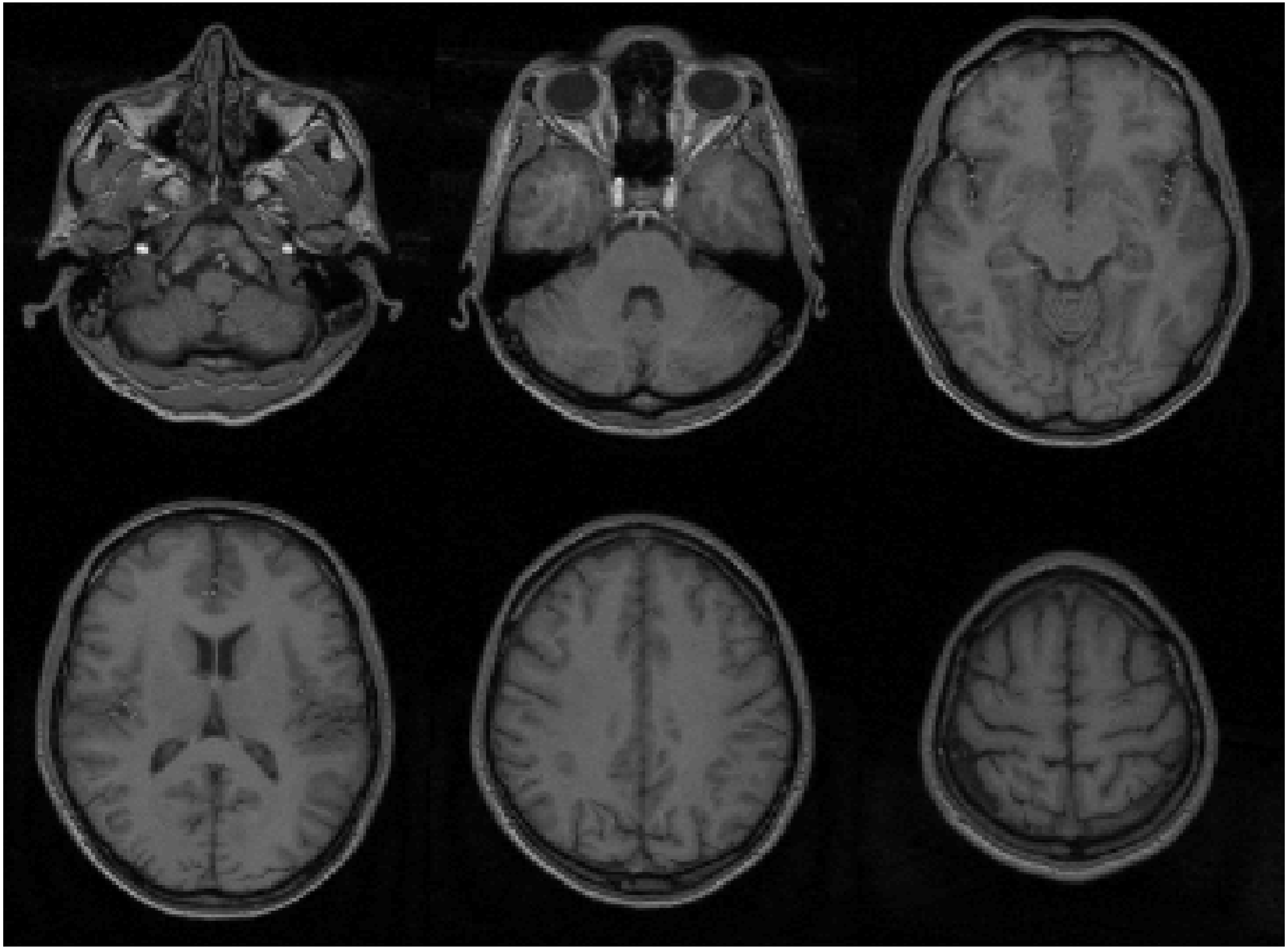
471 Subject Average



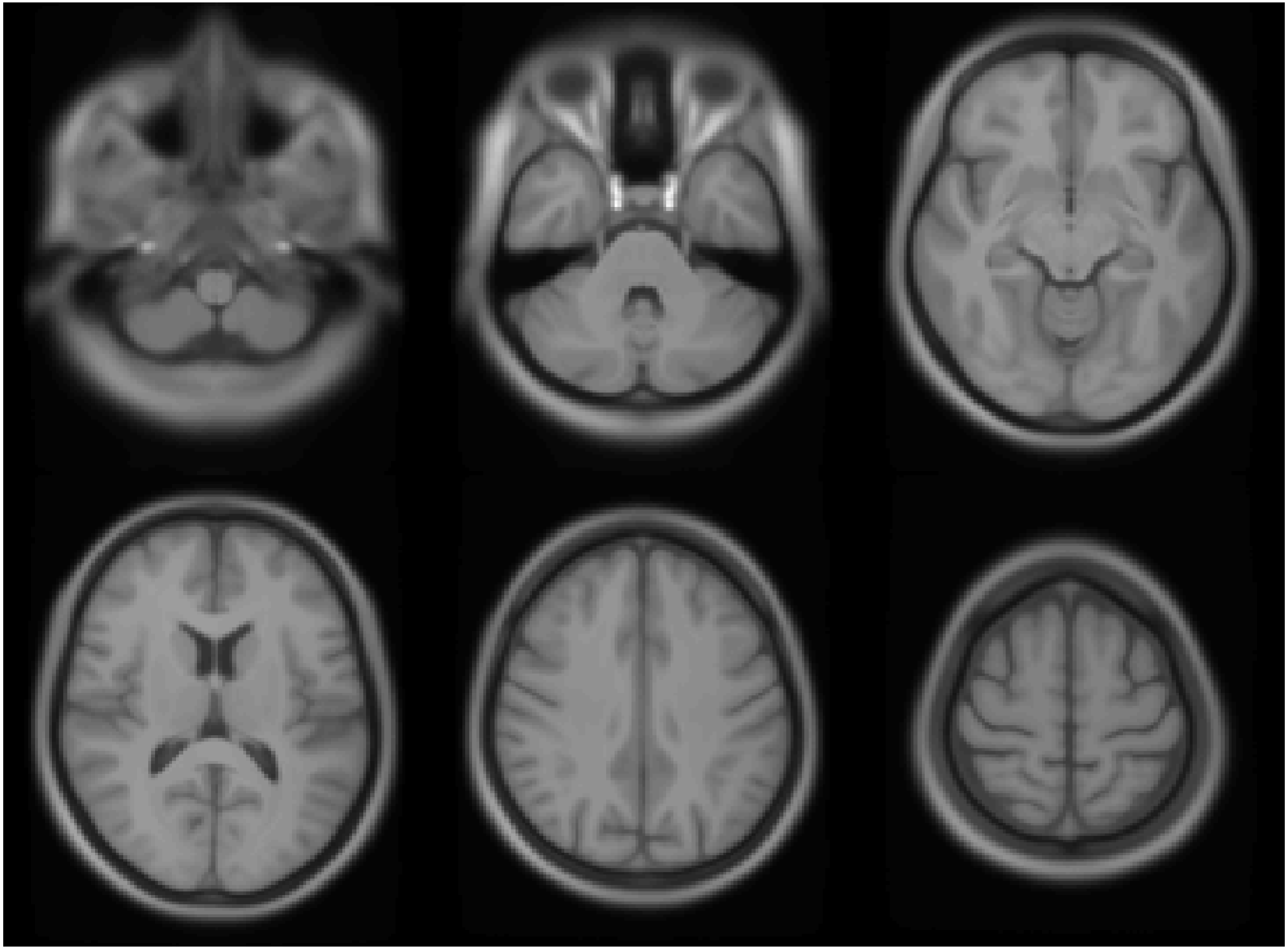
Subject 2



471 Subject Average

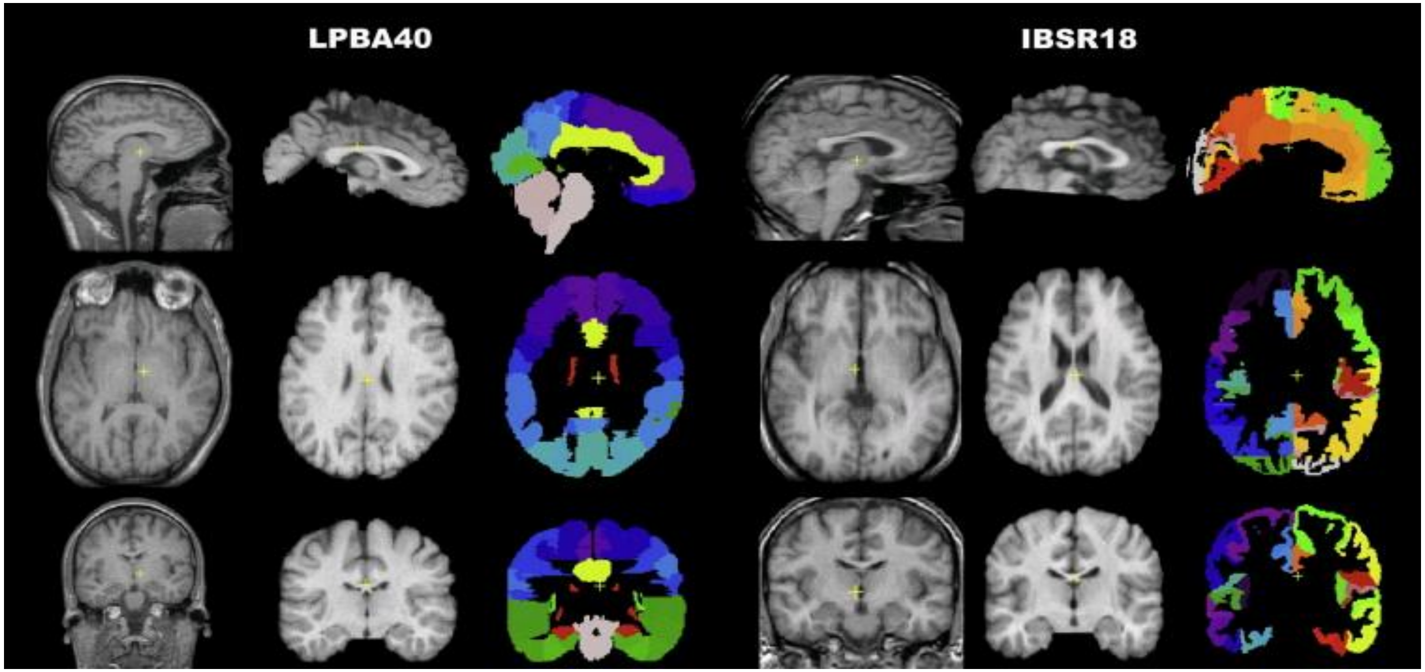


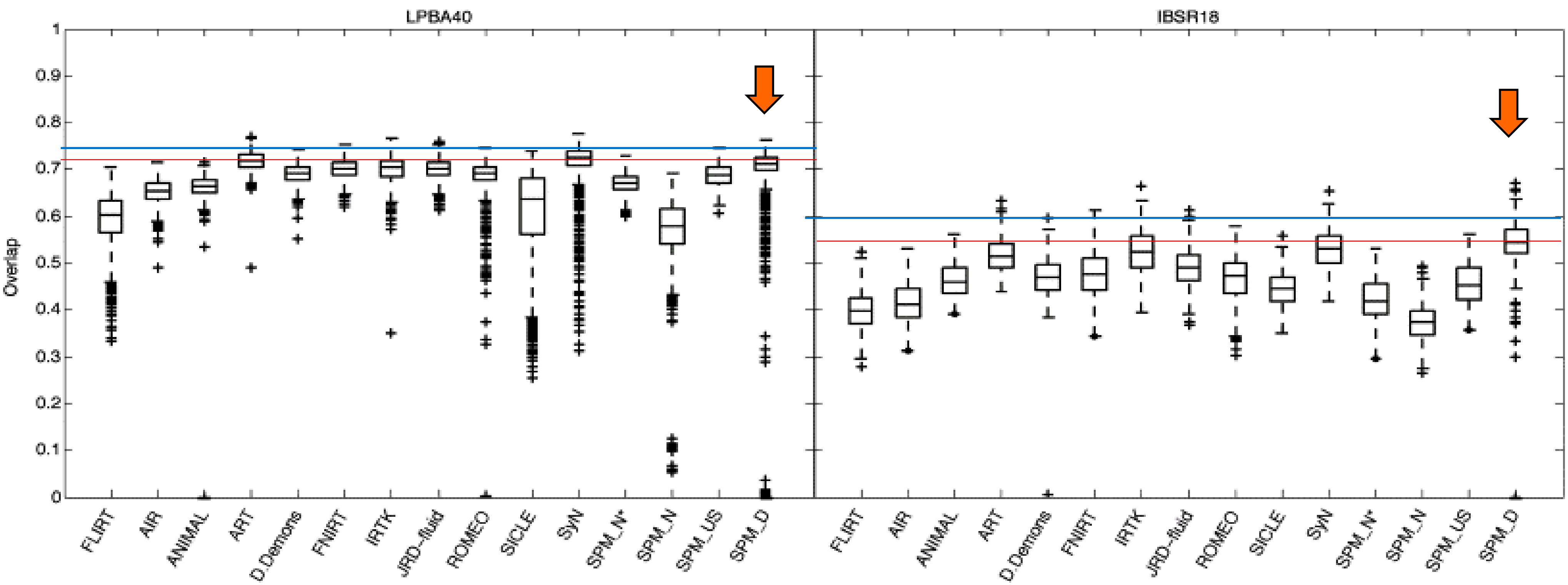
Subject 3

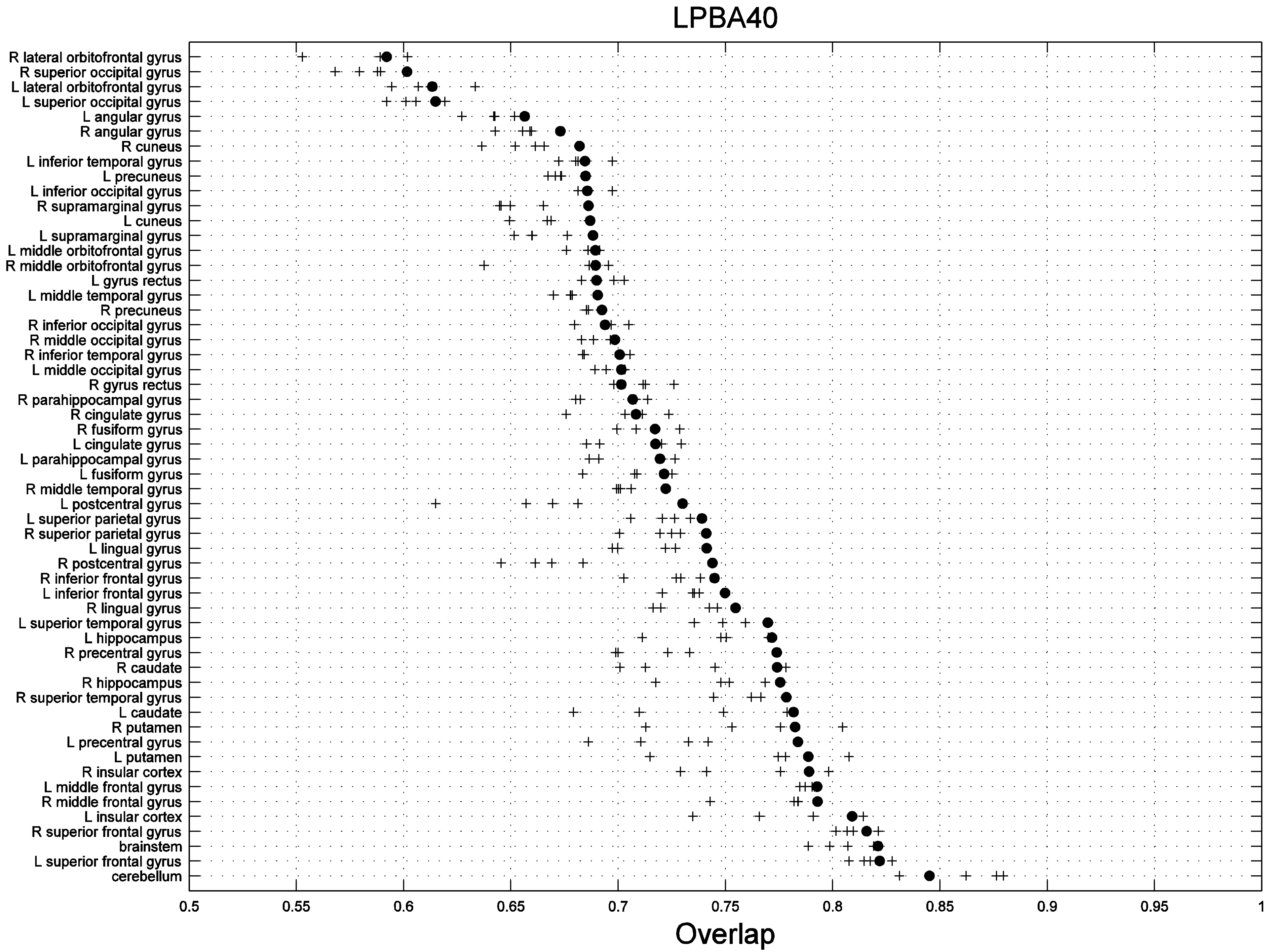


471 Subject Average

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

Selected References

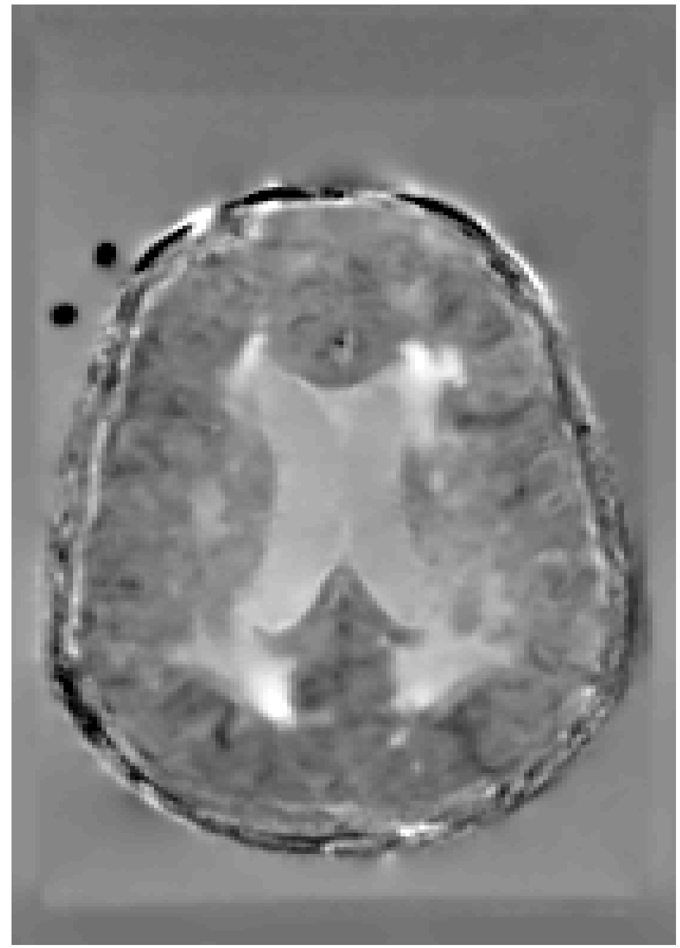
- Beg, Miller, Trouvé & Younes (2005). "*Computing large deformation metric mappings via geodesic flows of diffeomorphisms*." International journal of computer vision 61(2):139-157.
- Ashburner (2007). "*A Fast Diffeomorphic Image Registration Algorithm*". NeuroImage 38:95-113.
- Ashburner & Friston (2009). "*Computing Average Shaped Tissue Probability Templates*". NeuroImage 45:333-341.
- Klein et al (2009). "*Evaluation of 14 nonlinear deformation algorithms applied to human brain MRI registration*". NeuroImage 46(3):786-802.
- Ashburner & Friston (2011). "*Diffeomorphic registration using geodesic shooting and Gauss-Newton optimisation*". NeuroImage 55(3):954-967

Overview

- Morphometry
- Voxel-Based Morphometry
- Tissue Segmentation
- Diffeomorphic Registration
- **Longitudinal Registration**
- Multivariate Shape Models

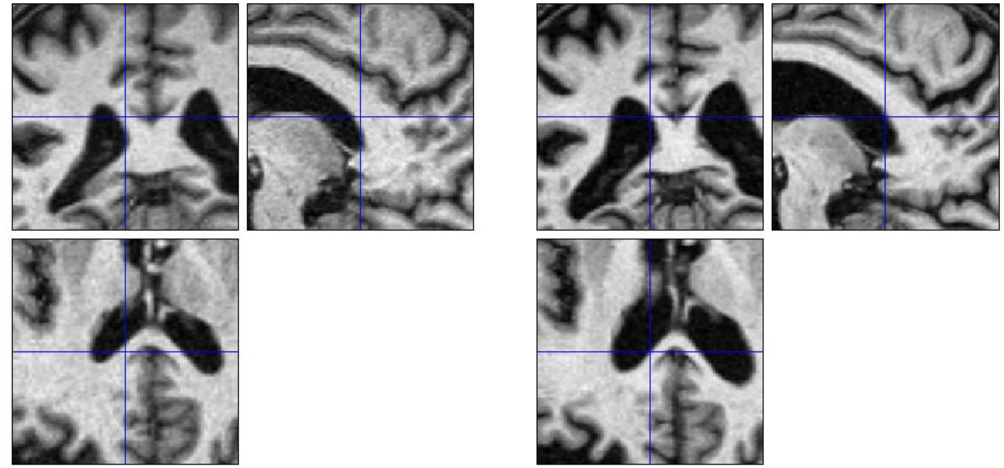
Longitudinal Registration

- Unified model combines:
  - Nonlinear diffeomorphic registration.
  - Rigid-body registration.
  - Intensity inhomoheneity correction.



Two Longitudinal Scans

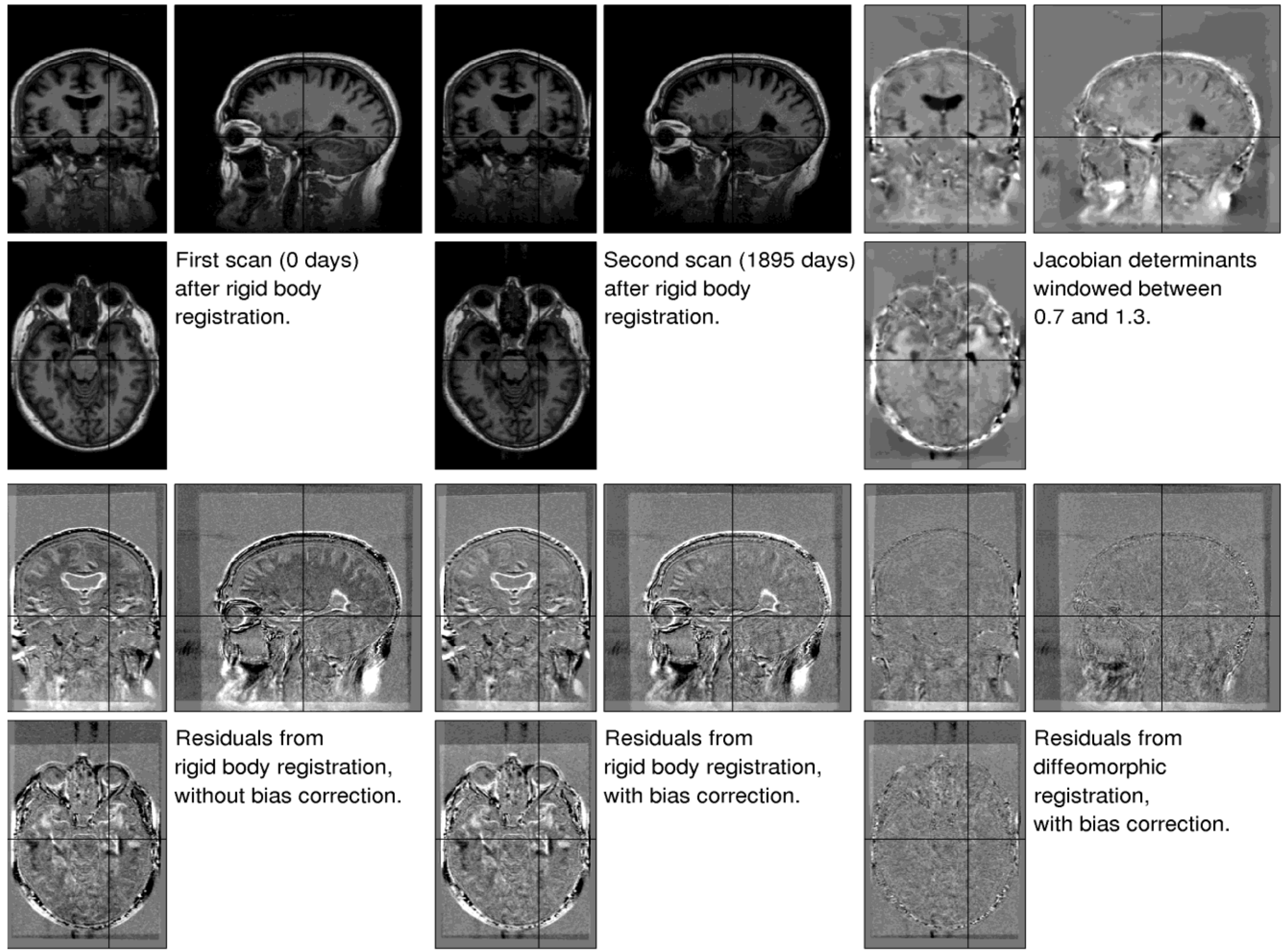
Two scans taken 6 years apart (after rigid registration).



Oasis Data

<u>OAS2 0002</u>

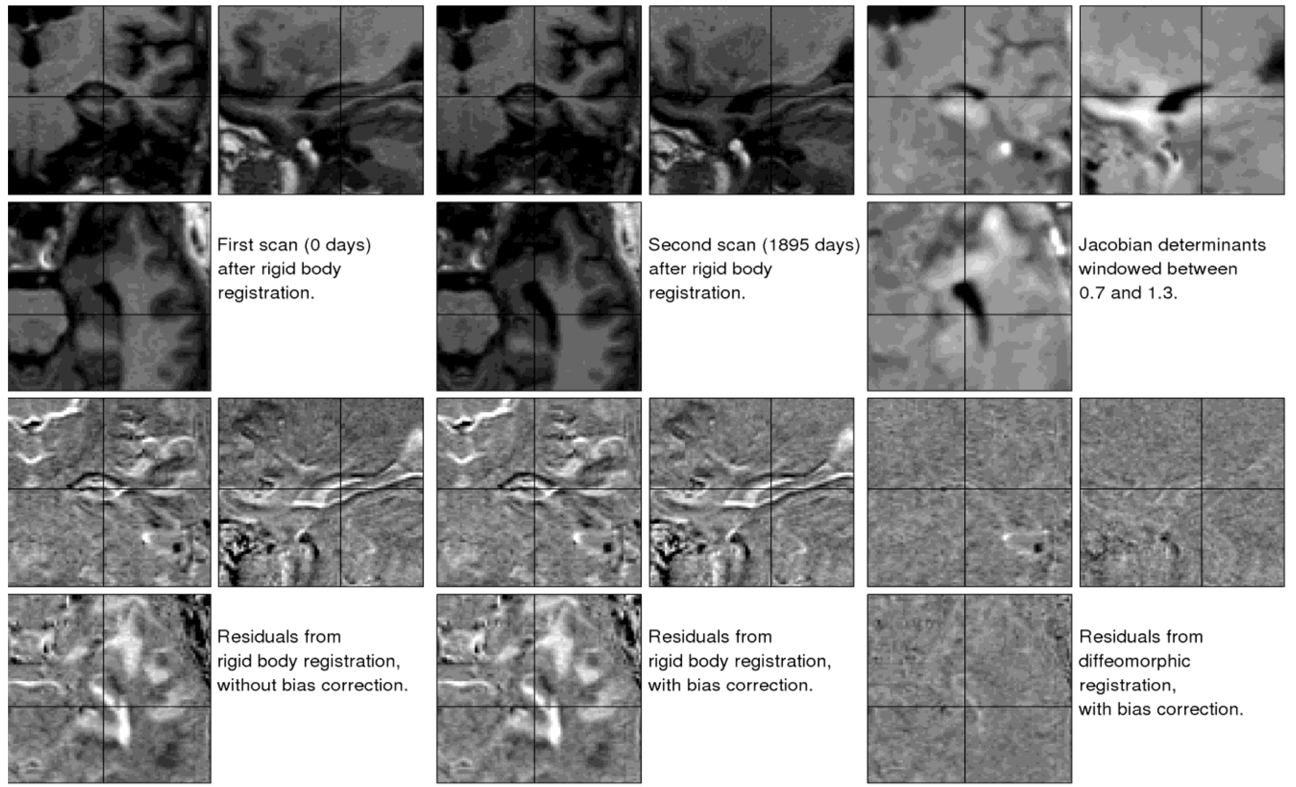
75 year old male, with MCI (MMSE=22, CDR=0.5).



Oasis Data

OAS2 0002

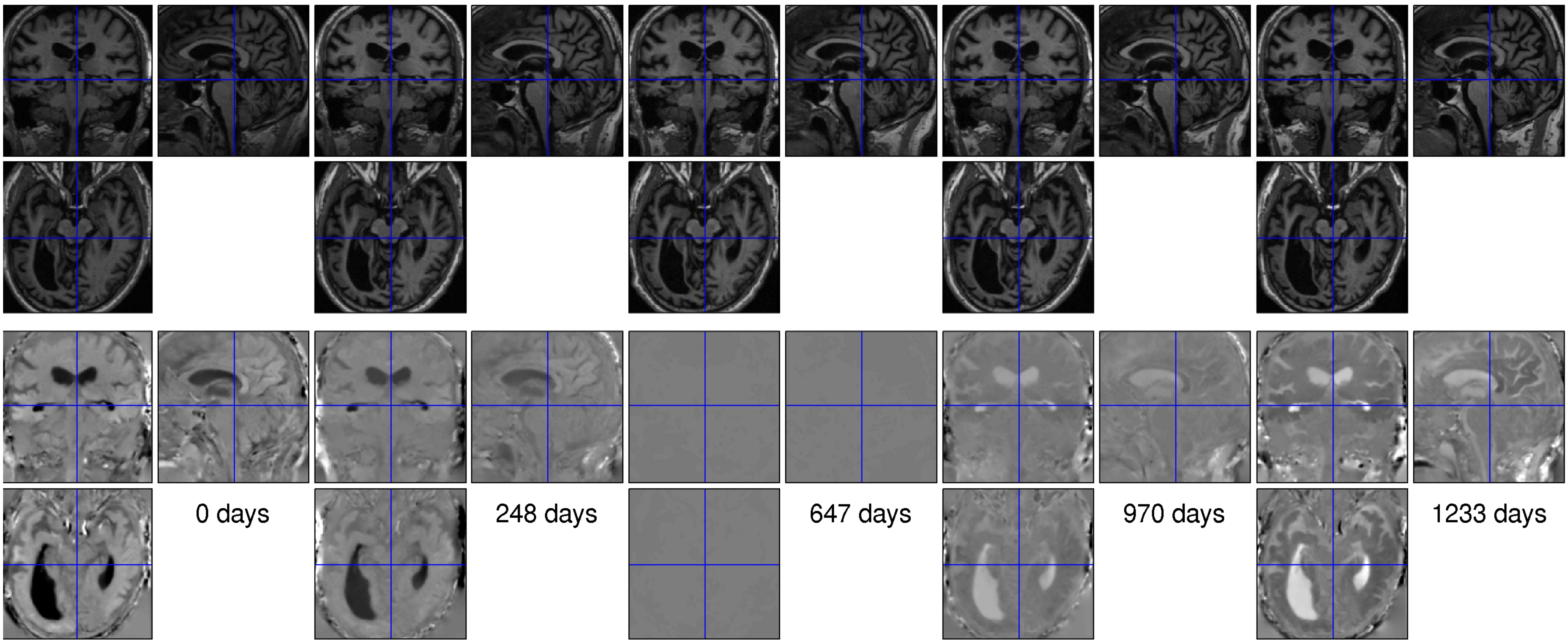
75 year old male, with MCI (MMSE=22, CDR=0.5).



Oasis Data

OAS2 0048

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



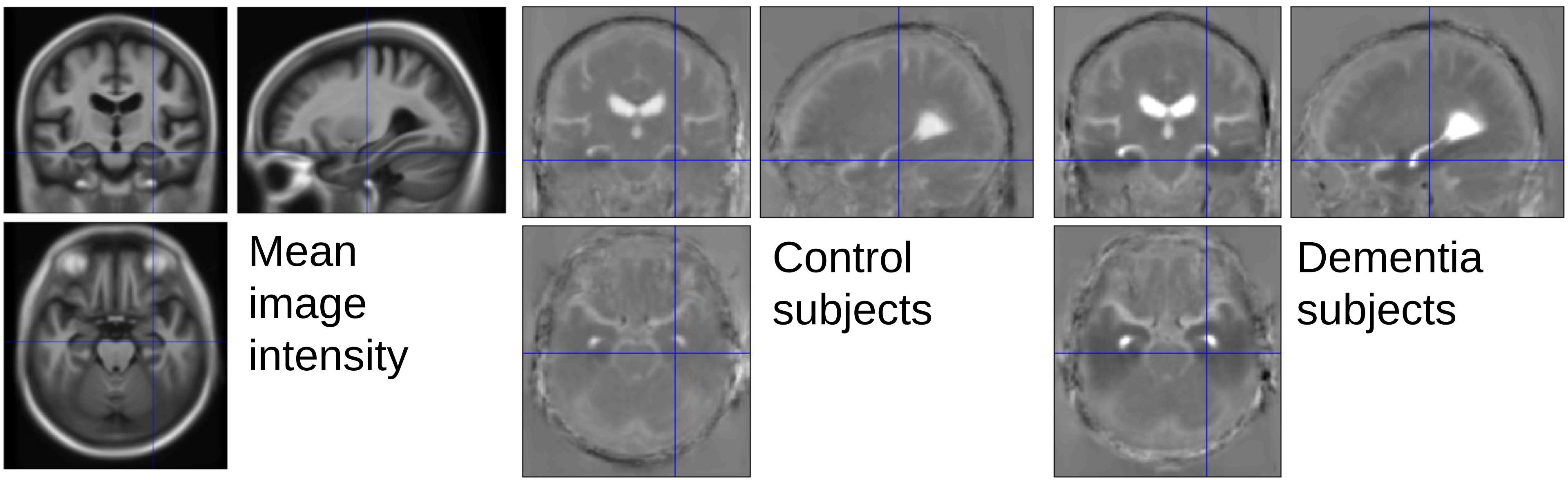
Oasis Data

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.



Selected References

- Fox, Ridgway & Schott (2011). "*Algorithms, atrophy and Alzheimer's disease: cautionary tales for clinical trials*". Neuroimage 57(1):15-18.
- Ashburner & Ridgway (2013). *"Symmetric diffeomorphic modelling of longitudinal structural MRI"*. Frontiers in Neuroscience 6(197).

Overview

- Morphometry
- Voxel-Based Morphometry
- Tissue Segmentation
- Diffeomorphic Registration
- Longitudinal Registration
- **Multivariate Shape Models**
  - **Multivariate nature of shape**
  - **“Scalar momentum”**
  - **Some evaluations**

Multivariate shape models

- 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.

Argument from authority I

“*The morphologist, when comparing one organism with another, describes the differences between them point by point, and “character” by “character”. If he is from time to time constrained to admit the existence of “correlation” between characters, yet all the while he recognises this fact of correlation somewhat vaguely, as a phenomenon due to causes which, except in rare instances, he cannot hope to trace ; and he falls readily into the habit of thinking and talking of evolution as though it had proceeded on the lines of his own descriptions, point by point, and character by character*.”

D’Arcy Thompson (Growth and Form, 1917).

Argument from authority II

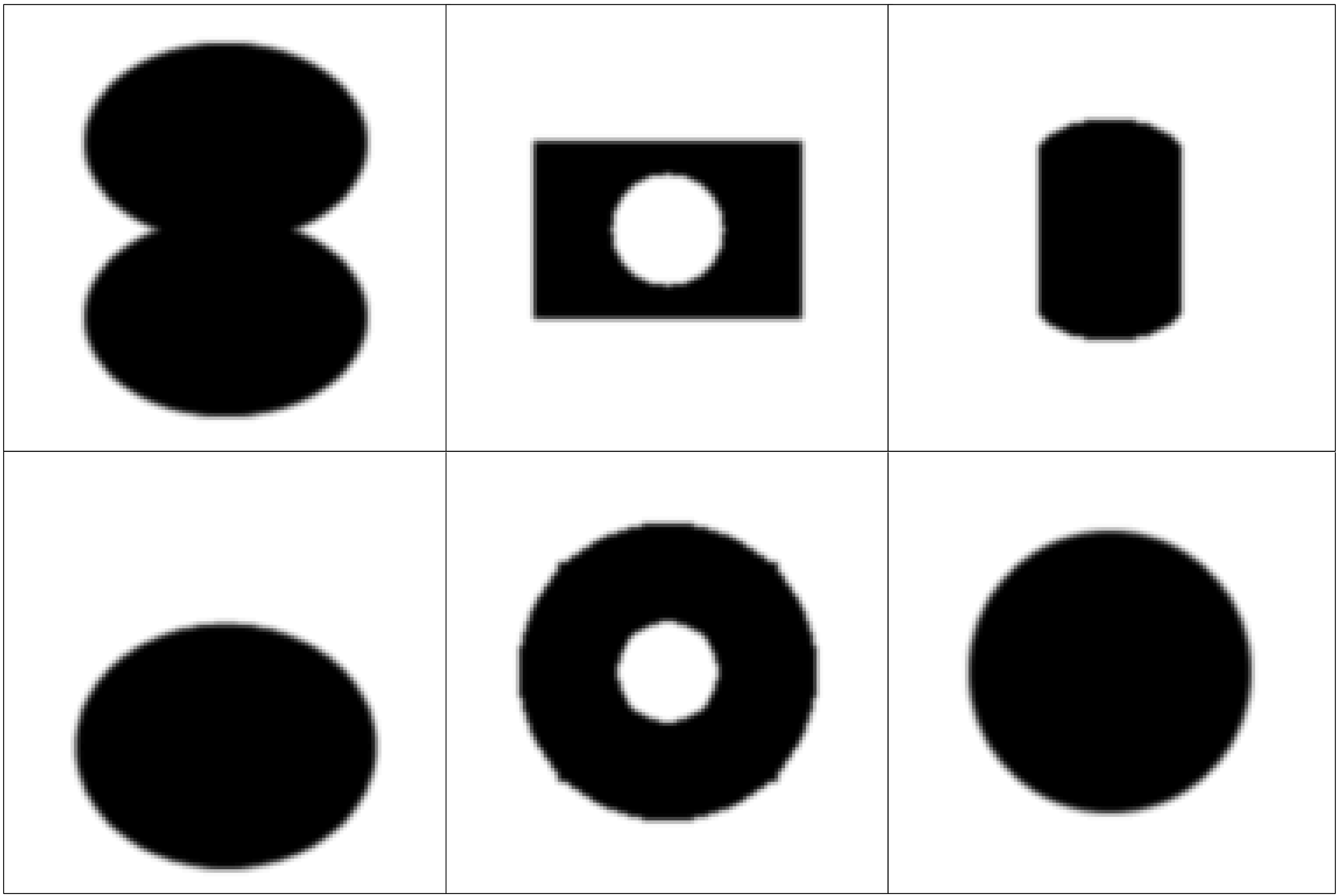
“This unhappy result can be traced to the piecemeal tests which have hitherto been used. A bone or a tooth is a unit ; it is not a discrete assembly of independent measurements.”

Jacob Bronowski & W.M. Long (Nature, 1951).

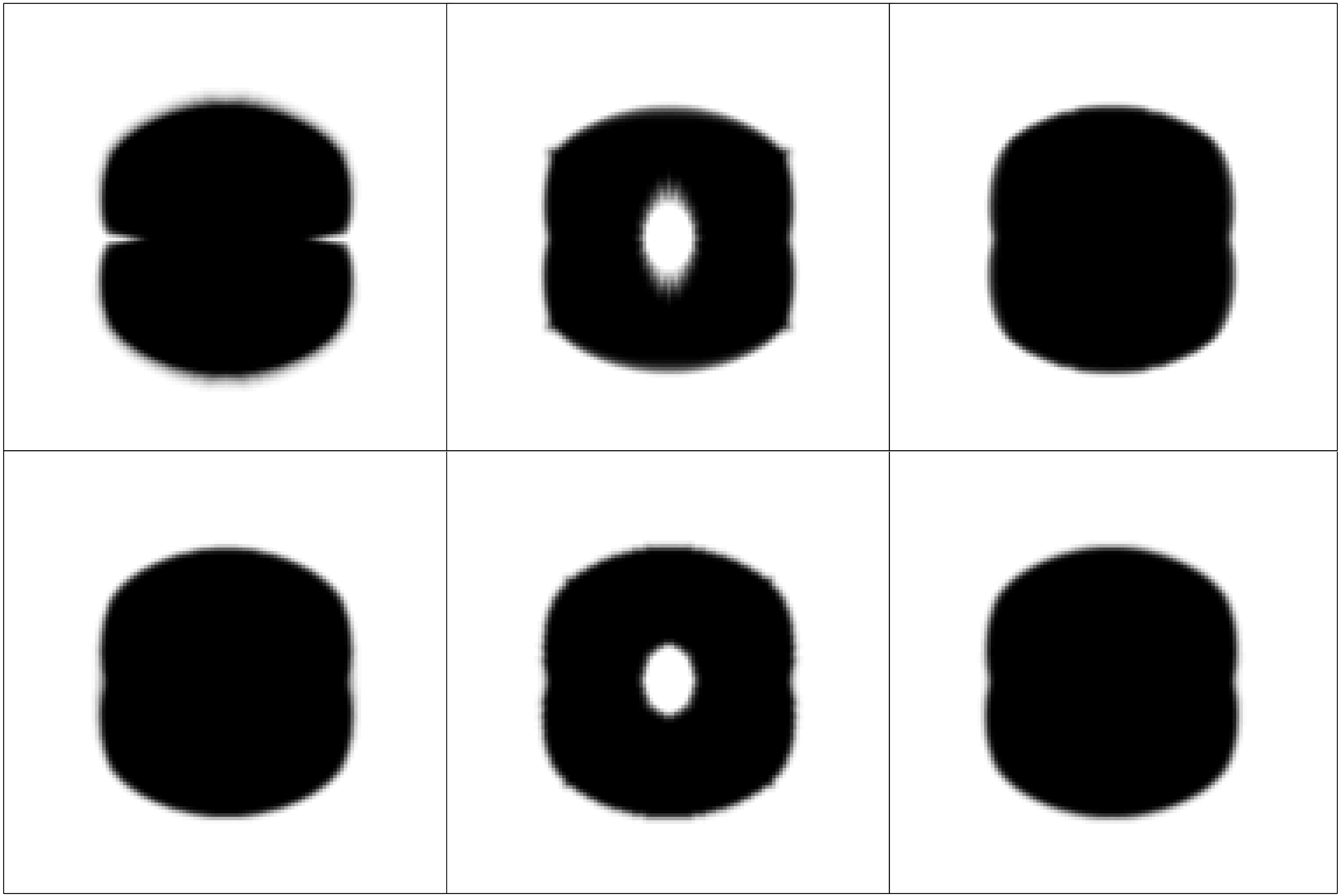
“*The right statistical method must treat the set of variates as a single coherent matrix ; and this is, in fact, the technique of multivariate analysis.”*

Jacob Bronowski & W.M. Long (Nature, 1951).

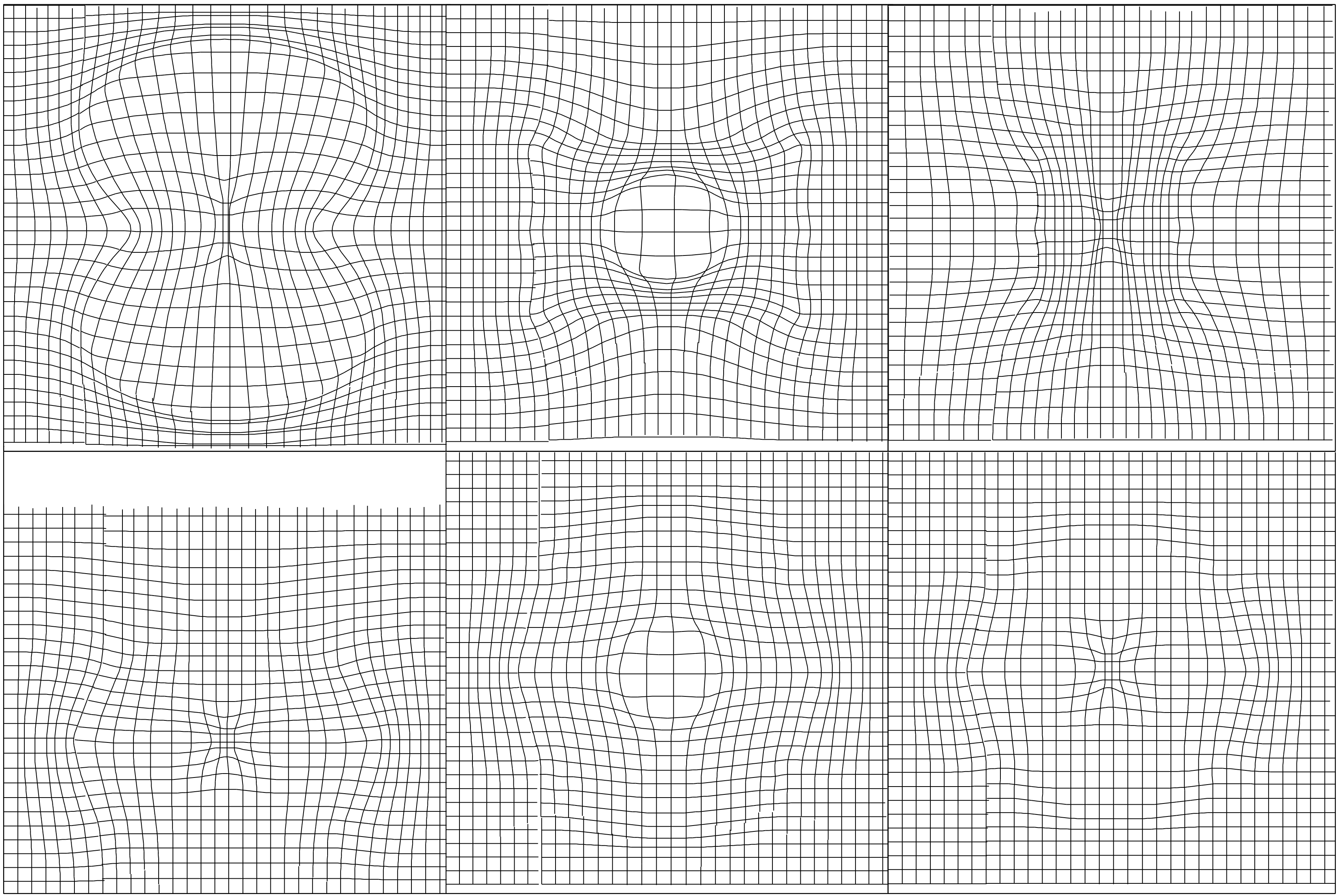
Some 2D Shapes



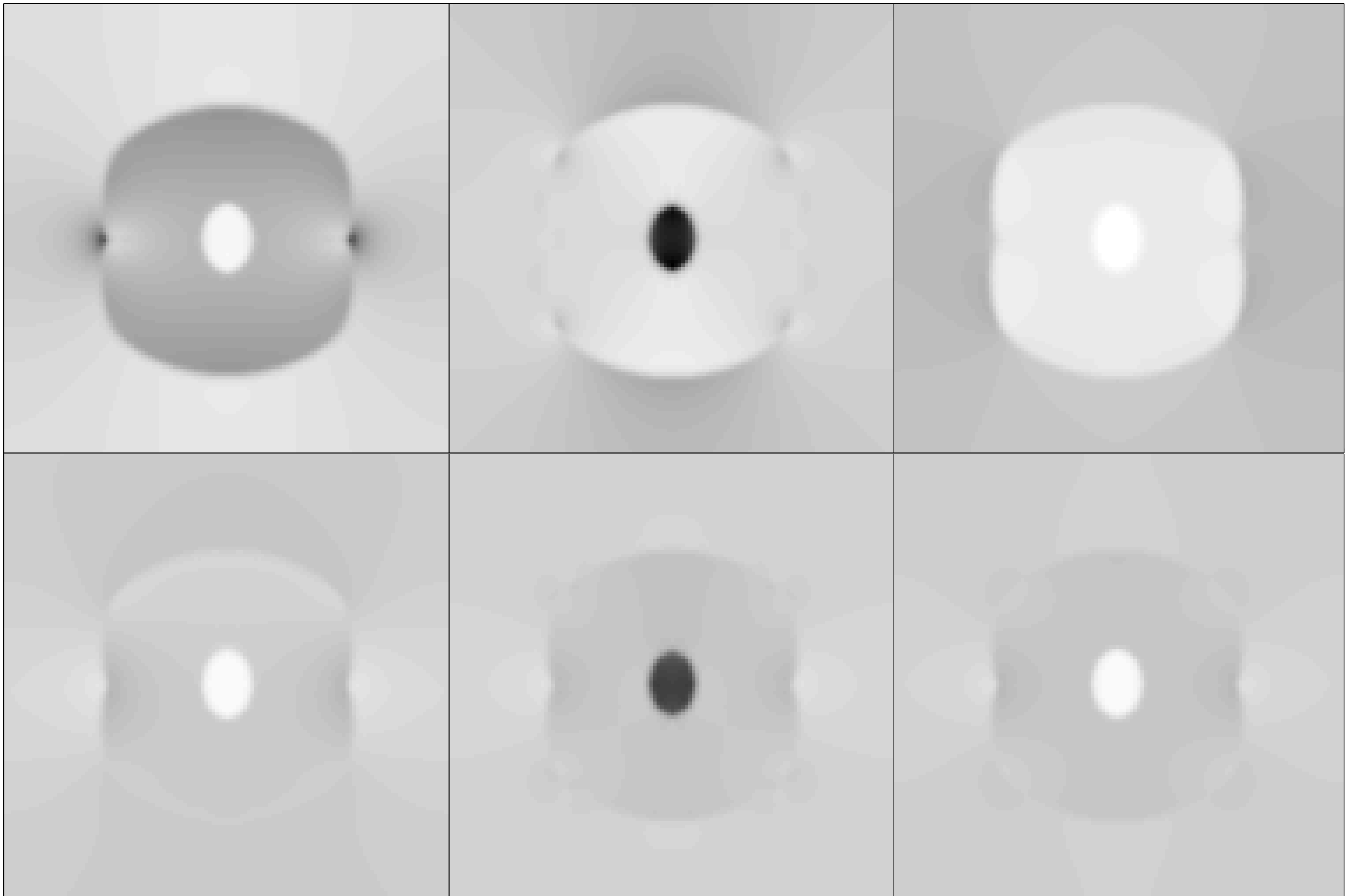
Shapes aligned to their average



These were the deformations for that

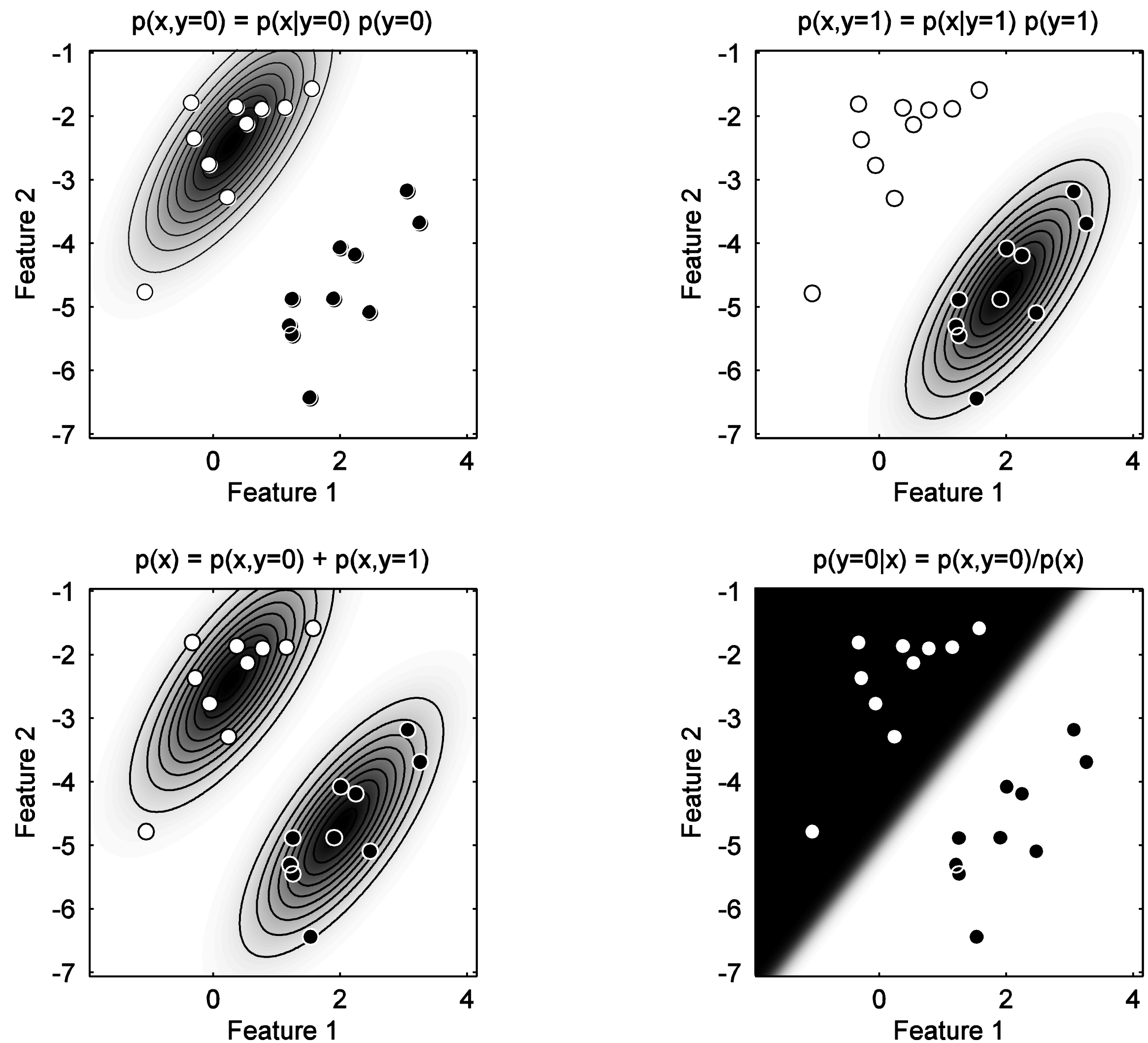


and these are the Jacobian determinants



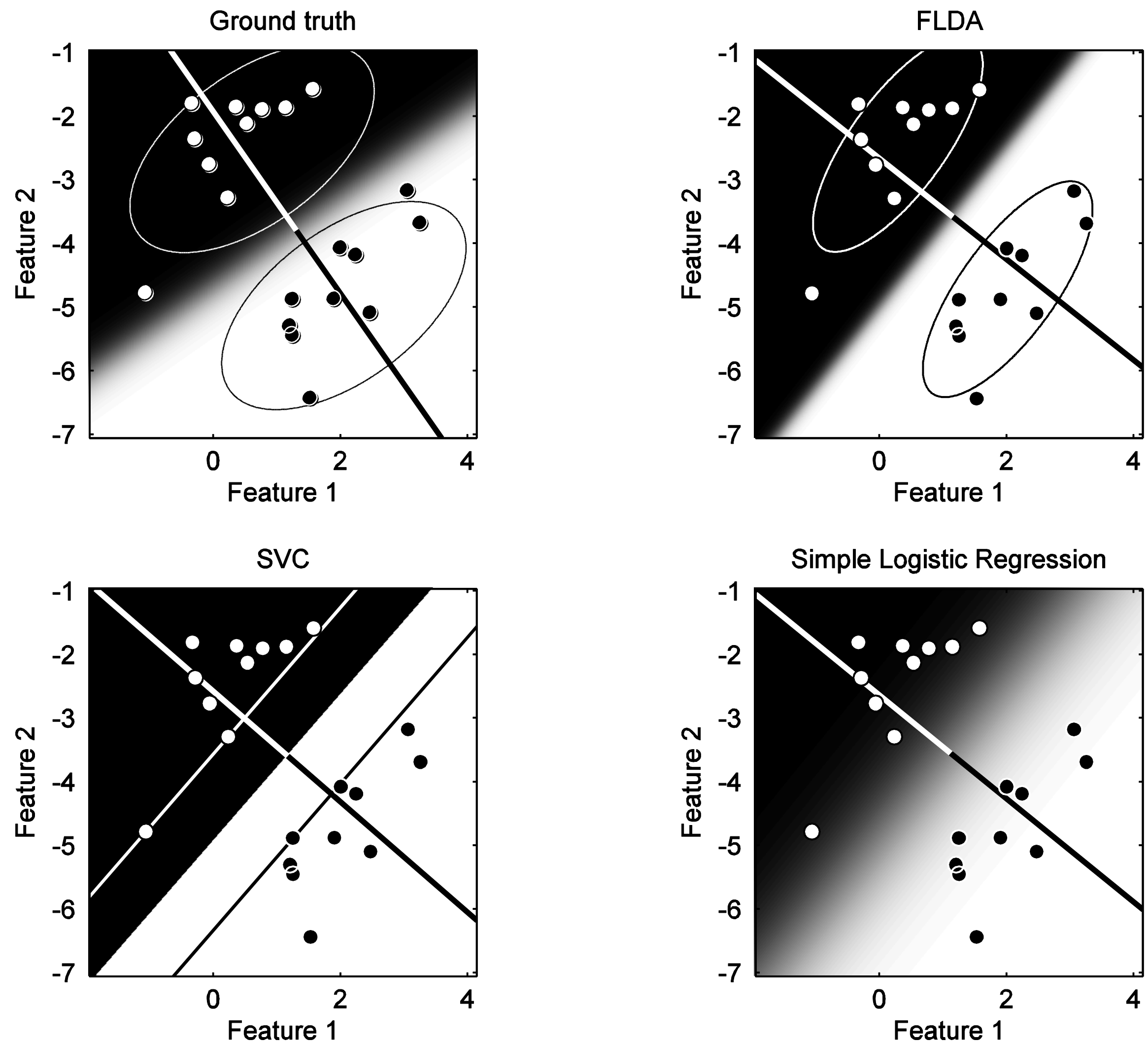
Fisher's Linear Discriminant Analysis

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



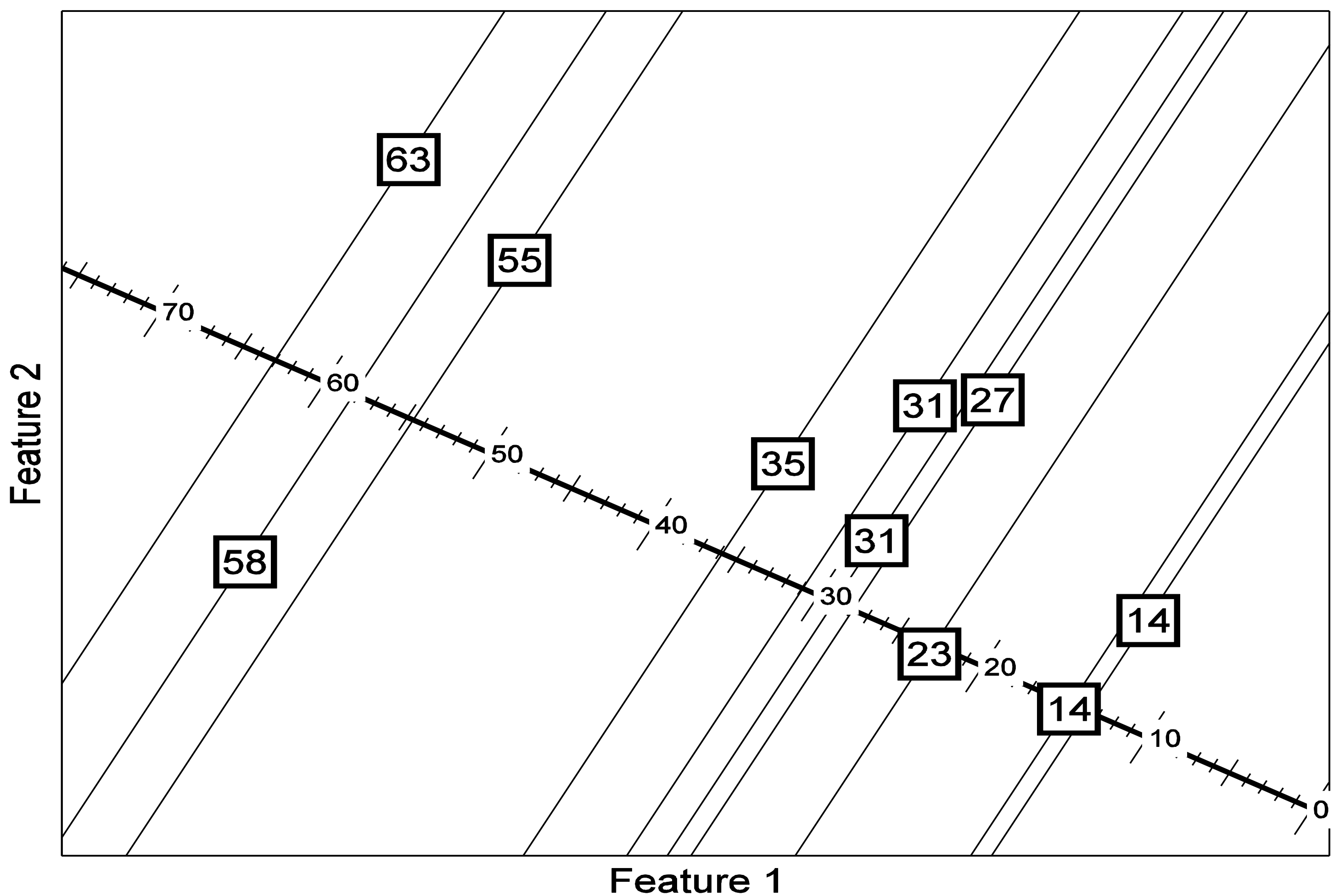
Other linear discrimination approaches

- 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



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

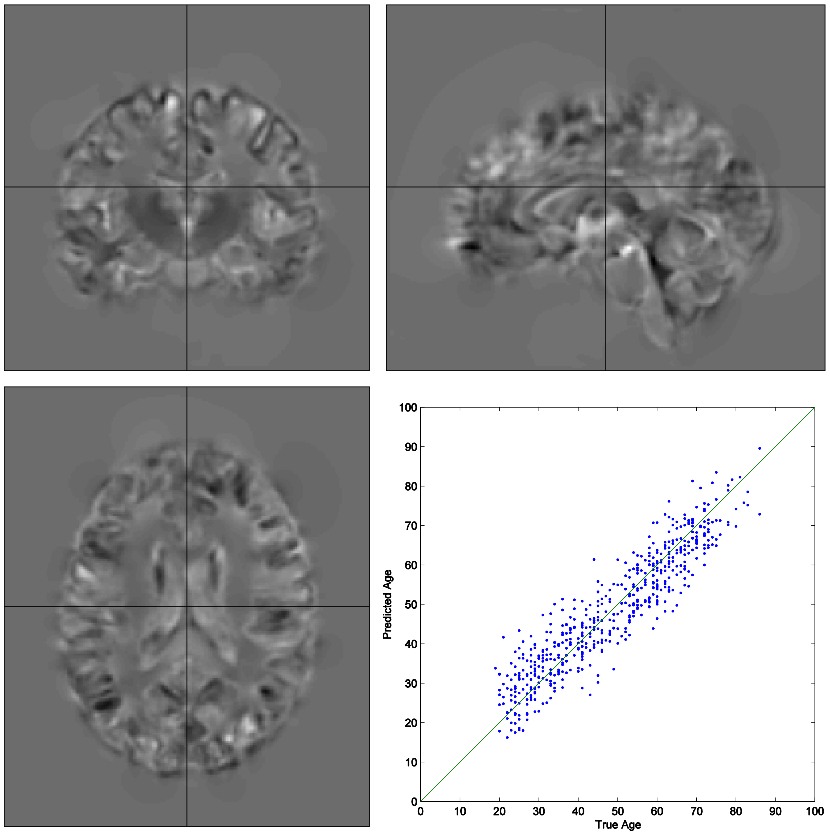
a_1, a_2, a_3 etc are voxels in a weight map

b is a constant offset.

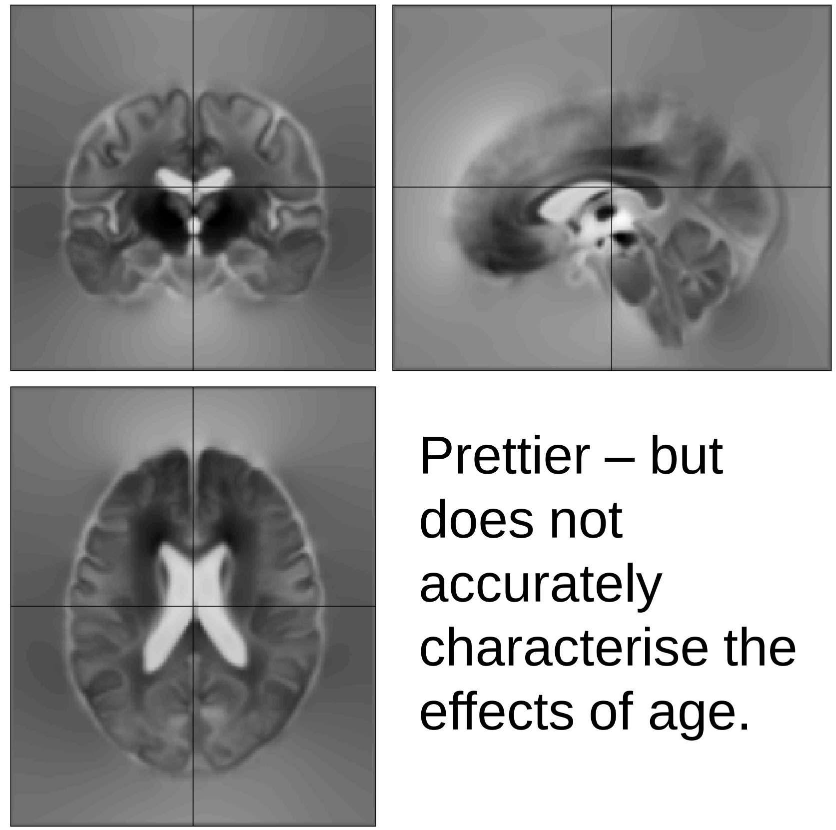
The weight map can be visualised

Maps

Multivariate weight map



Simple T statistic image



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

"Scalar Momentum"

- For diffeomorphic registration by least-squares matching, the warps (φ) are encoded by an initial velocity ($v(0)$):

$$Lv(0) = \frac{1}{\sigma^2} |\det d\varphi| (I_0 - I_1 \circ \varphi) \nabla I_0$$

Initial Momentum

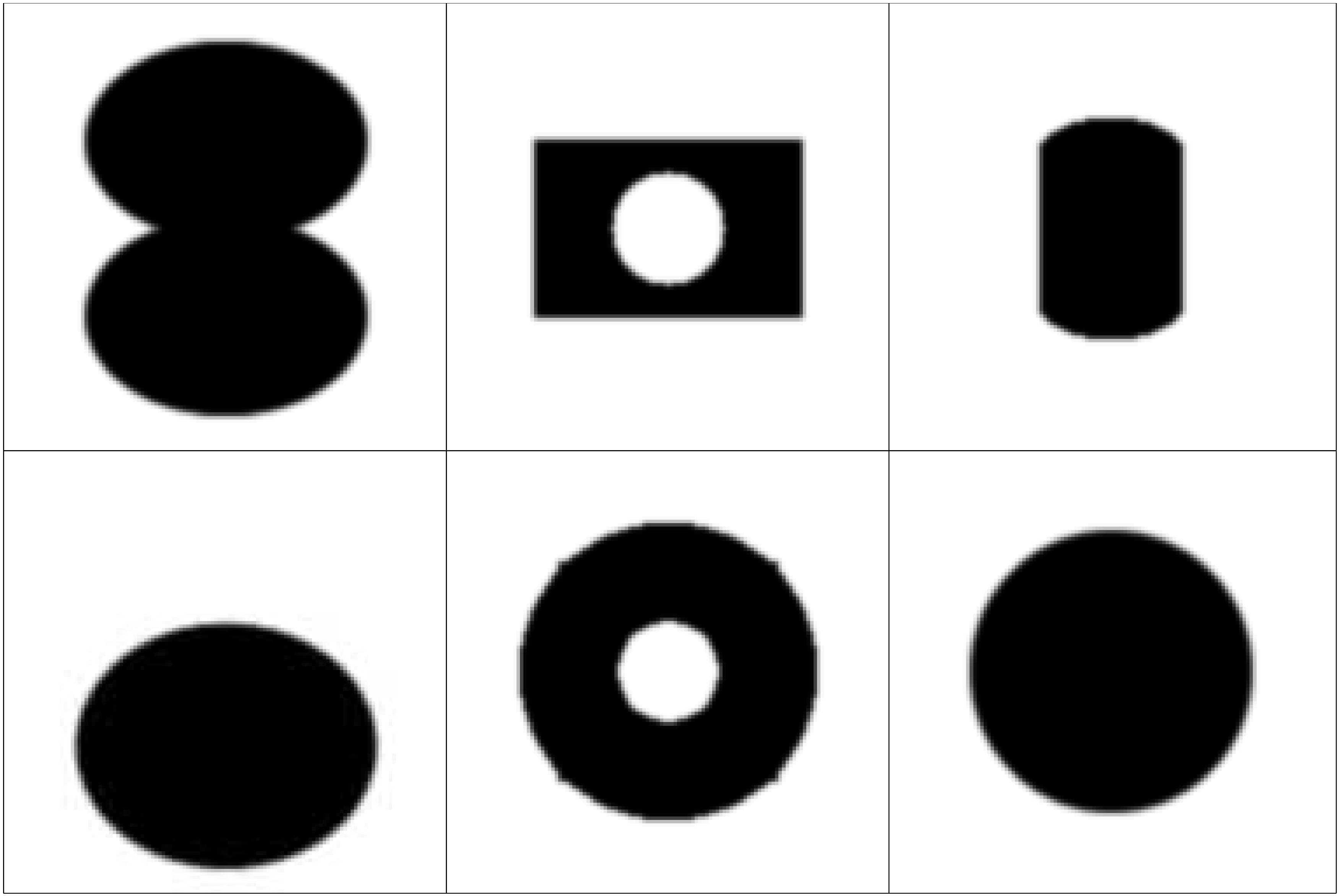
Jacobian determinants

Template

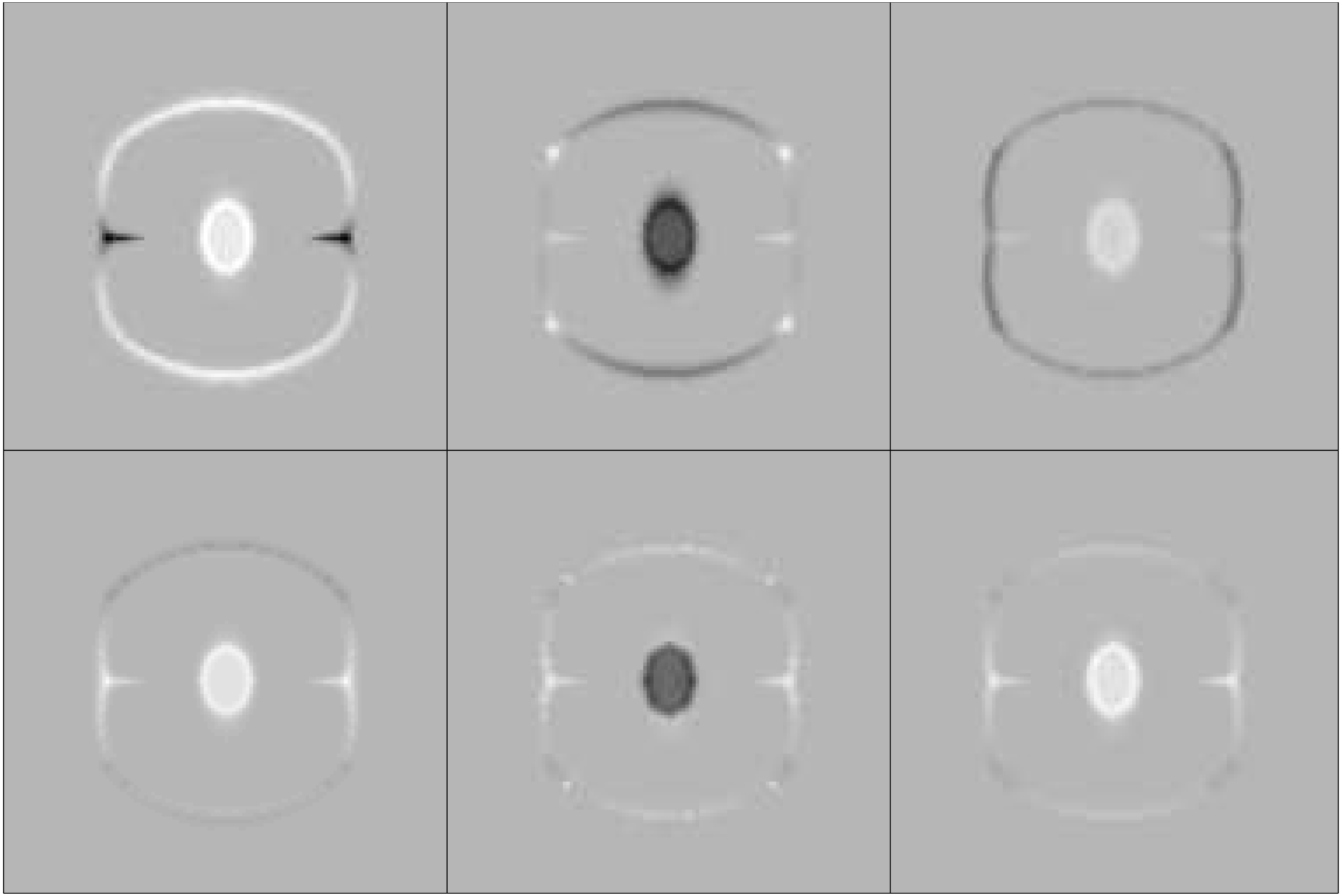
Warped individual

Gradient of template

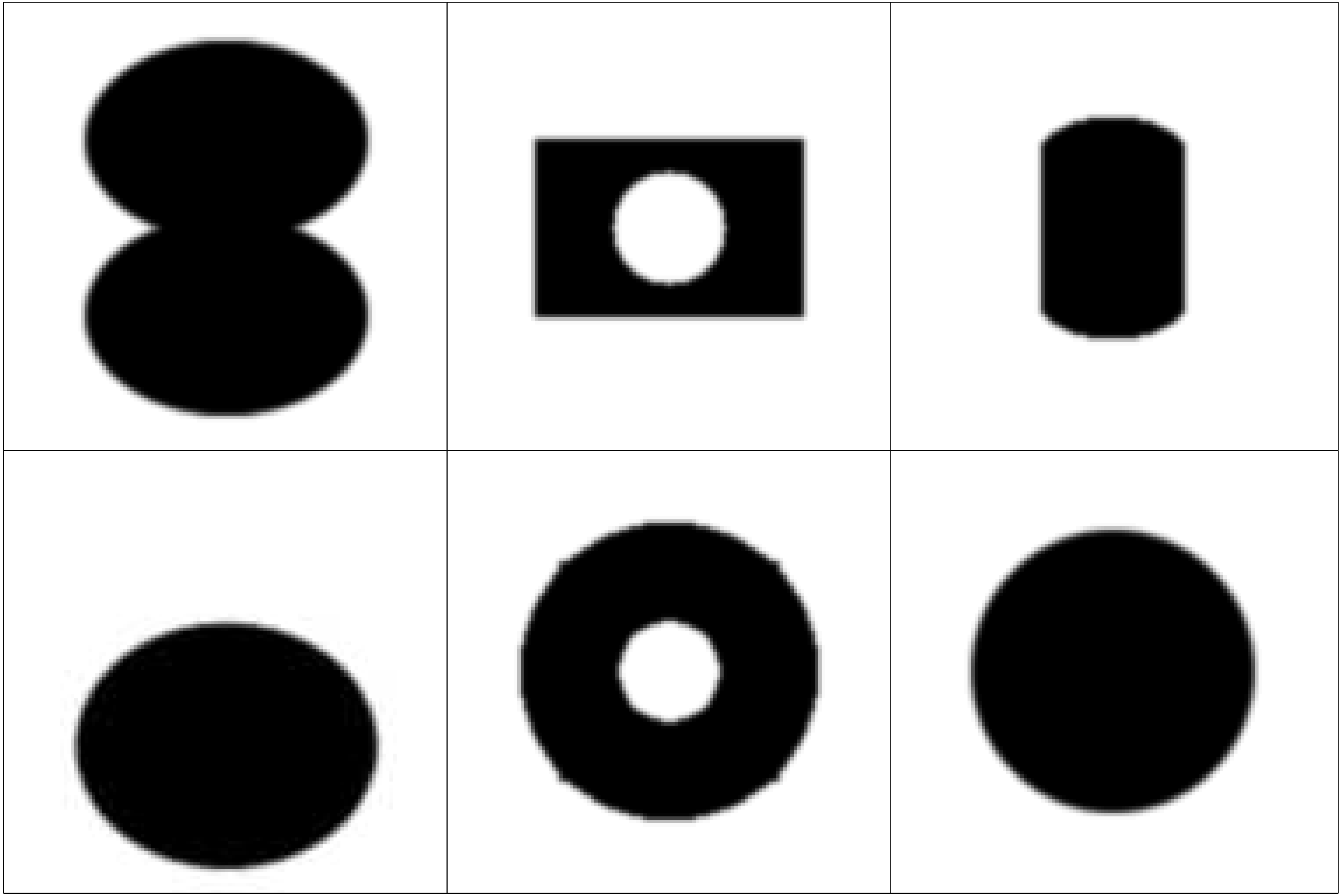
The 2D shapes (again)



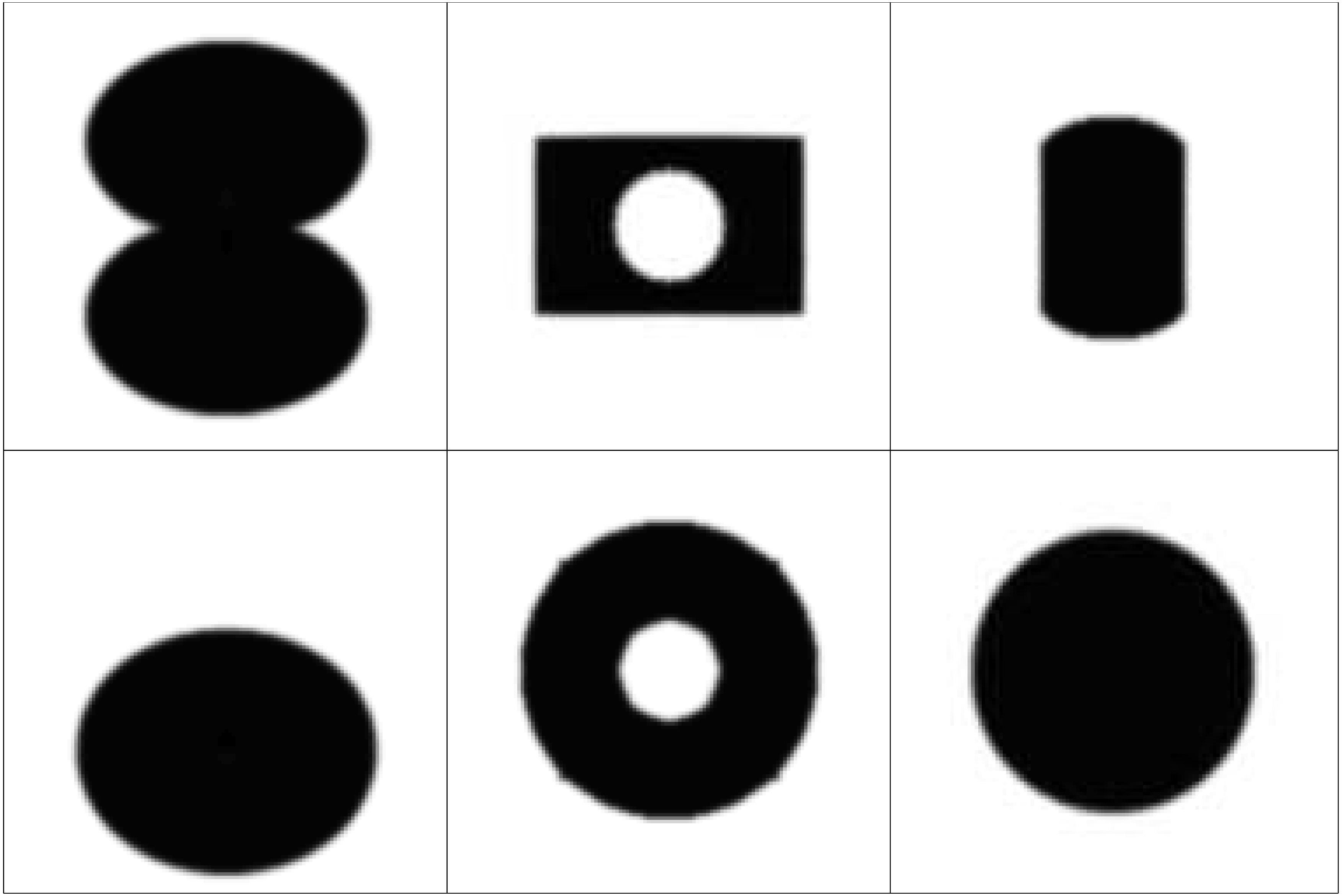
“Scalar momentum” $|\det d\varphi|(I_0 - I_1 \circ \varphi)$



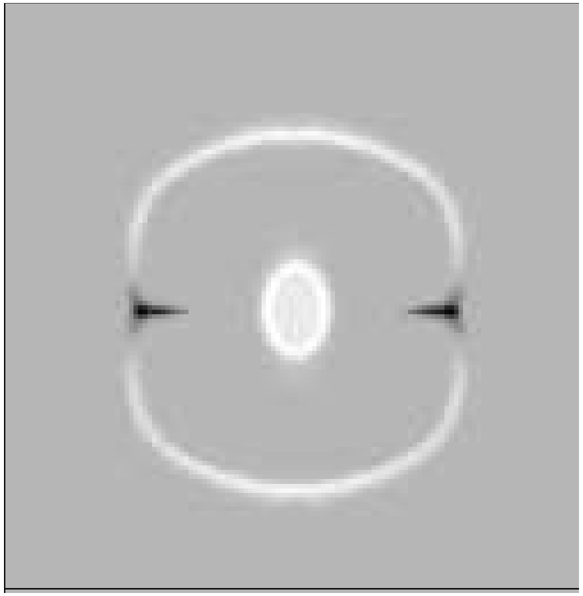
The 2D shapes (yet again)



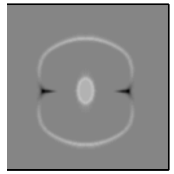
Reconstructed from scalar momentum and template.



“Scalar momentum” – encodes the original shapes

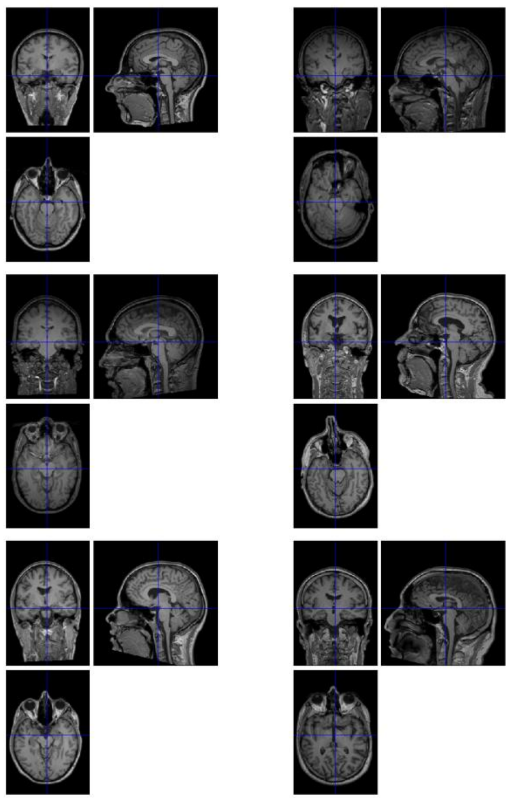


Residuals

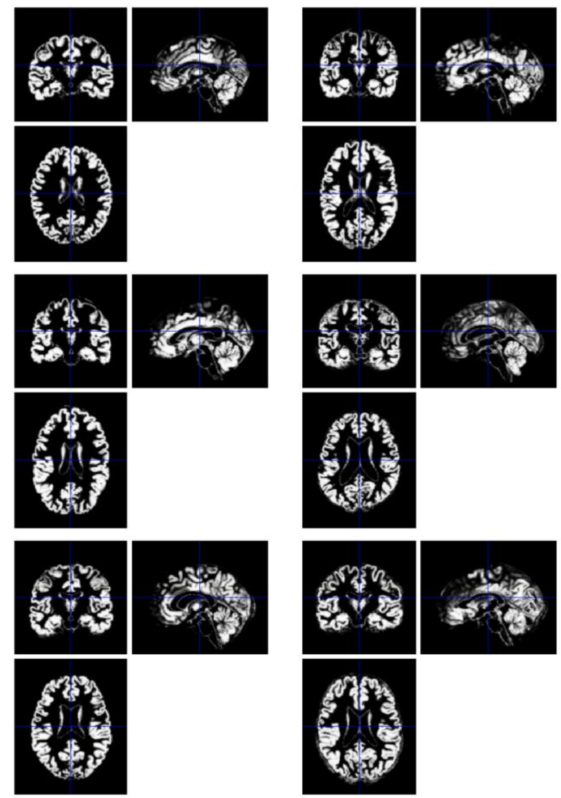


IXI Data

Original Images

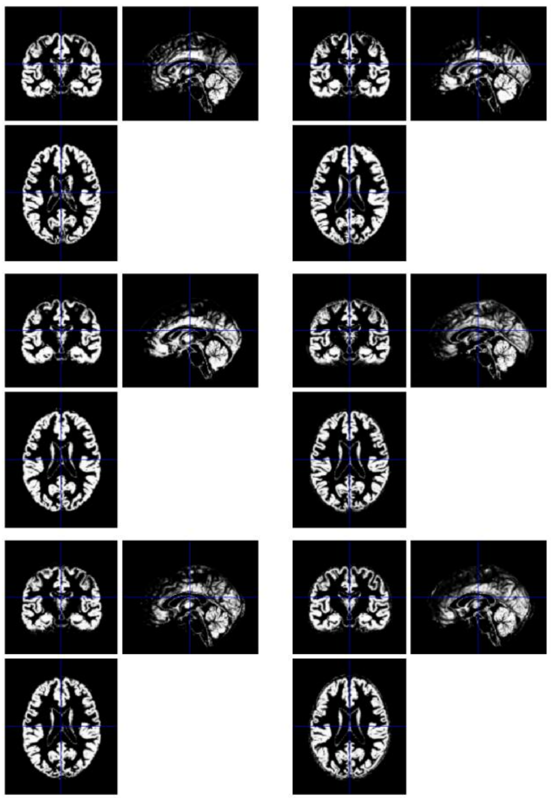


Rigidly Aligned Grey Matter

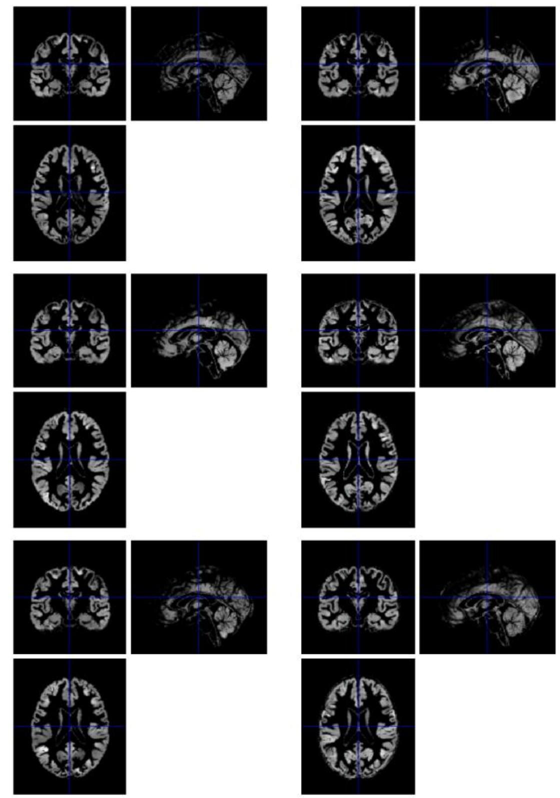


VBM-type Features

Warped Grey Matter

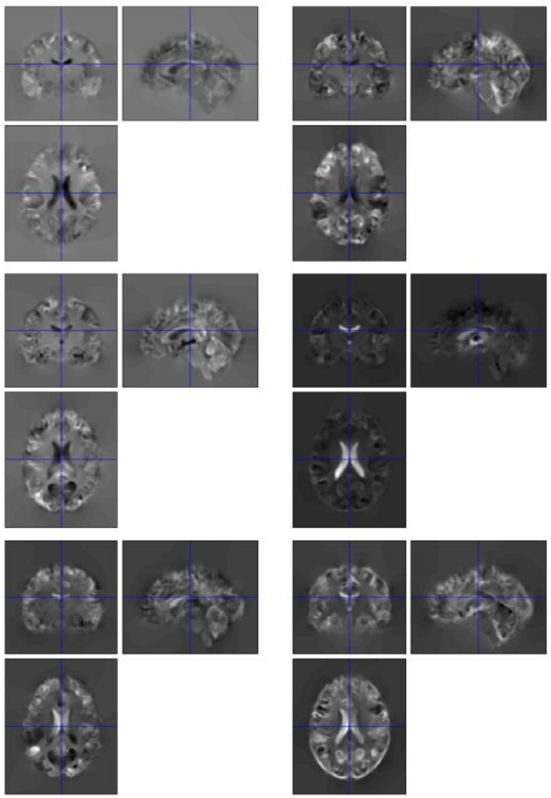


“Modulated” Warped GM

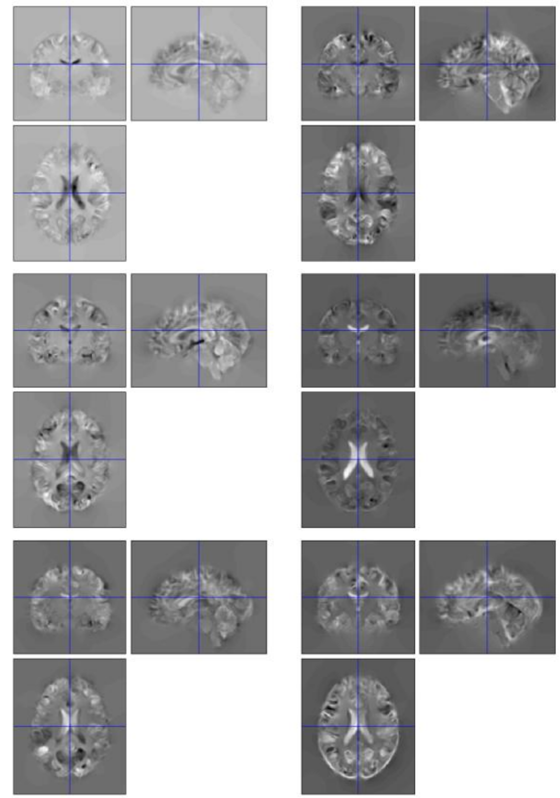


Volumetric Measures from Deformation Fields

Jacobian determinants

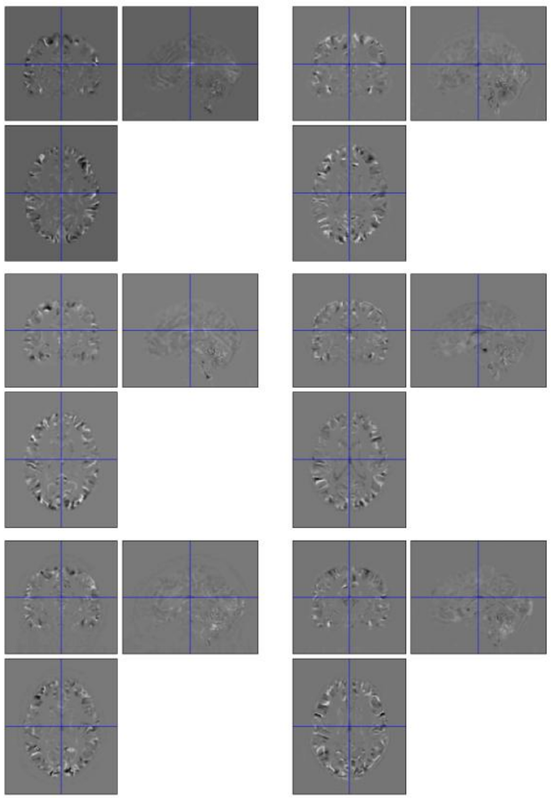


Initial Velocity Divergence

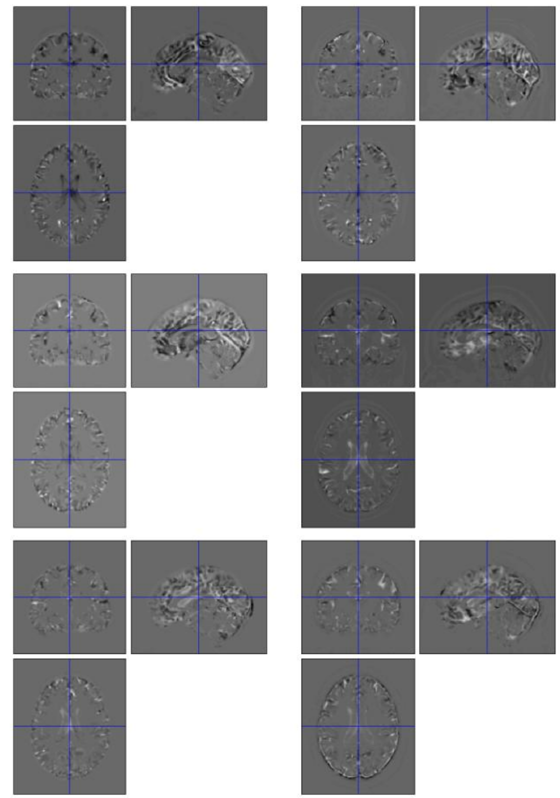


Scalar Momentum

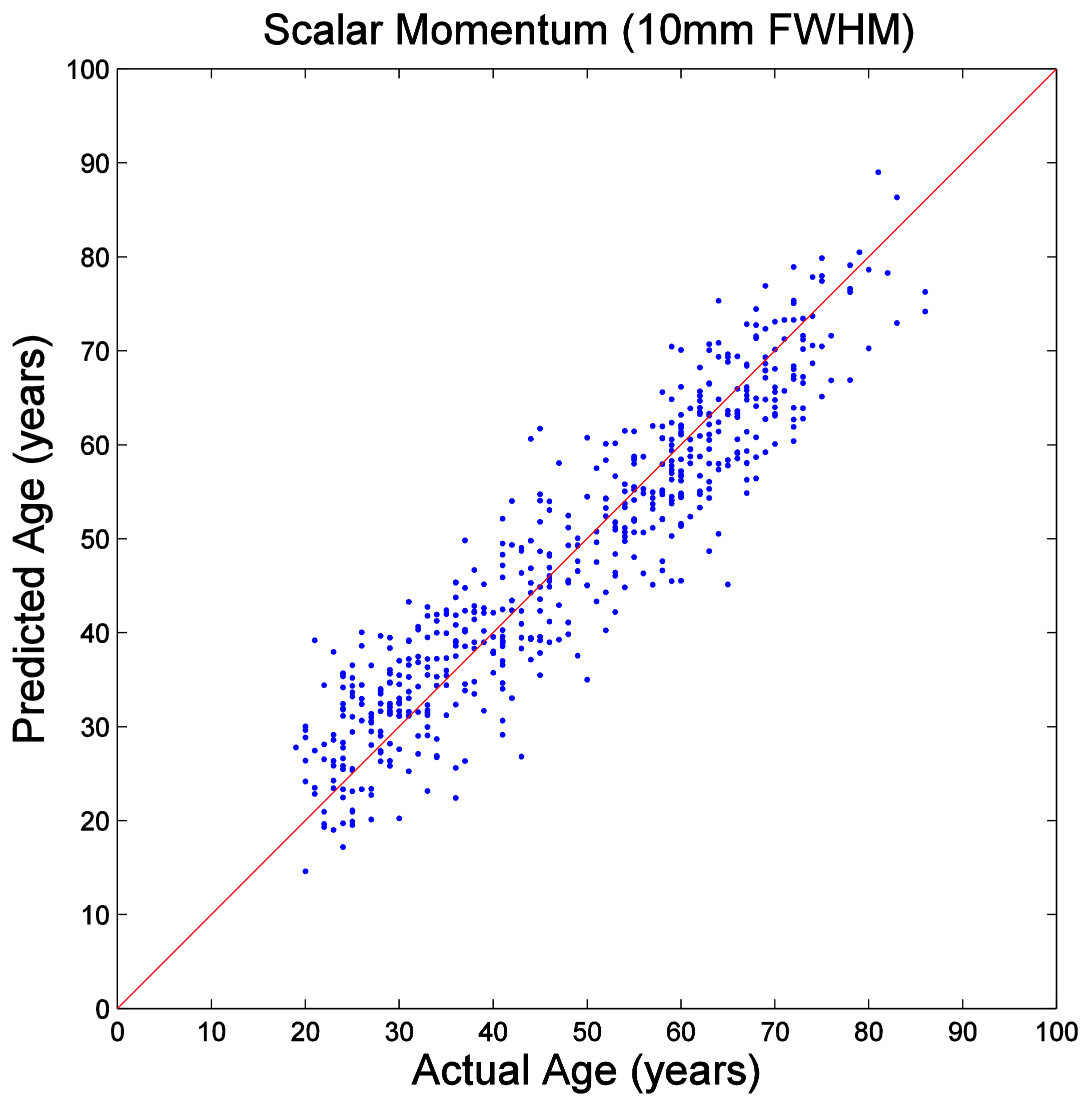
1st Component



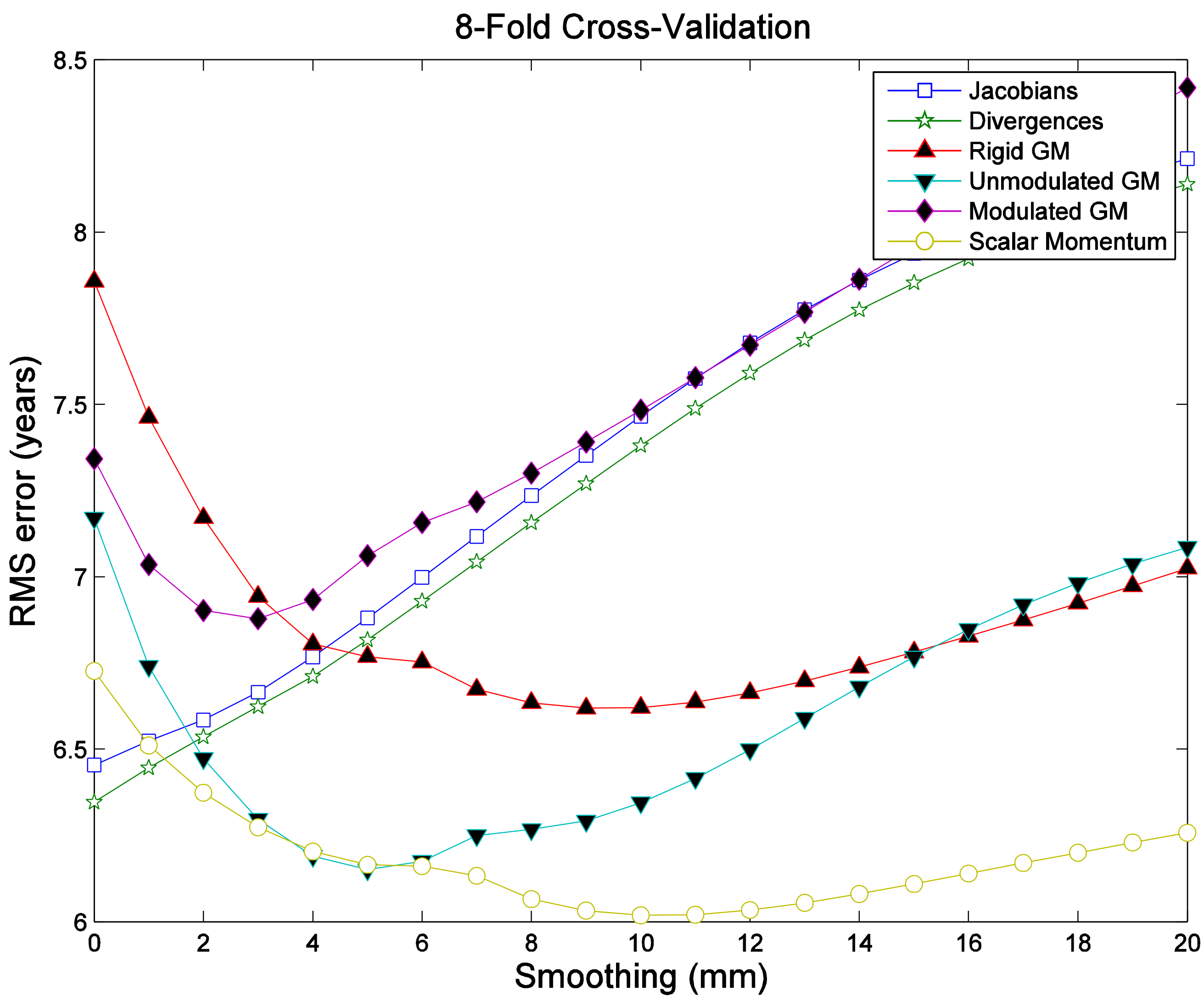
2nd Component



Age Prediction - Best Result

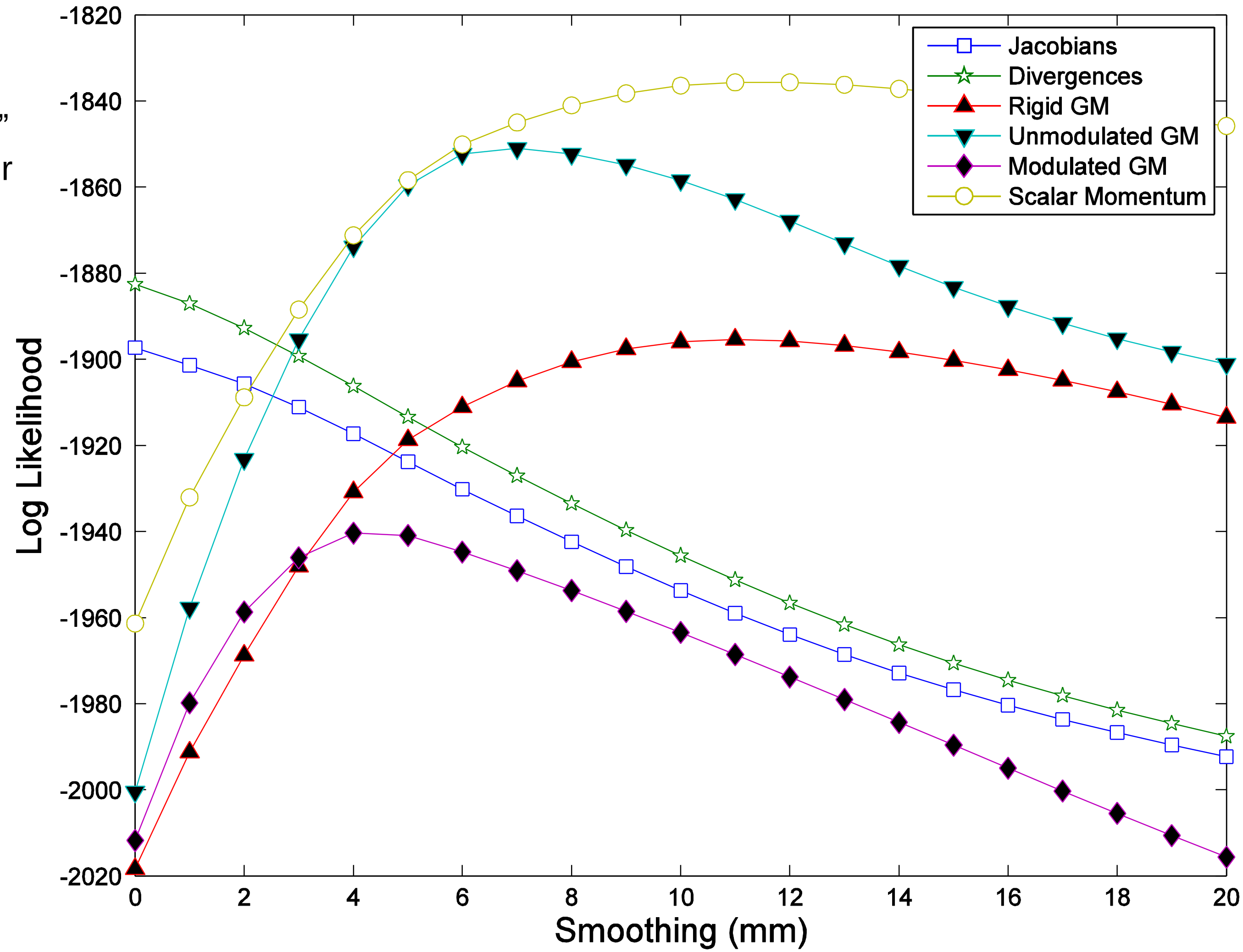


Age Prediction – Comparison Among Features

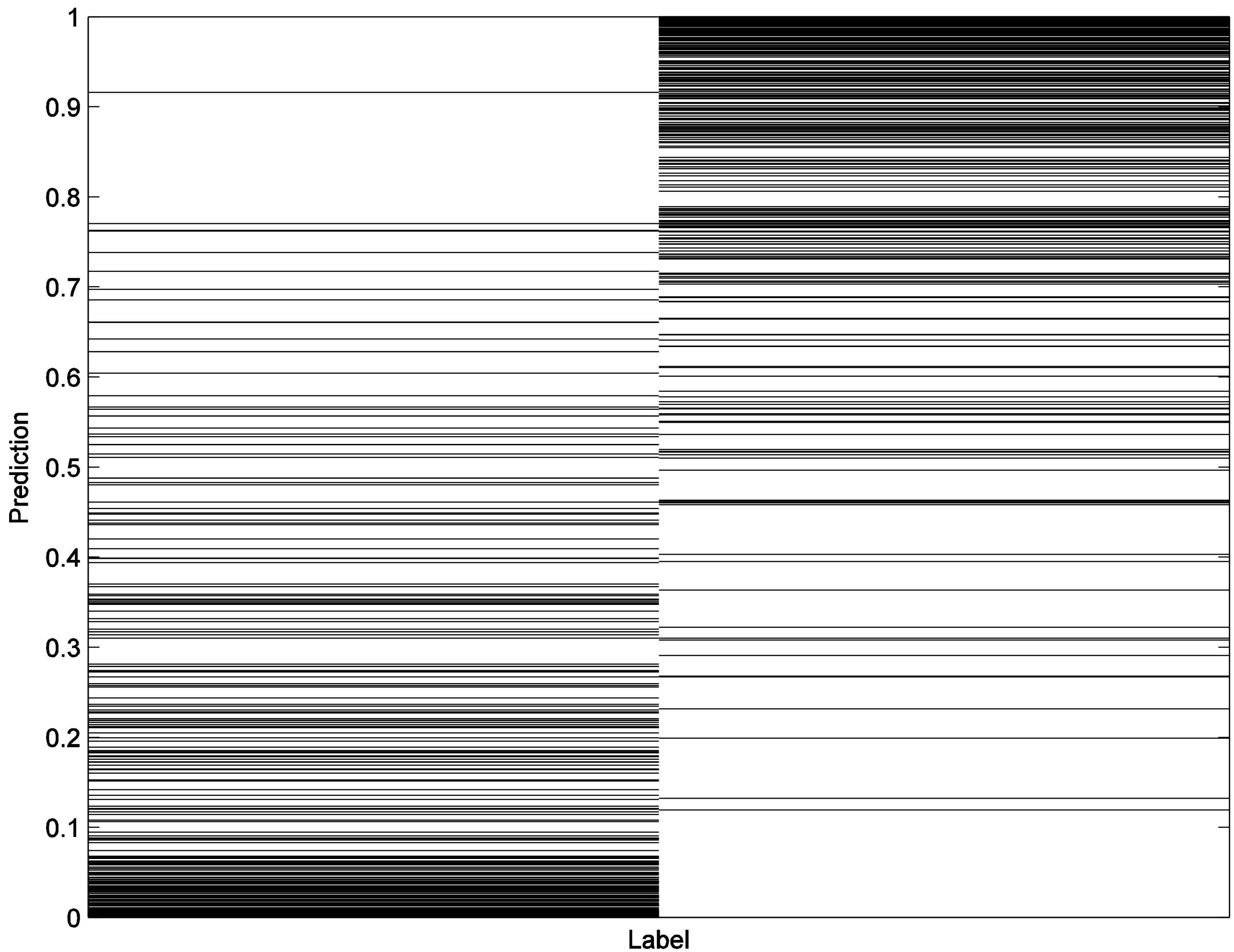


Age Prediction – Model Log Likelihoods

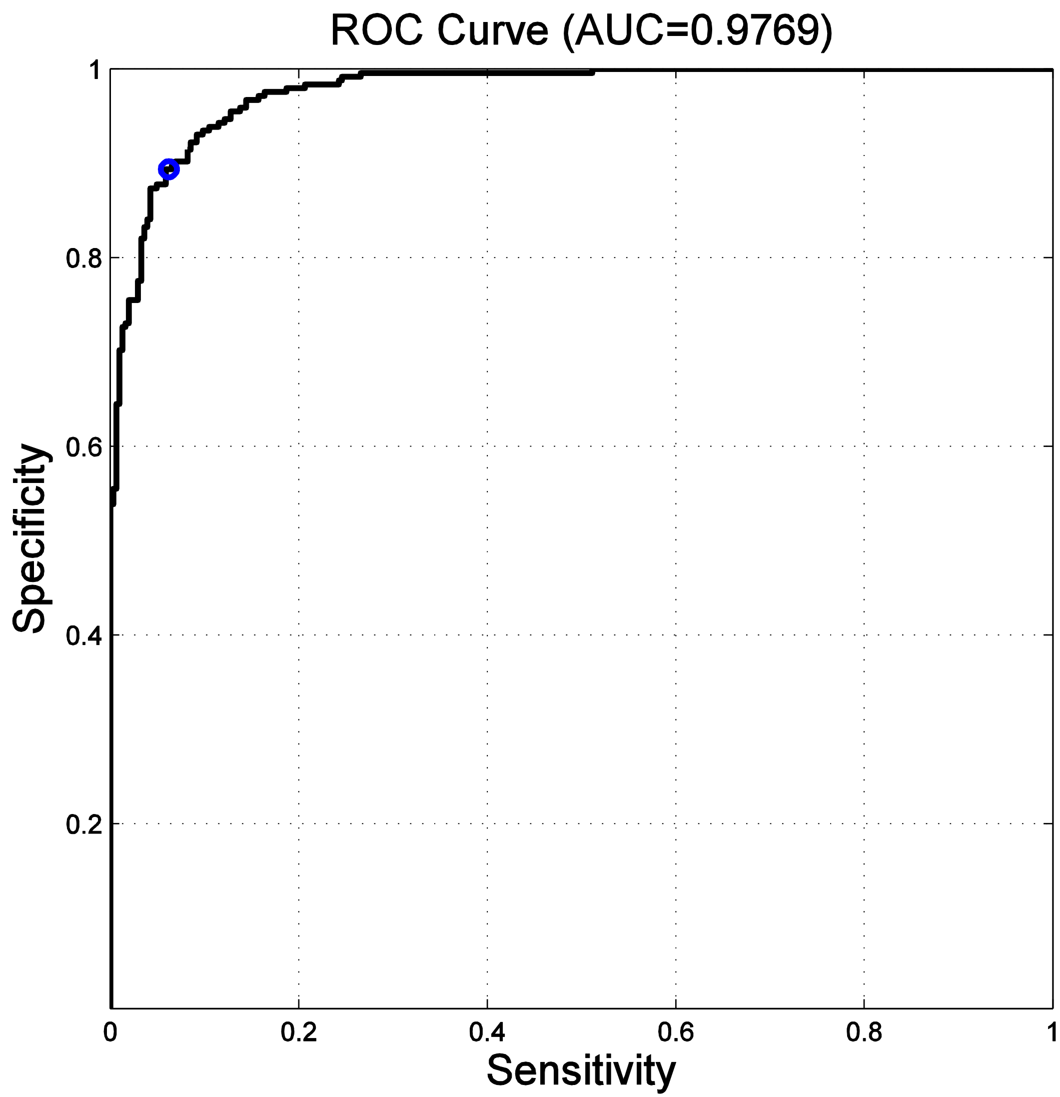
Differences > 4.6 indicate “decisive” evidence in favour of one approach over another.



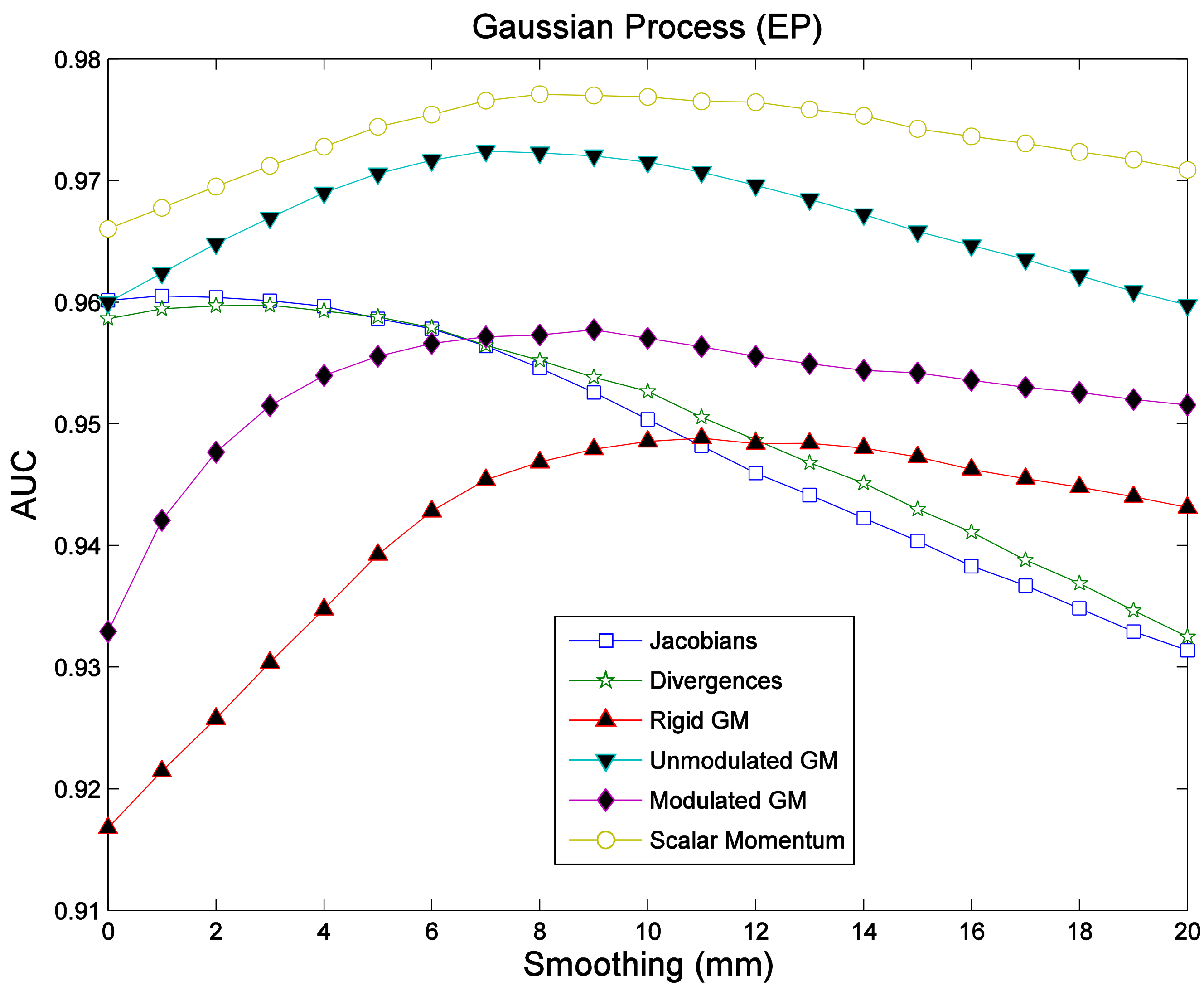
Sex Prediction – Best Result



Sex Prediction – Best Result

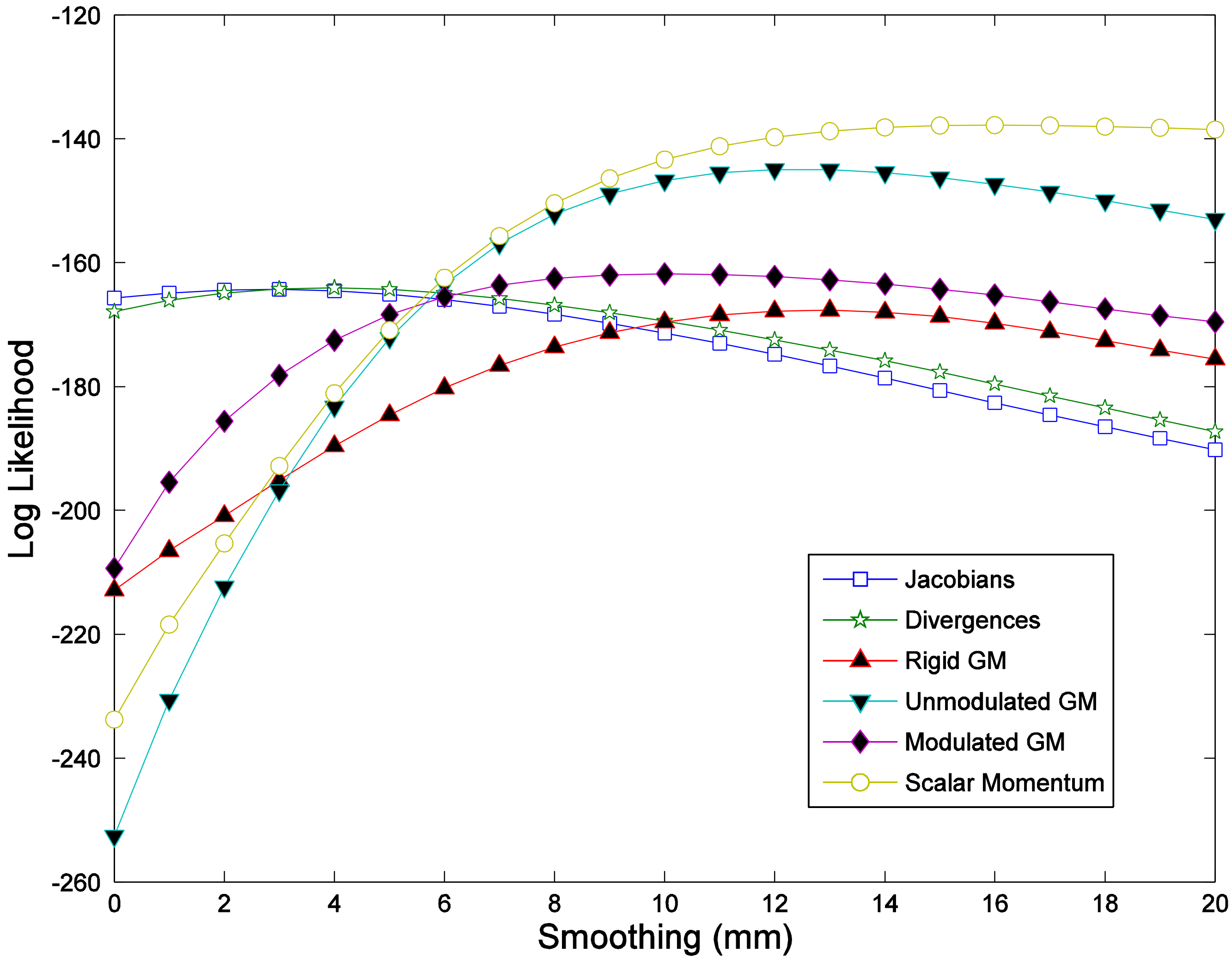


Sex Prediction – Comparison Among Features



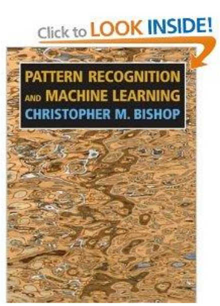
Sex Prediction – Model Log Likelihoods

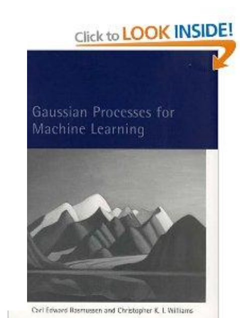
Differences > 4.6 indicate “decisive” evidence in favour of one approach over another.

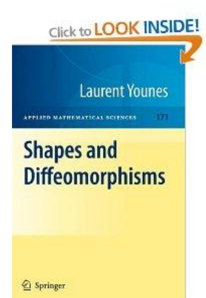


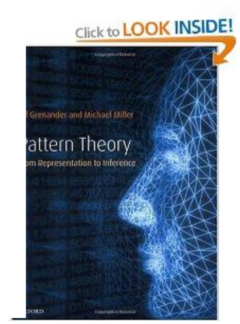
Selected References

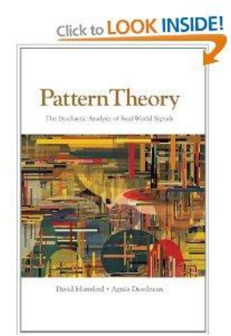
- Bishop. *Pattern Recognition and Machine Learning*. 2006.
- Rasmussen & Williams. *Gaussian Processes for Machine Learning*. MIT Press, 2006. ISBN-10 0-262-18253-X, ISBN-13 978-0-262-18253-9. http://www.gaussianprocess.org/gpml/
- Younes, Arrate & Miller. "*Evolutions equations in computational anatomy*".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












For the harmony of
the world is made
manifest in Form and
Number, and the heart
and soul and all the
poetry of Natural
Philosophy are embodied
in the concept of
mathematical beauty.
D'Arcy Thompson
On Growth and Form
(Dundee, 1917)