Morphometry

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Morphometry is defined as:

Measurement of the form of organisms or of their parts.

The American Heritage® Medical Dictionary

The measurement of the structures and parts of organisms.

Mosby's Medical Dictionary, 8th edition. © 2009, Elsevier.

The measurement of forms.

Saunders Comprehensive Veterinary Dictionary, 3 ed. © 2007 Elsevier, Inc.

What kind of differences are we looking for?

- 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.

Overview

- A Mass-Univariate Approach
  - Voxel-based morphometry
  - Preprocess, followed by SPM

- A Multivariate Approach
  - Multivariate methods
  - Shape models
  - A 2D simulation
  - A real 3D example

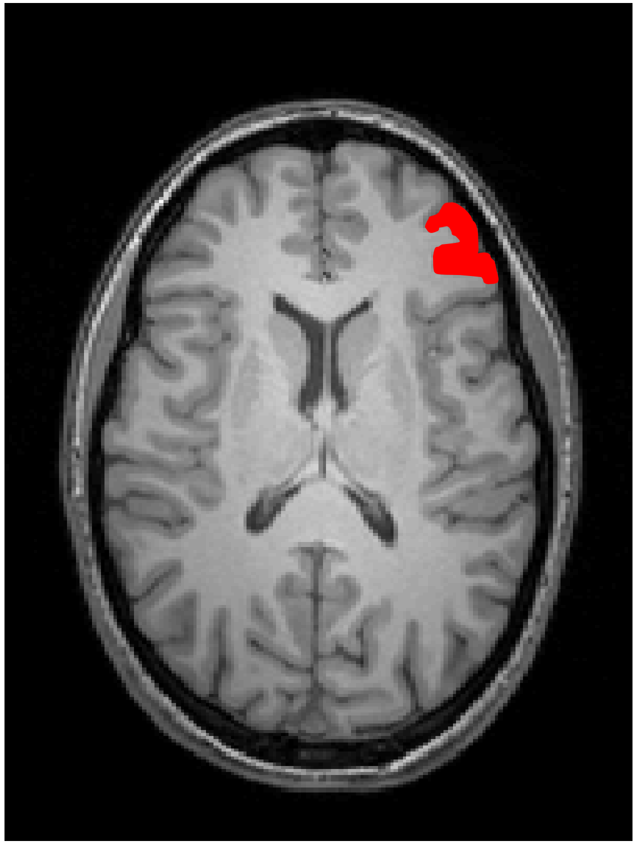
A Univariate Approach - VBM

- Based on comparing **regional volumes of tissue**.
- Suitable for studying focal volumetric differences of grey matter.
- Assumes independence among voxels
  - Not very biologically plausible
  - But shows differences that are easier to interpret

Voxel-Based Morphometry

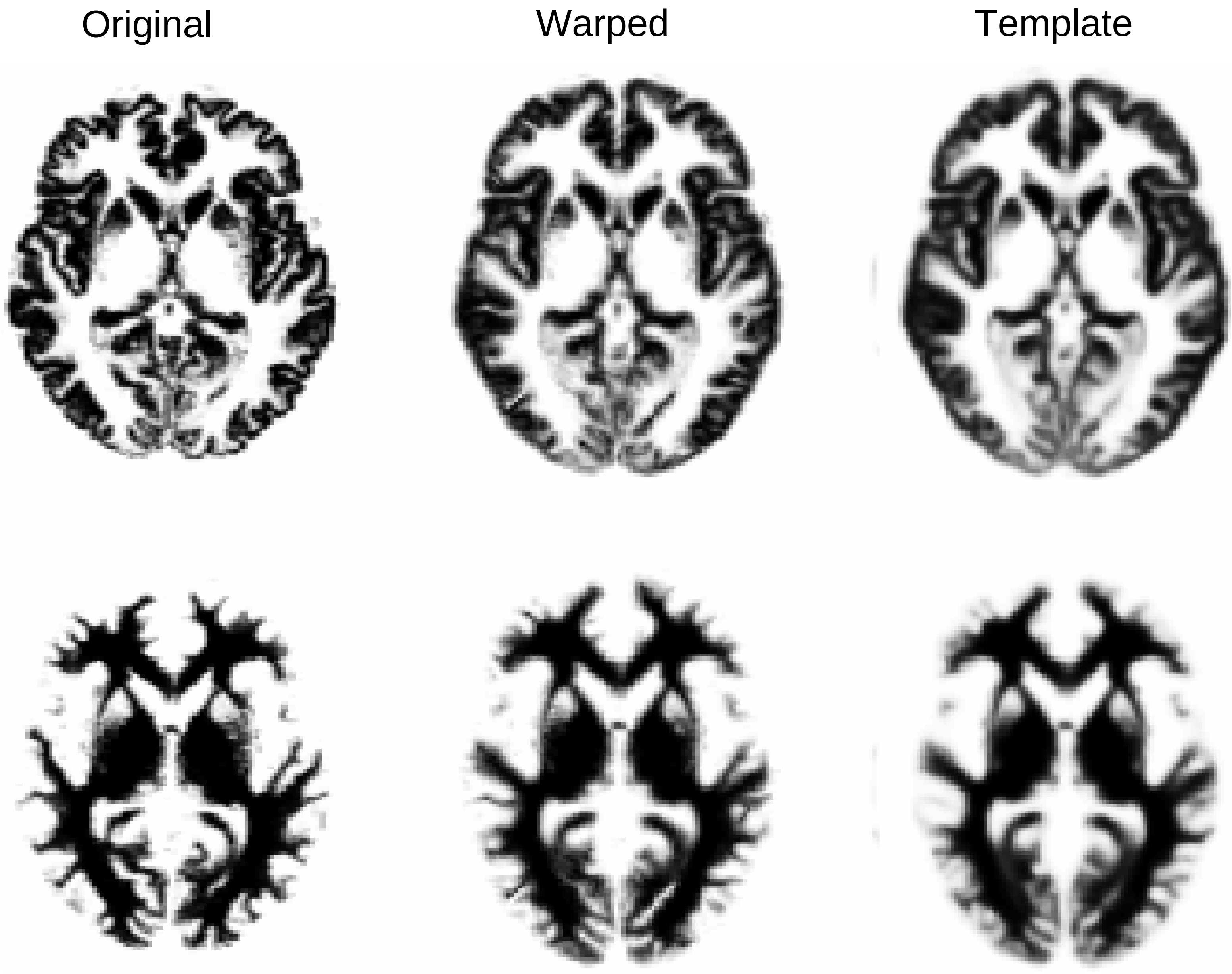
- Produce a map of statistically significant differences among populations of subjects.
  - e.g. compare a patient group with a control group.
  - or identify correlations with age, test-score etc.
- The data are pre-processed to sensitise the tests to regional tissue volumes.
  - Usually grey or white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

Volumetry

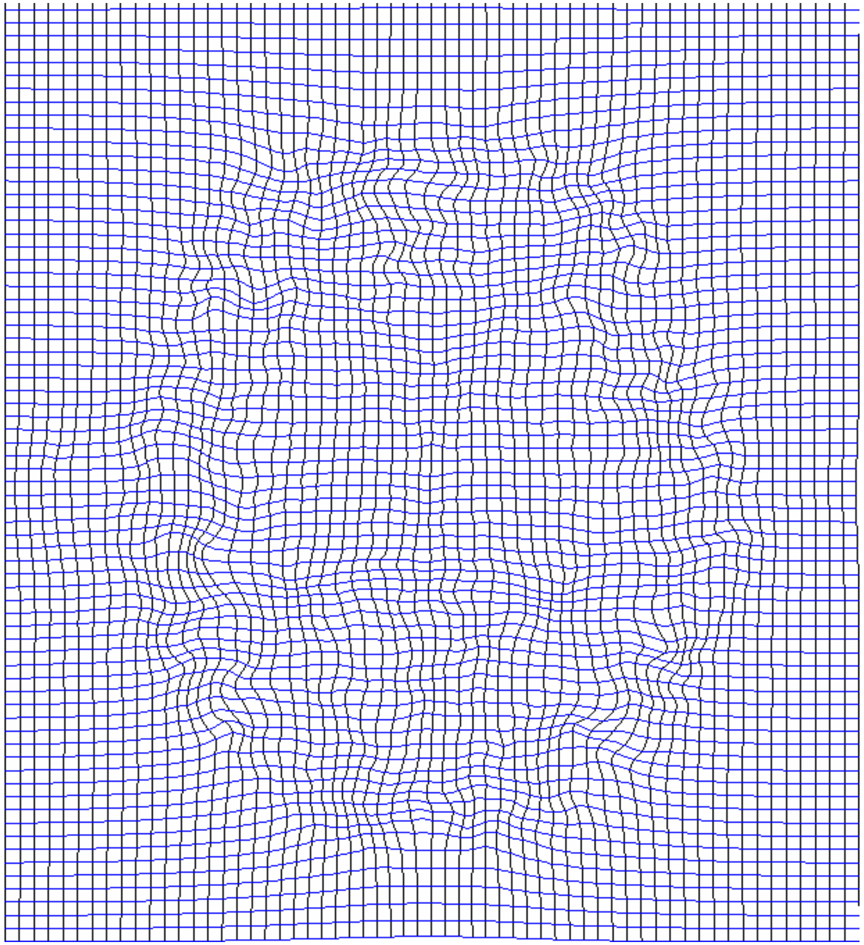


T1-Weighted MRI

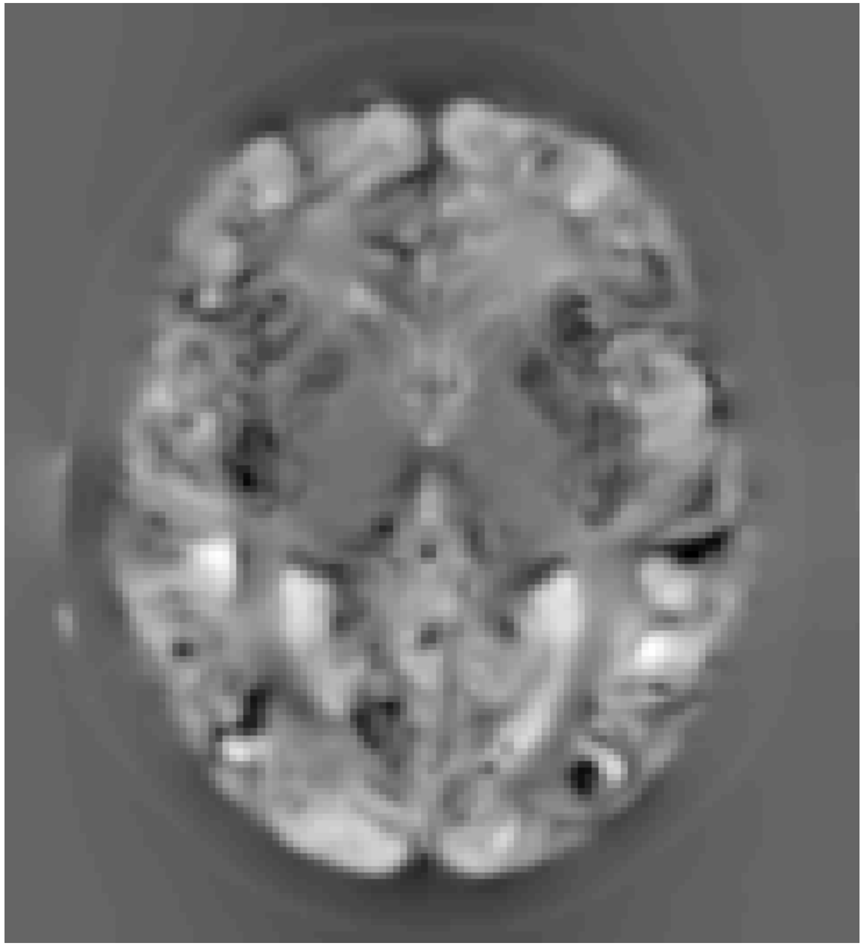
Grey Matter


Original
Warped
Template

“Modulation” – change of variables.



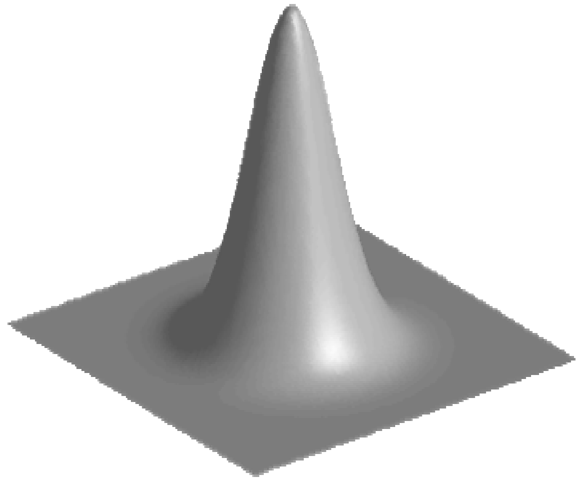
Deformation Field



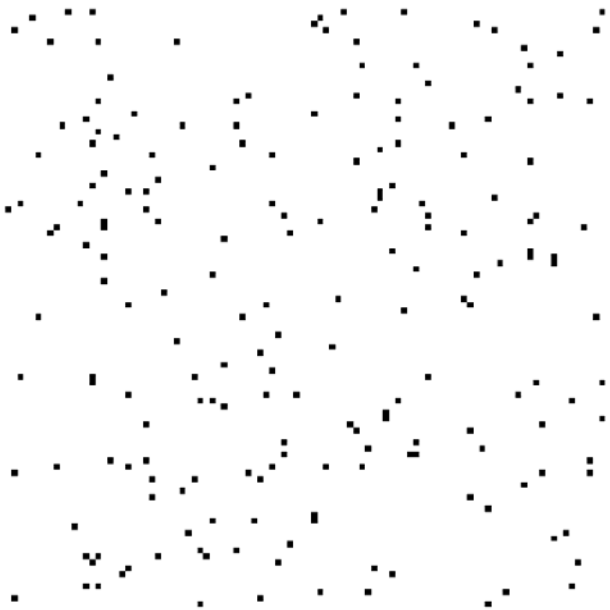
Jacobians determinants
Encode relative volumes.

Smoothing

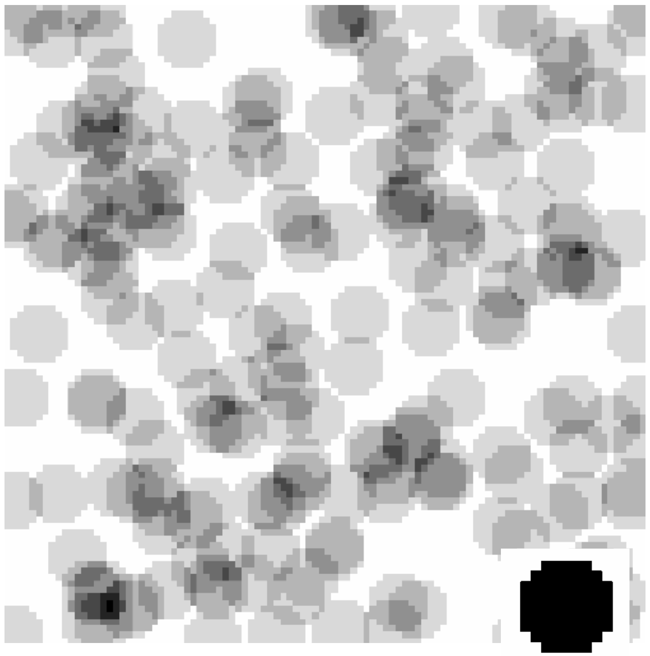
Each voxel after smoothing effectively becomes the result of applying a weighted region of interest (ROI).



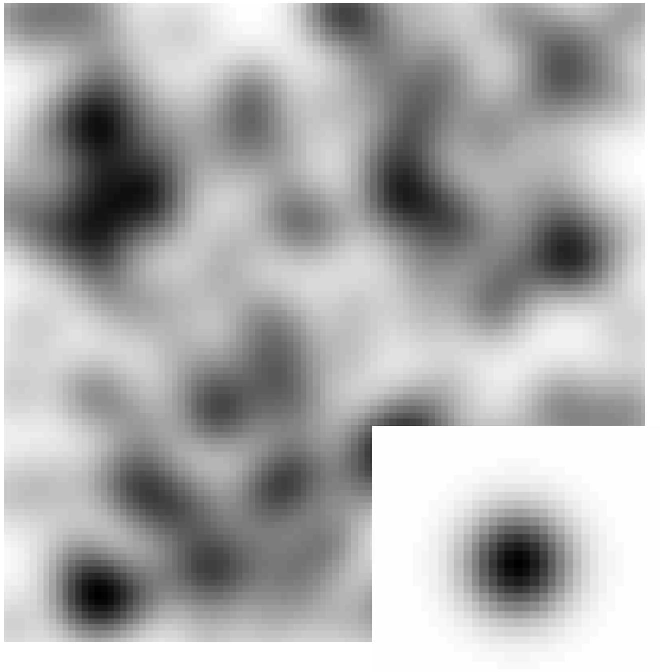
Before convolution



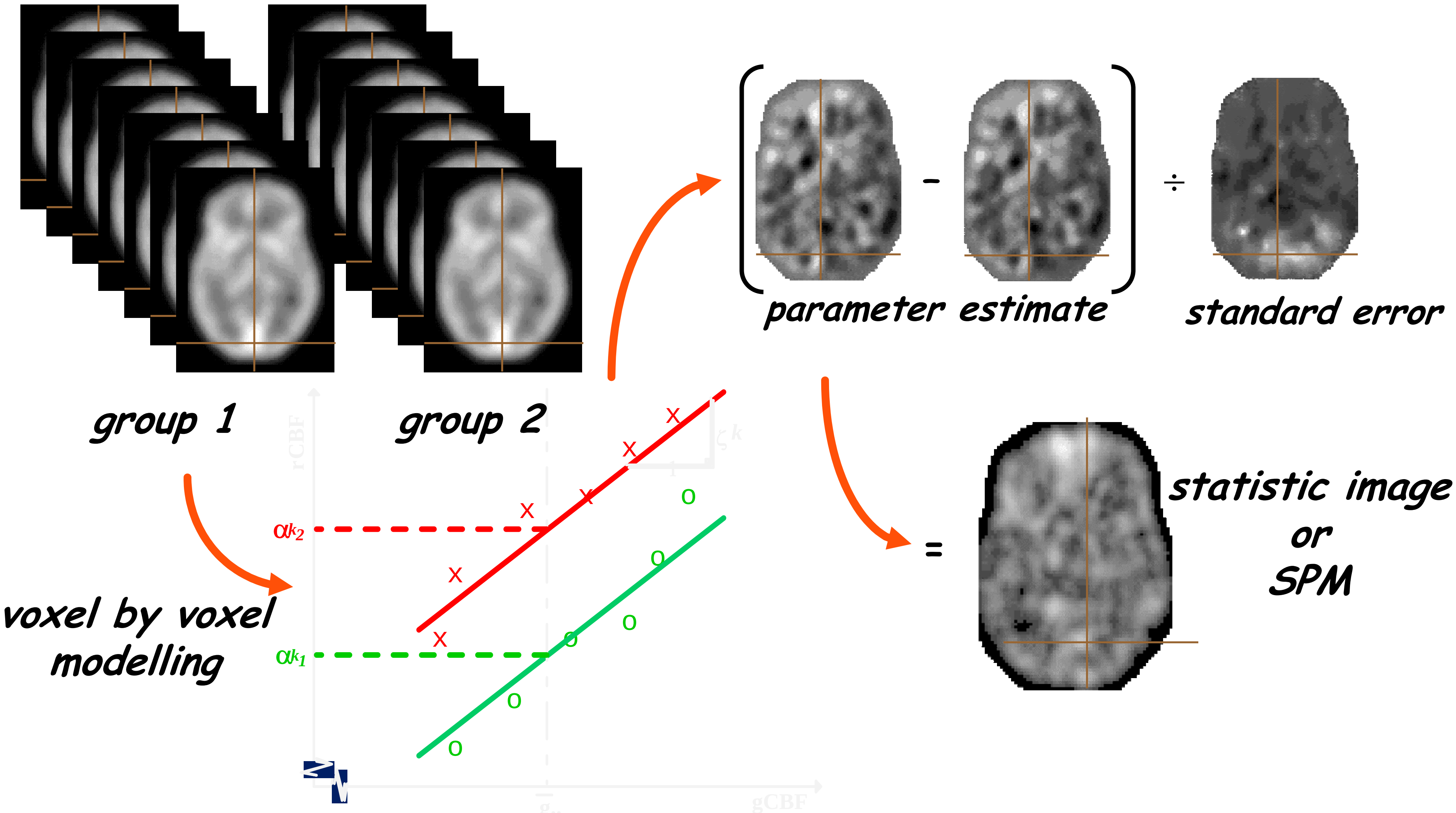
Convolved with a circle



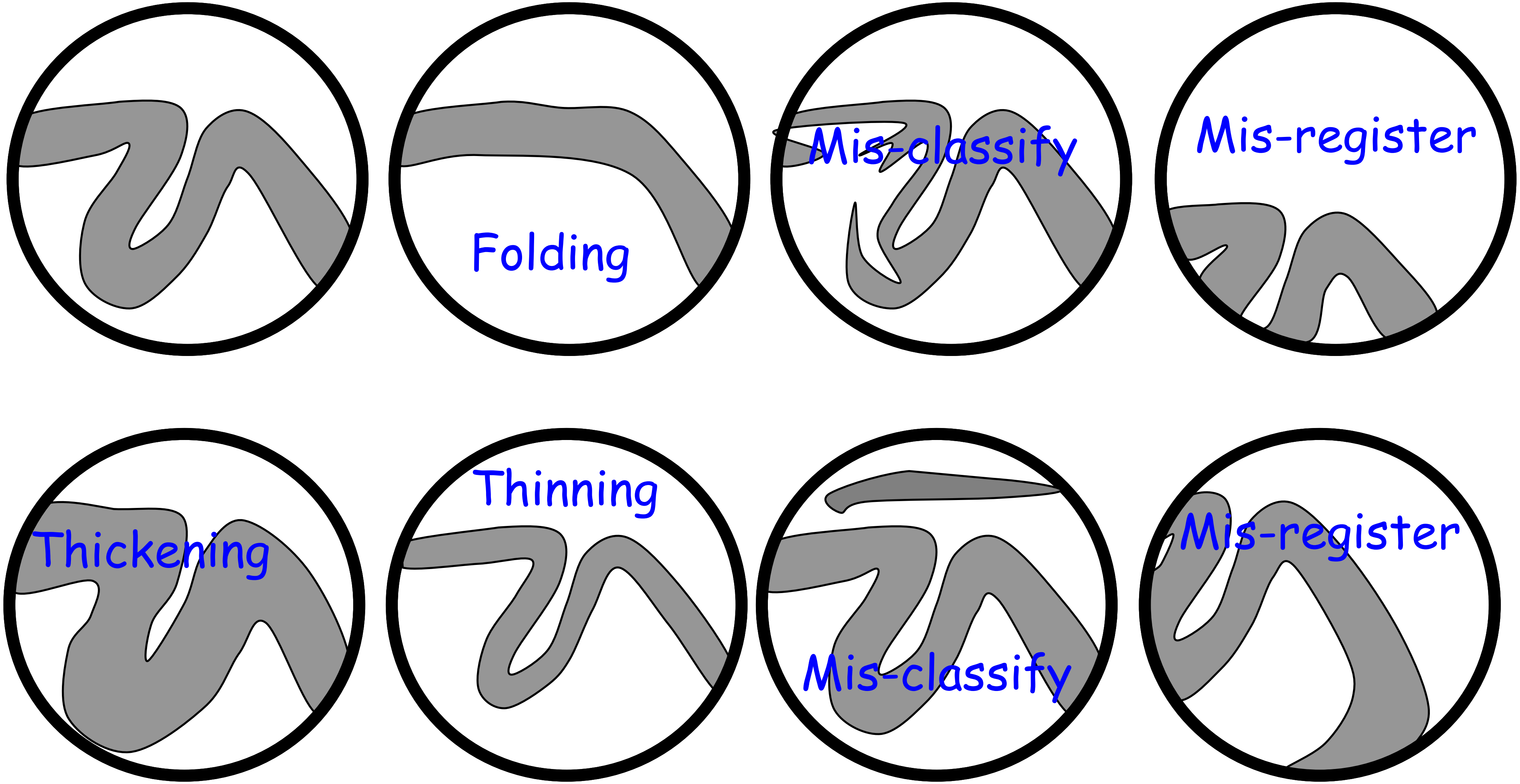
Convolved with a Gaussian



Statistical Parametric Mapping…

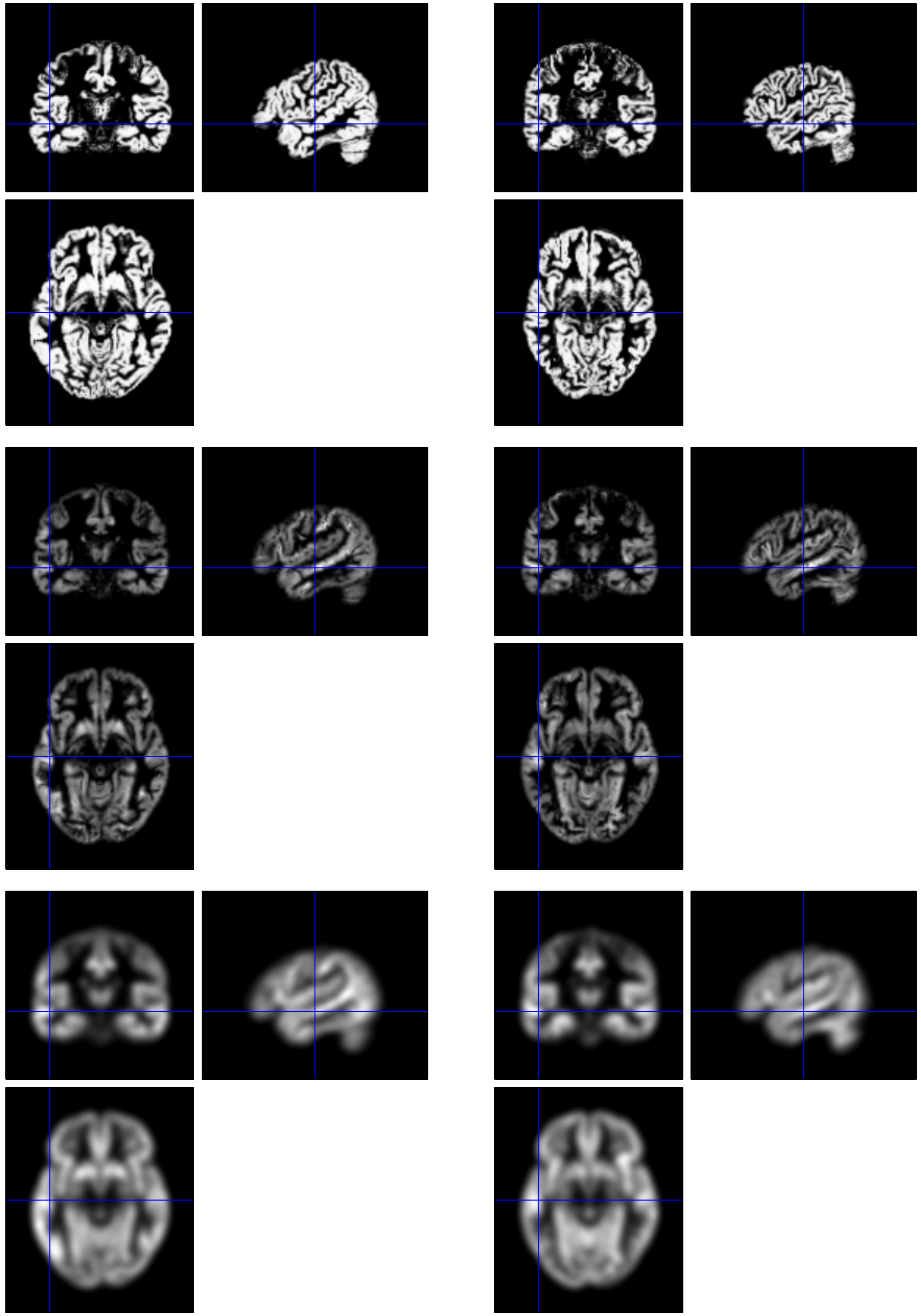


Some Explanations of the Differences



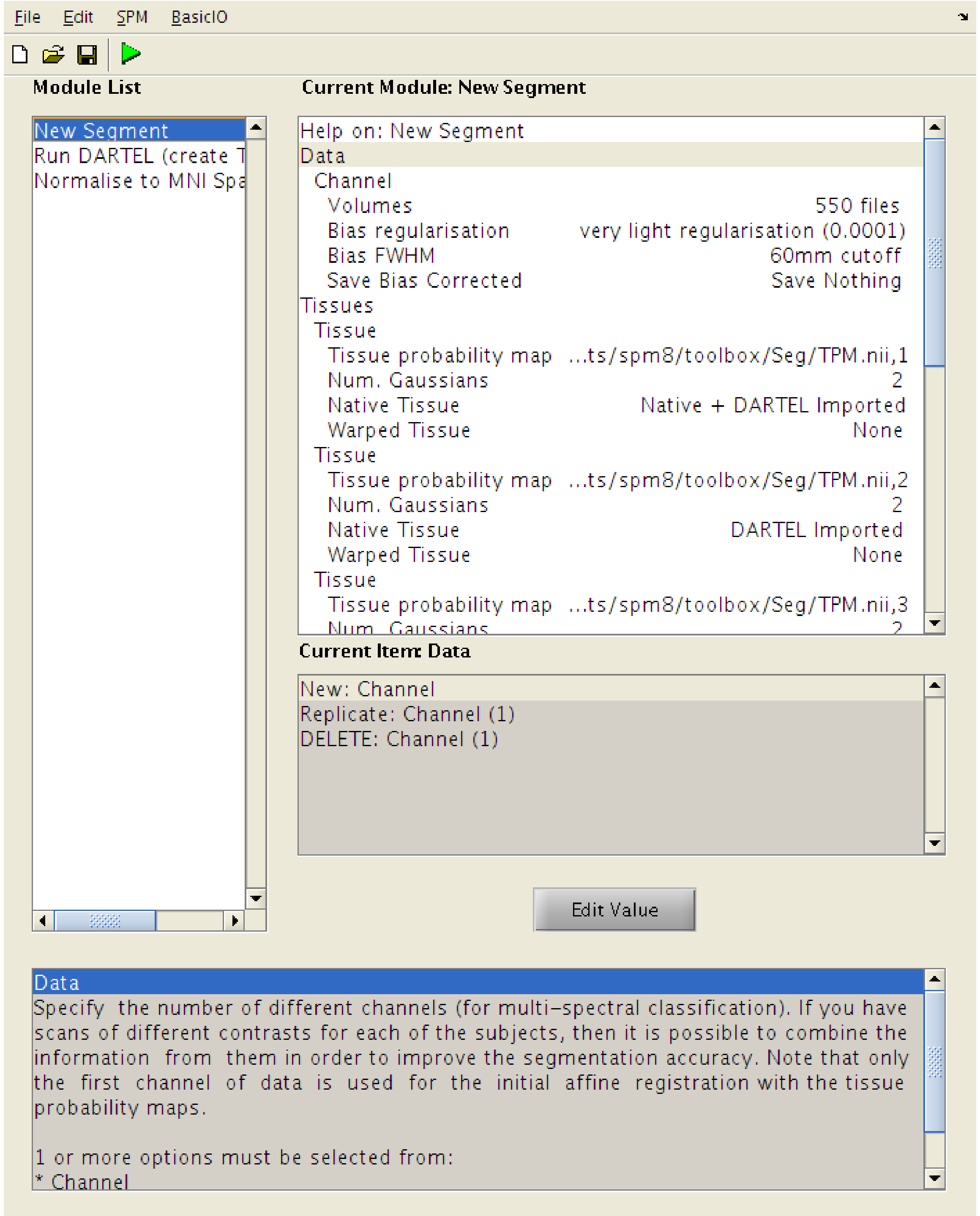
VBM Pre-processing in SPM8

- Use New 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.



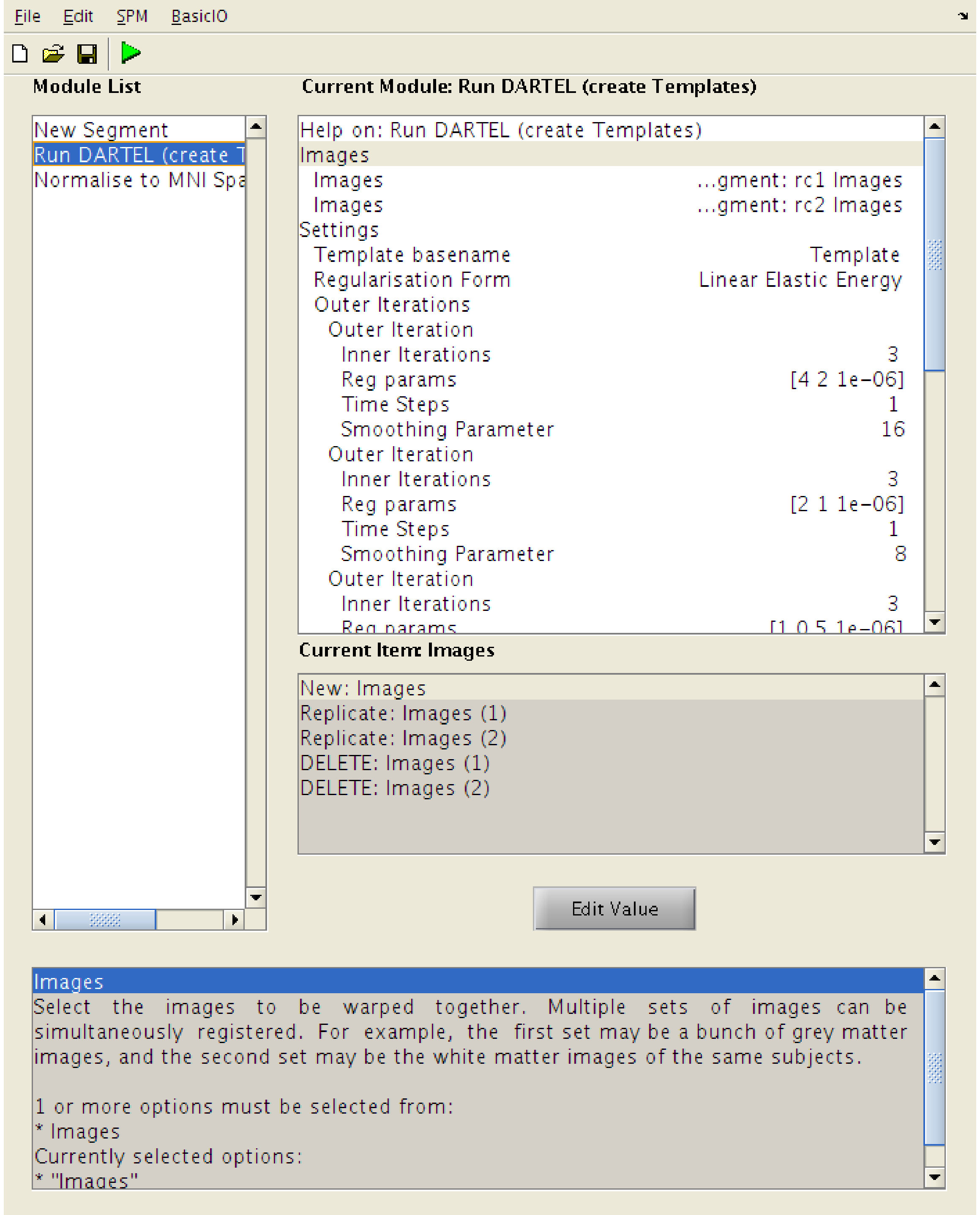
New Segment

- **Generate low resolution GM and WM images for each subject ("DARTEL imported").**
- **Generate full resolution GM map for each subject.**



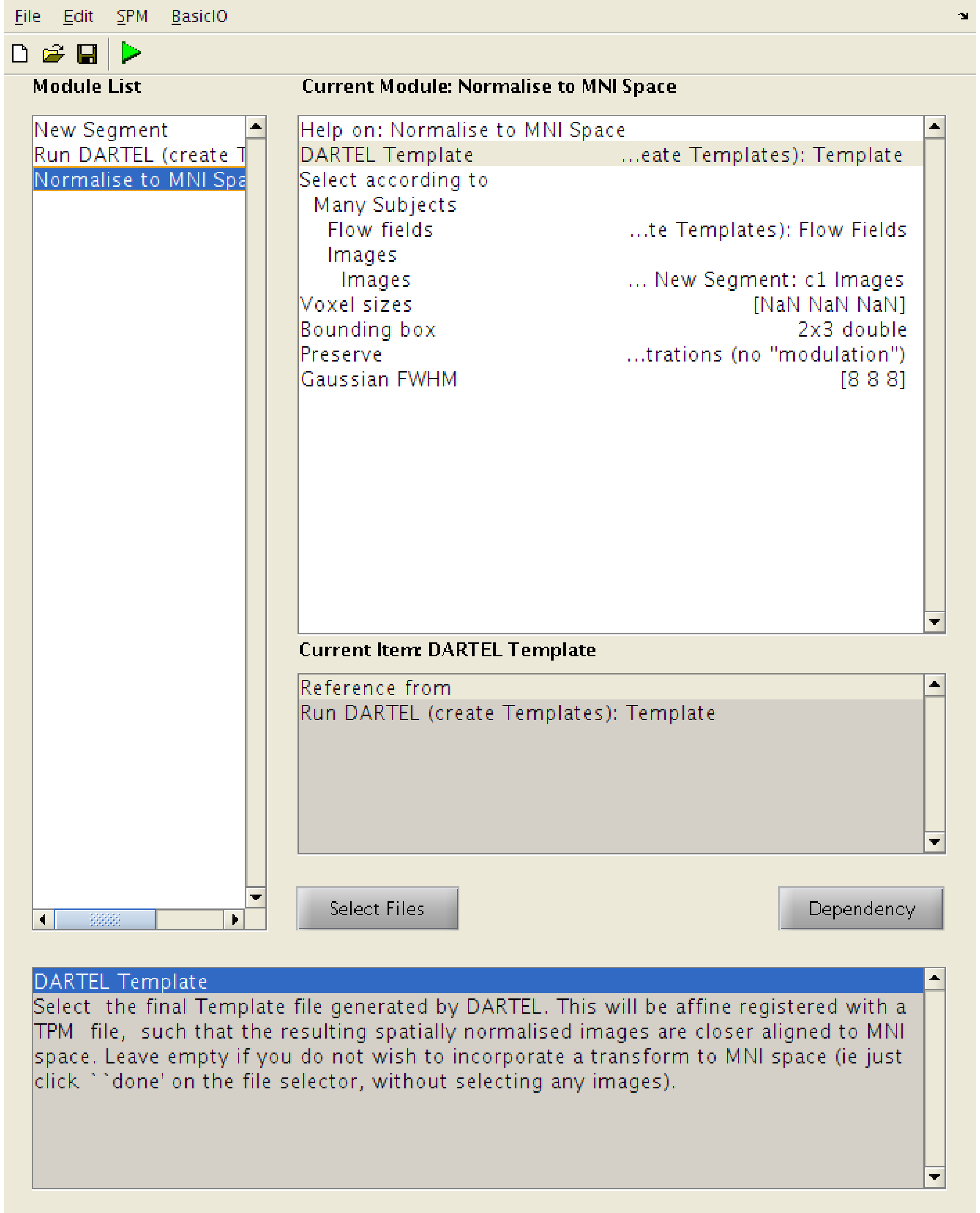
Run DARTEL (create Templates)

- Simultaneously align “DARTEL imported” GM and WM for all subjects.
- Generates templates and parameterisations of relative shapes.



Normalise to MNI Space

- **Use shape parameterisations to generate smoothed Jacobian scaled and spatially normalised GM images for each subject.**



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Overview

- A Mass-Univariate Approach
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- A Multivariate Approach
  - Multivariate methods
  - Shape models
  - A 2D simulation
  - A real 3D example

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.

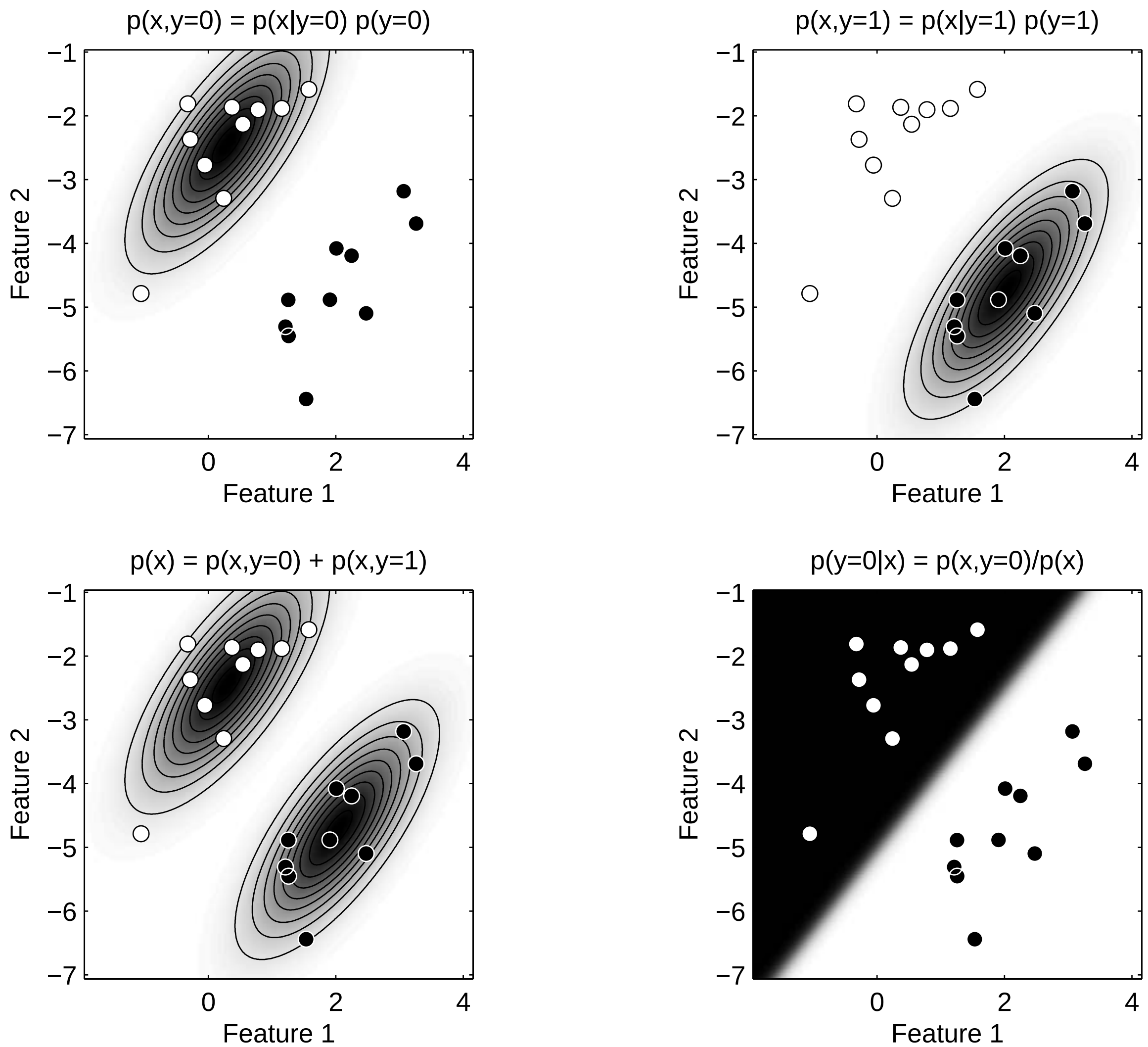
- Empirical evidence in (eg)

  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.

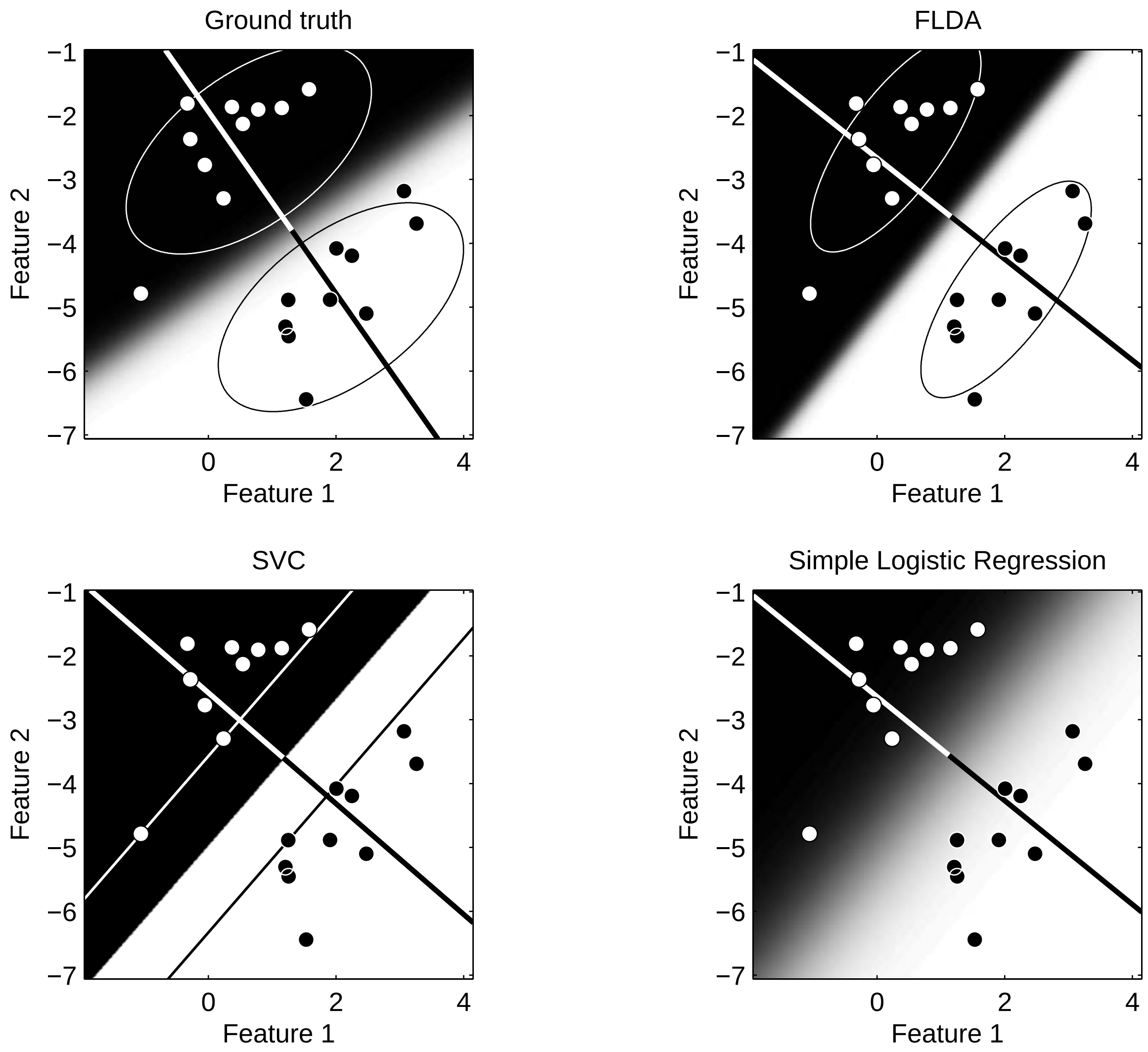
Fisher's Linear Discriminant Analysis

- A multivariate model.
- Special case of canonical variates analysis.
- Also a special case of a mixture of Gaussians
- A **generative model**.

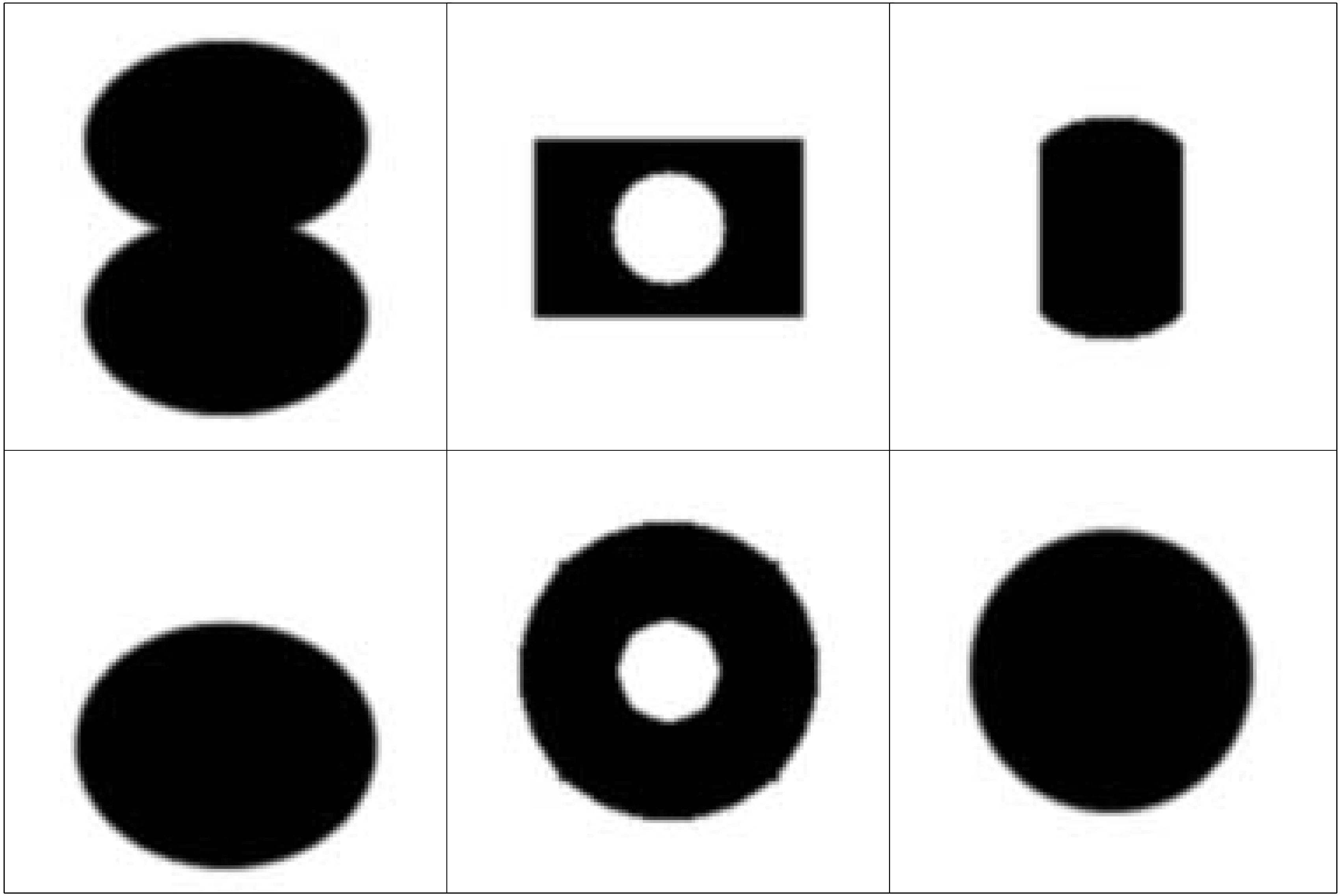


Other linear discrimination approaches

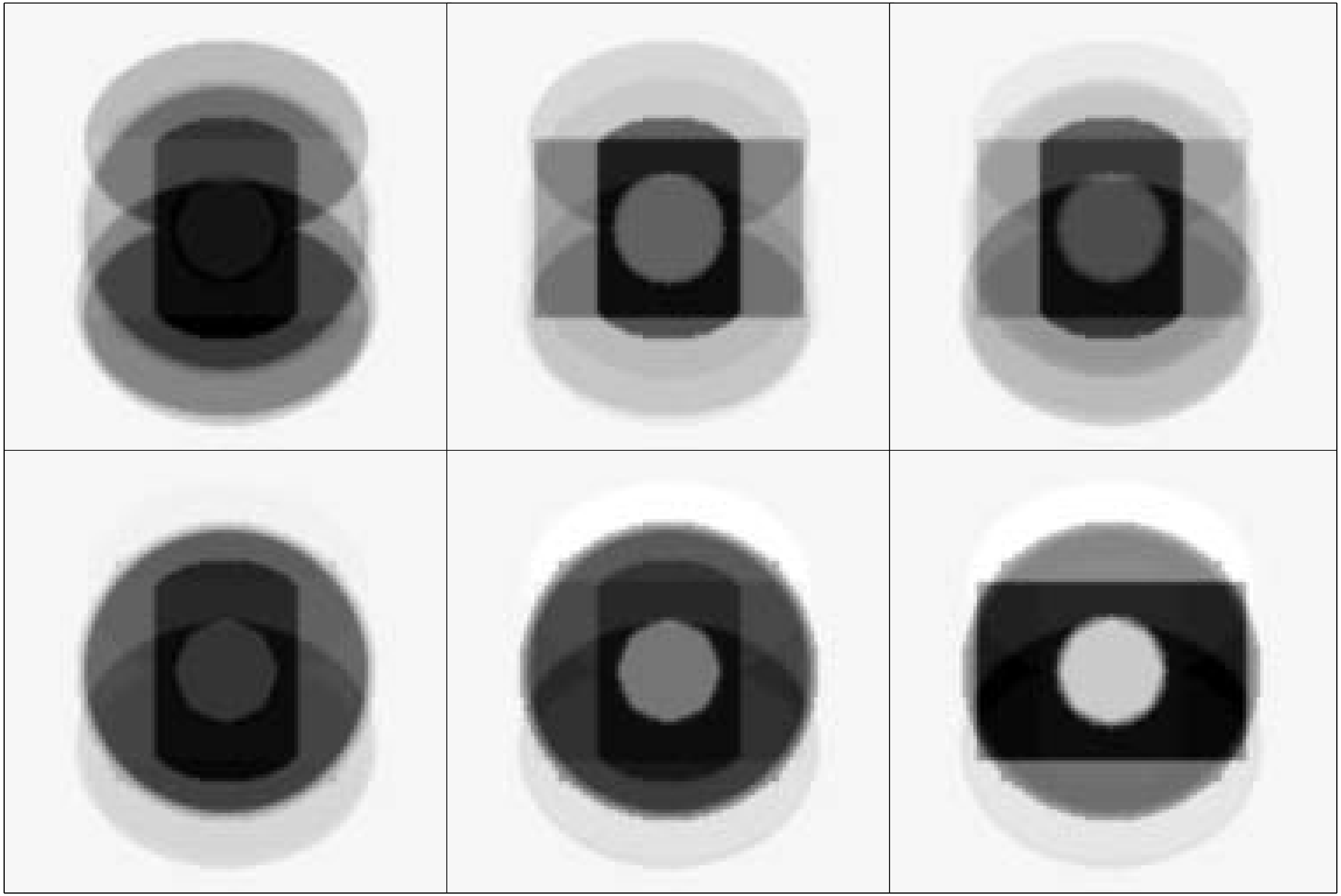
- Can also use **discriminative models**.
- Anatomical differences are encoded by the vector orthogonal to the separating hyper-plane.
- The most accurate model of difference is the one that best separates the groups.



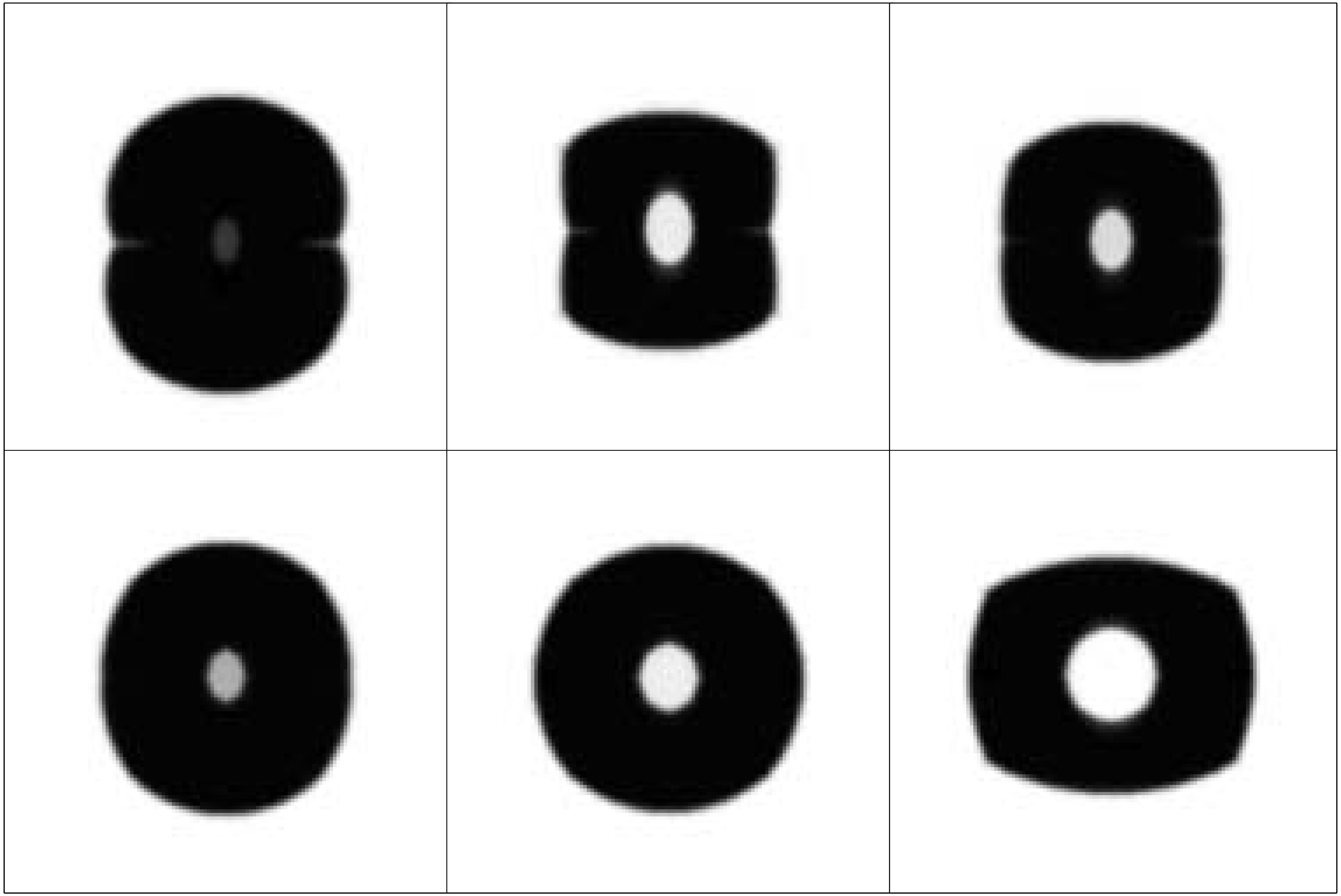
Some 2D Shapes



Simulations using a simple linear model



Simulations using a nonlinear model



D'Arcy Thompson (1917). ***GROWTH AND FORM.***

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 (as a hundred years ago Cuvier first showed the way), 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. But if, on the other hand, diverse and dissimilar fish [brains] can be referred as a whole to identical functions of very different coordinate systems, this fact will of itself constitute a proof that a comprehensive "law of growth" has pervaded the whole structure in its integrity, and that some more or less simple and recognizable system of forces has been at work.

Julian Huxley (1932). ***PROBLEMS OF RELATIVE GROWTH***

One essential fact about growth is that it is a process of self-multiplication of living substance – i.e. that the rate of growth of an organism growing equally in all its parts is at any moment proportional to the size of the organism.

A constant partition of growth intensity between different regions implies constant differences in their rates of growth. Thus any genes controlling relative size of parts will have to exert their action by influencing the rates of processes, …

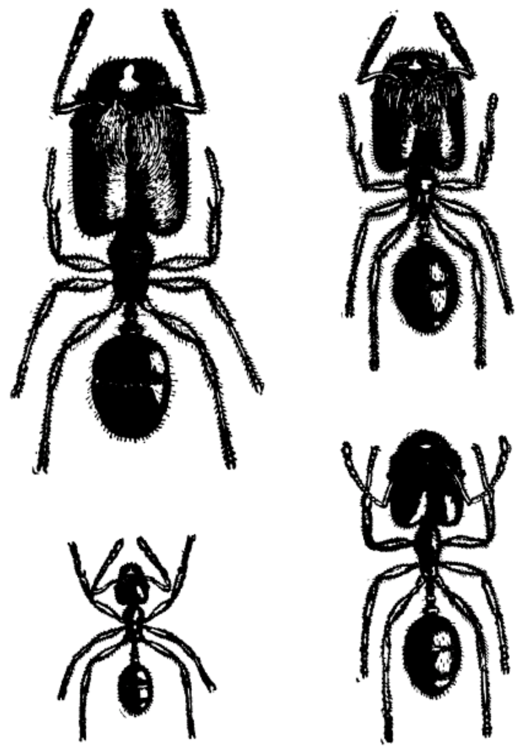
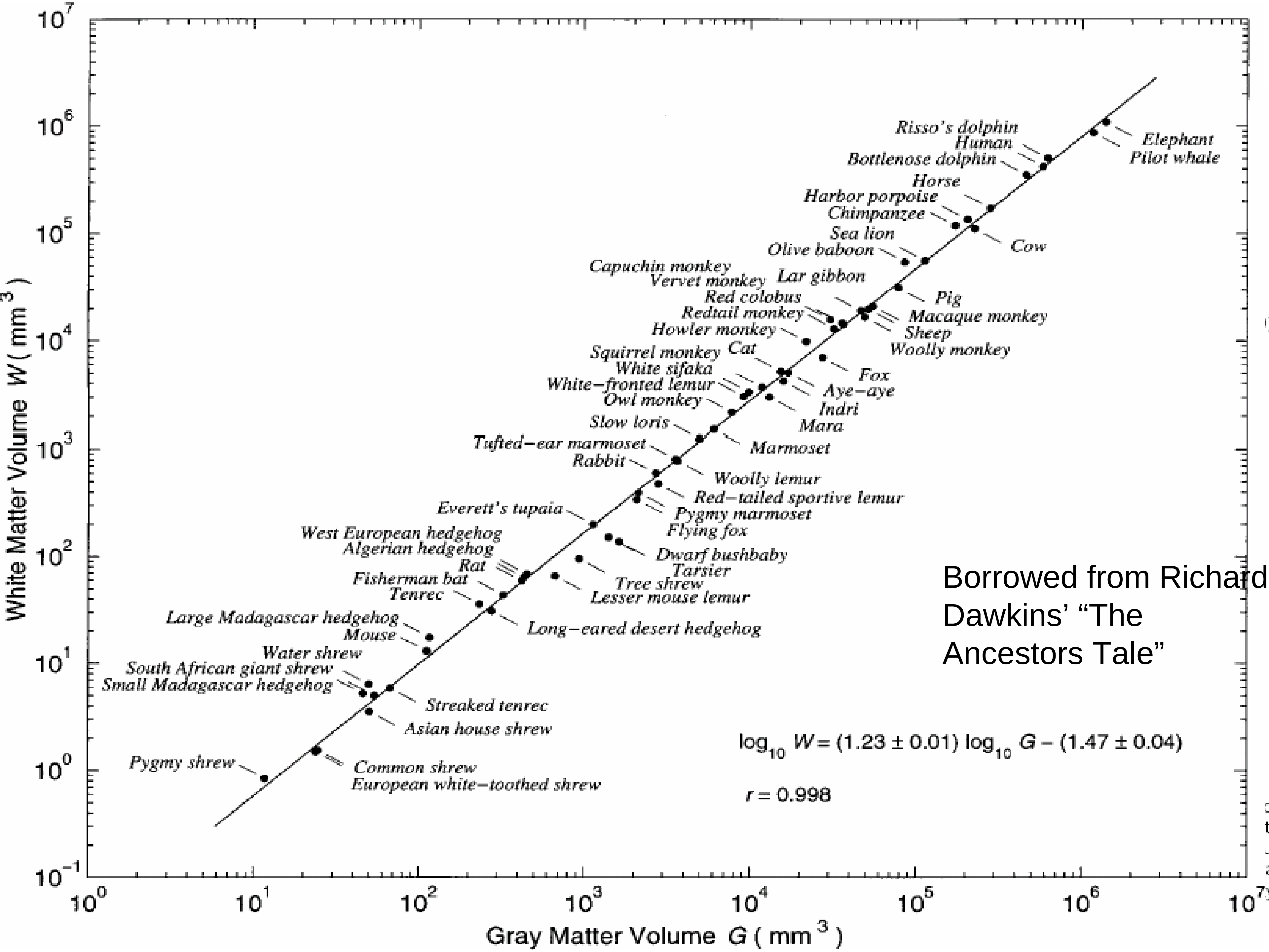


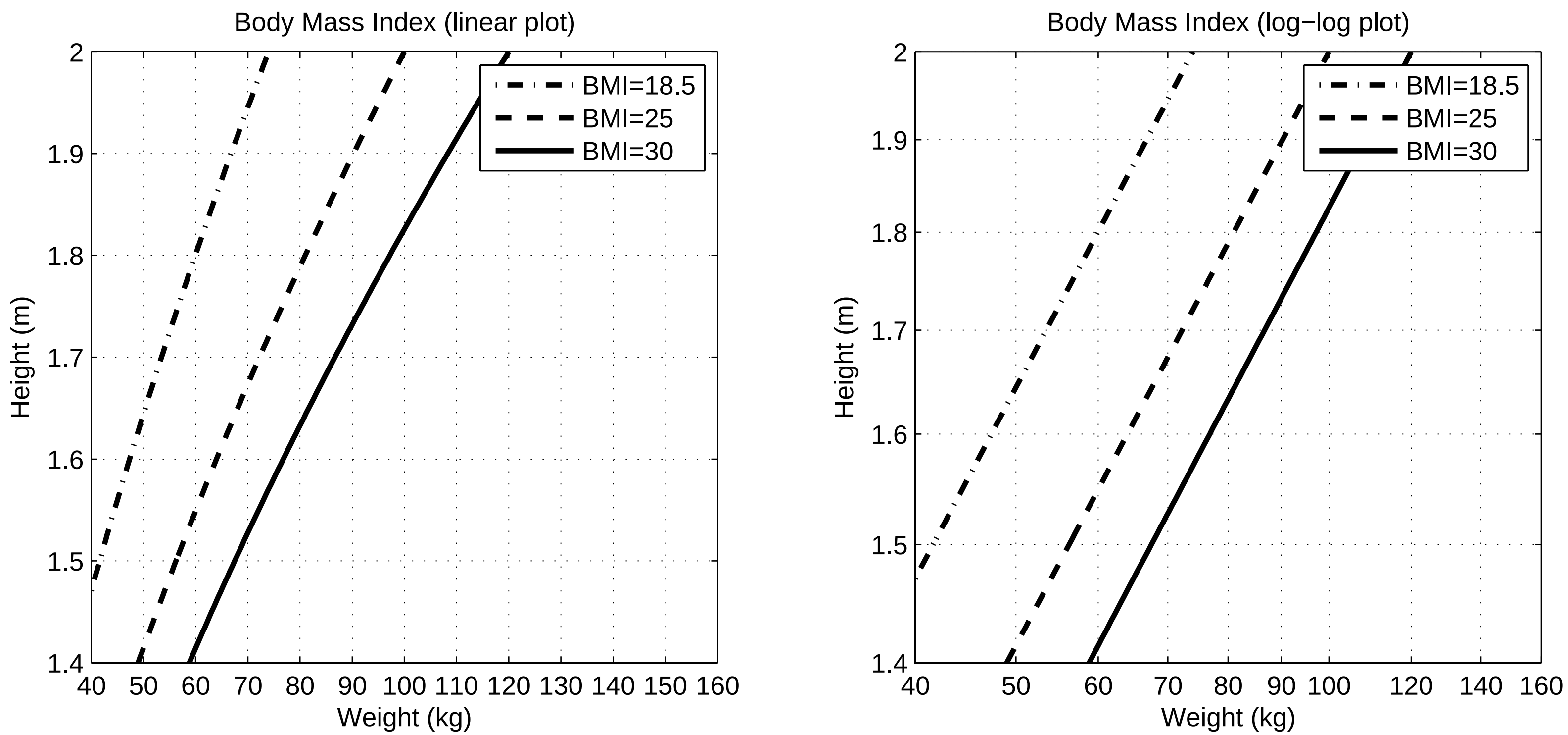
FIG. 36.—Increase of relative size of head with absolute size of body in the neuters of the ant, *Pheidole instabilis*.



Borrowed from Richard Dawkins' "The Ancestors Tale"

Another allometric Relationship

- A simple example based on Body Mass Index.
  - BMI = weight/height^2



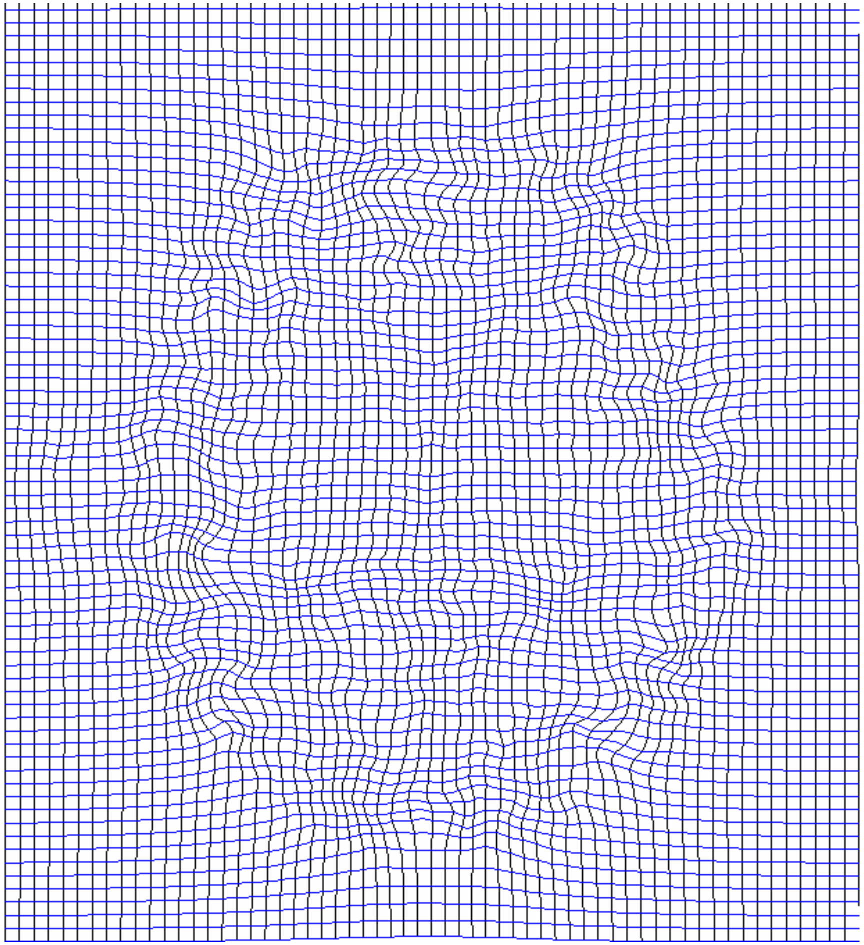
- Working with logarithms (of some kind) may be more appropriate.

Requirements…

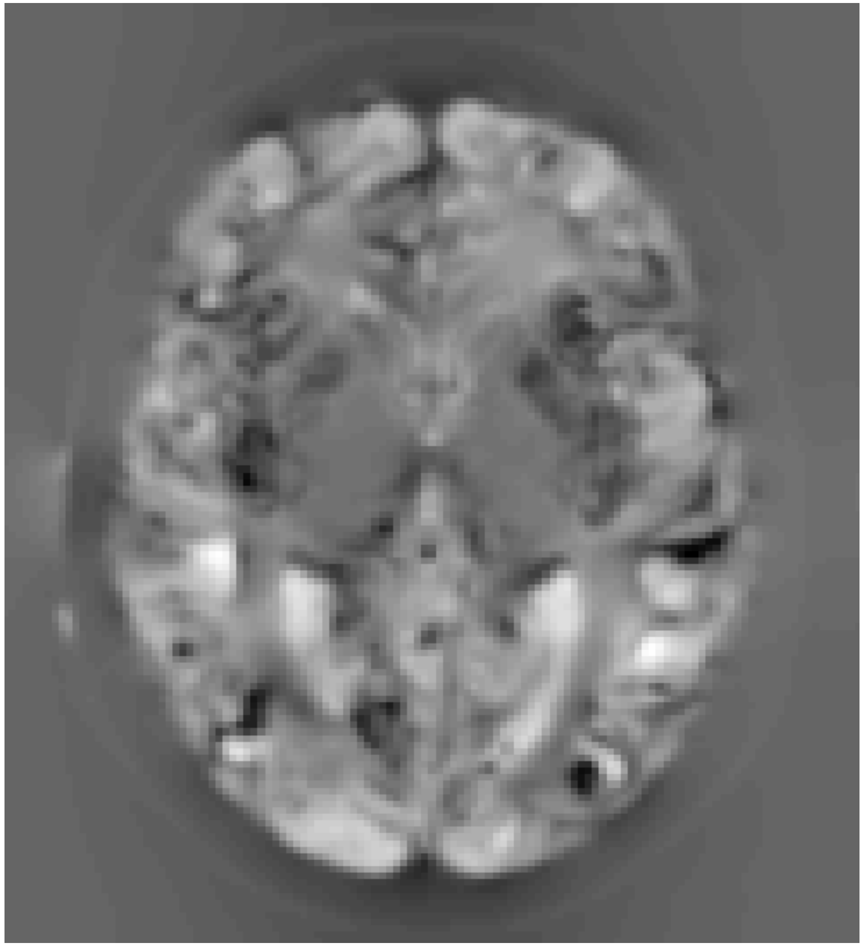
- Different models have different parameterisations and will therefore give different findings.
- Need to have a good model, before reporting details about differences among parameters.
- Shape models (image registration models) are no exception.

- Accurate multivariate analysis of form needs a suitable registration model.
  - Can’t fit a general linear model, and interpret the parameters in terms of a dynamic causal model.
  - Can’t fit any old registration model, and interpret the parameters in any meaningful way.

Deformations and Jacobian



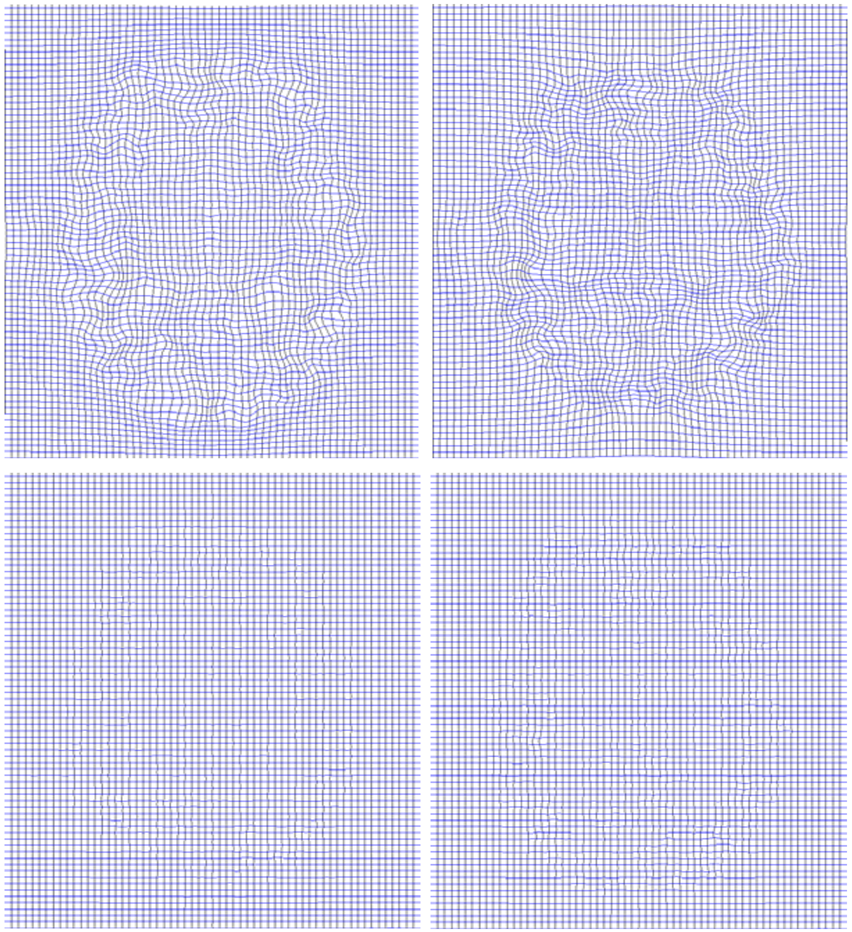
Deformation Field



Jacobians determinants
(should be positive)

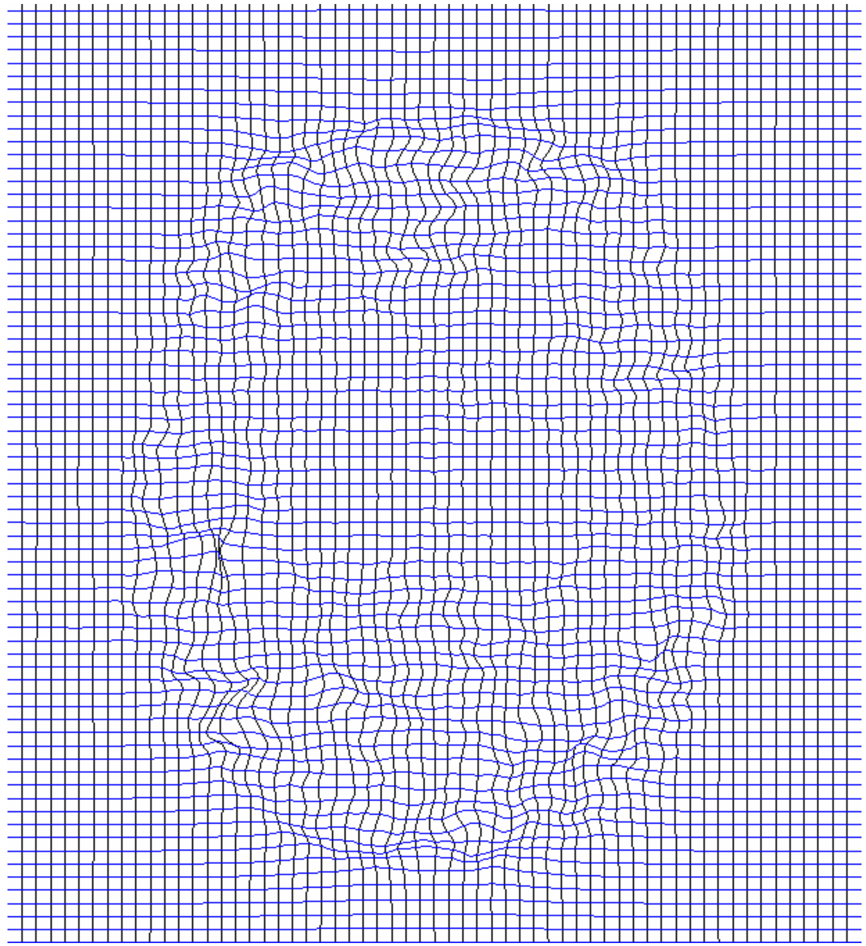
Displacements don’t add linearly

Forward Inverse

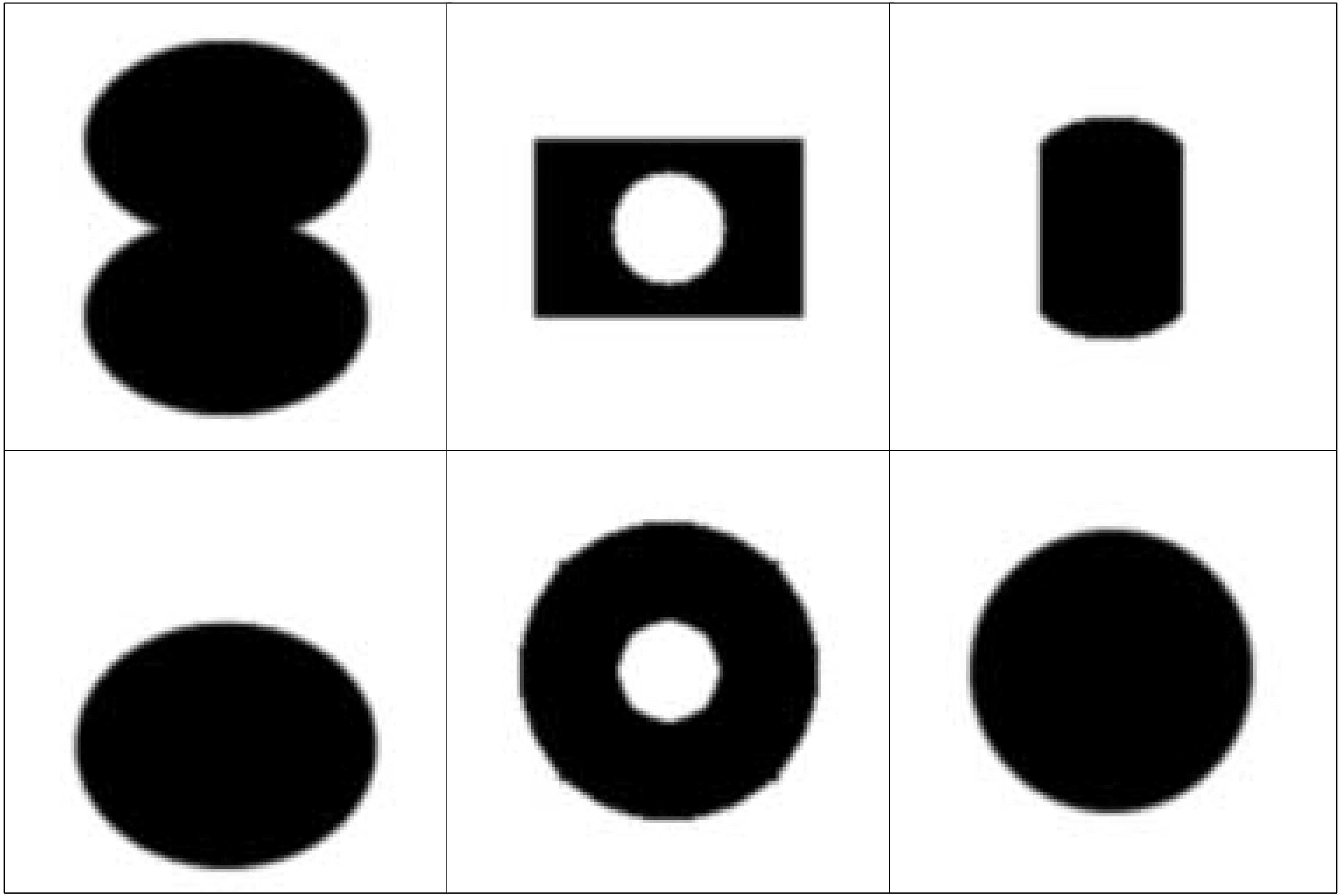


Composed

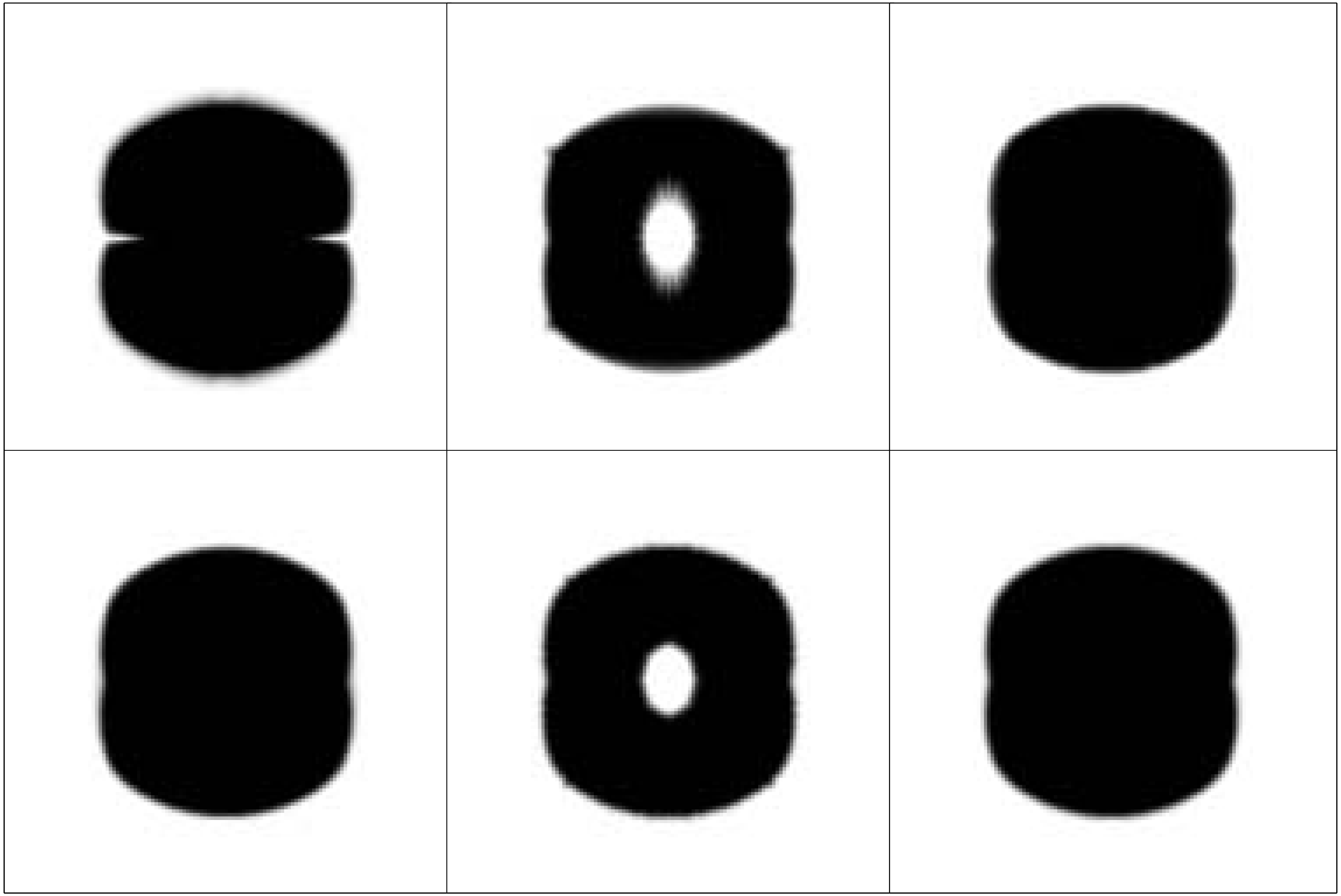
Subtracted



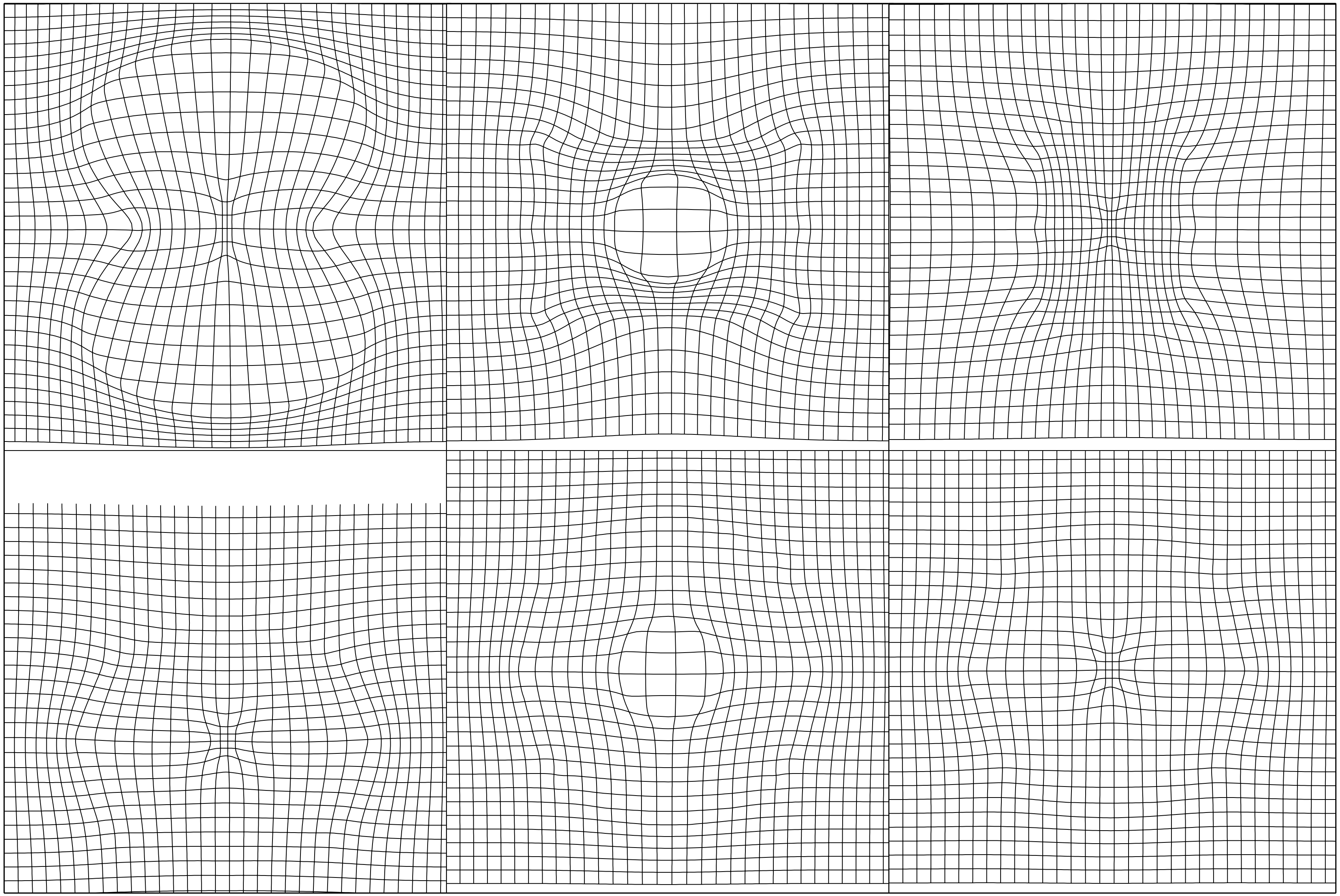
The 2D Shapes (again)



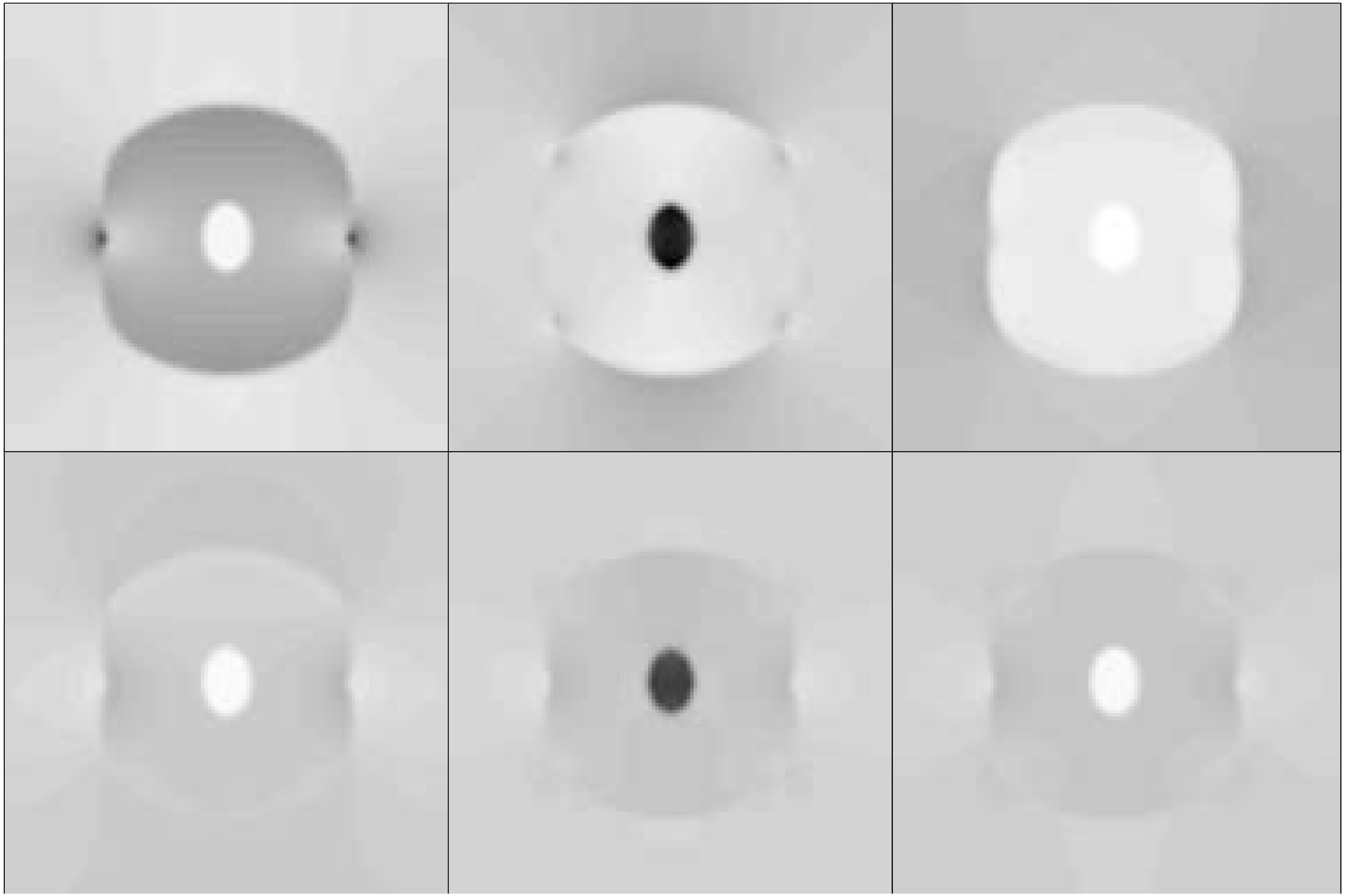
Shapes aligned to their average



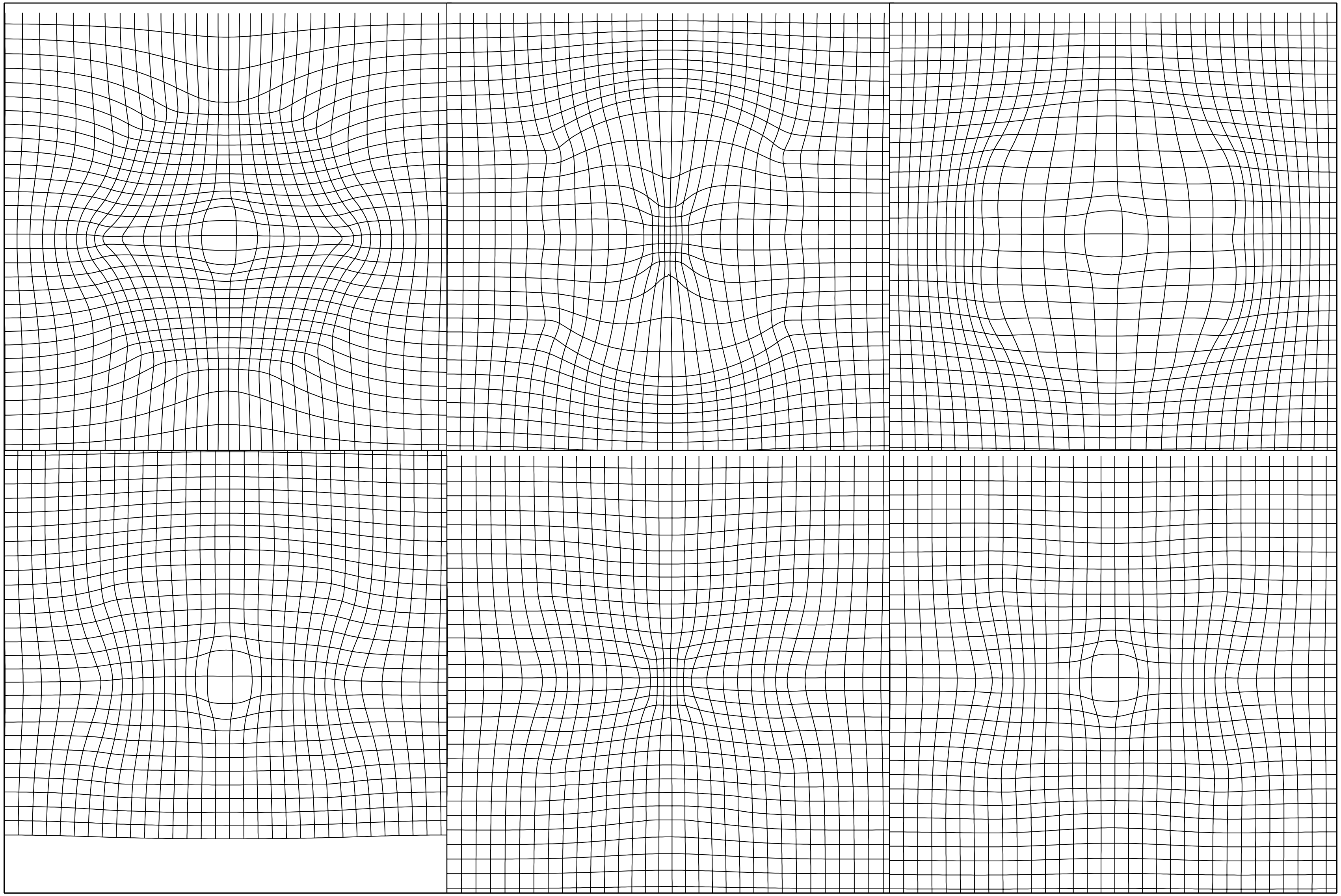
These were the deformations for that



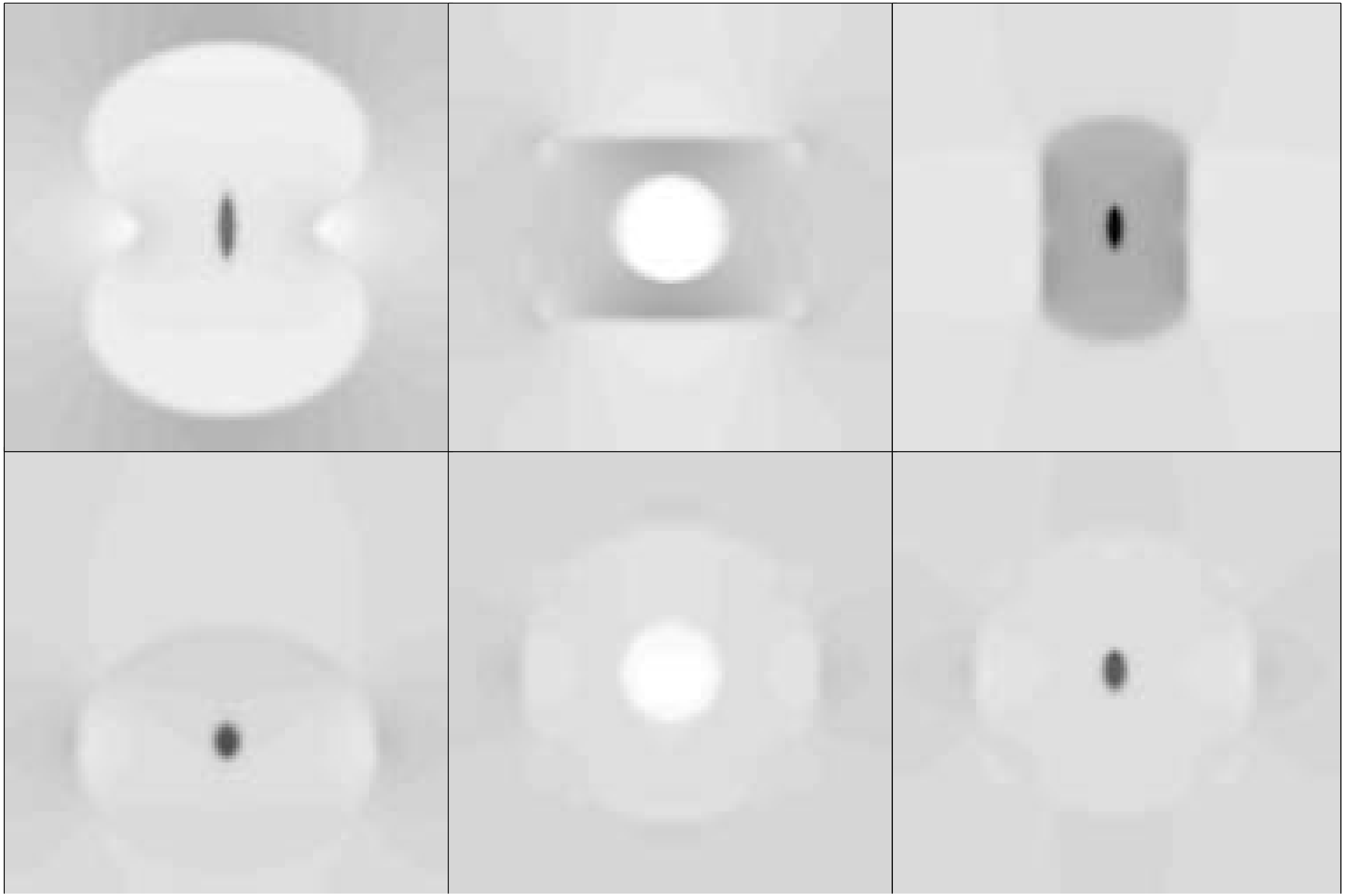
and these are the Jacobian determinants



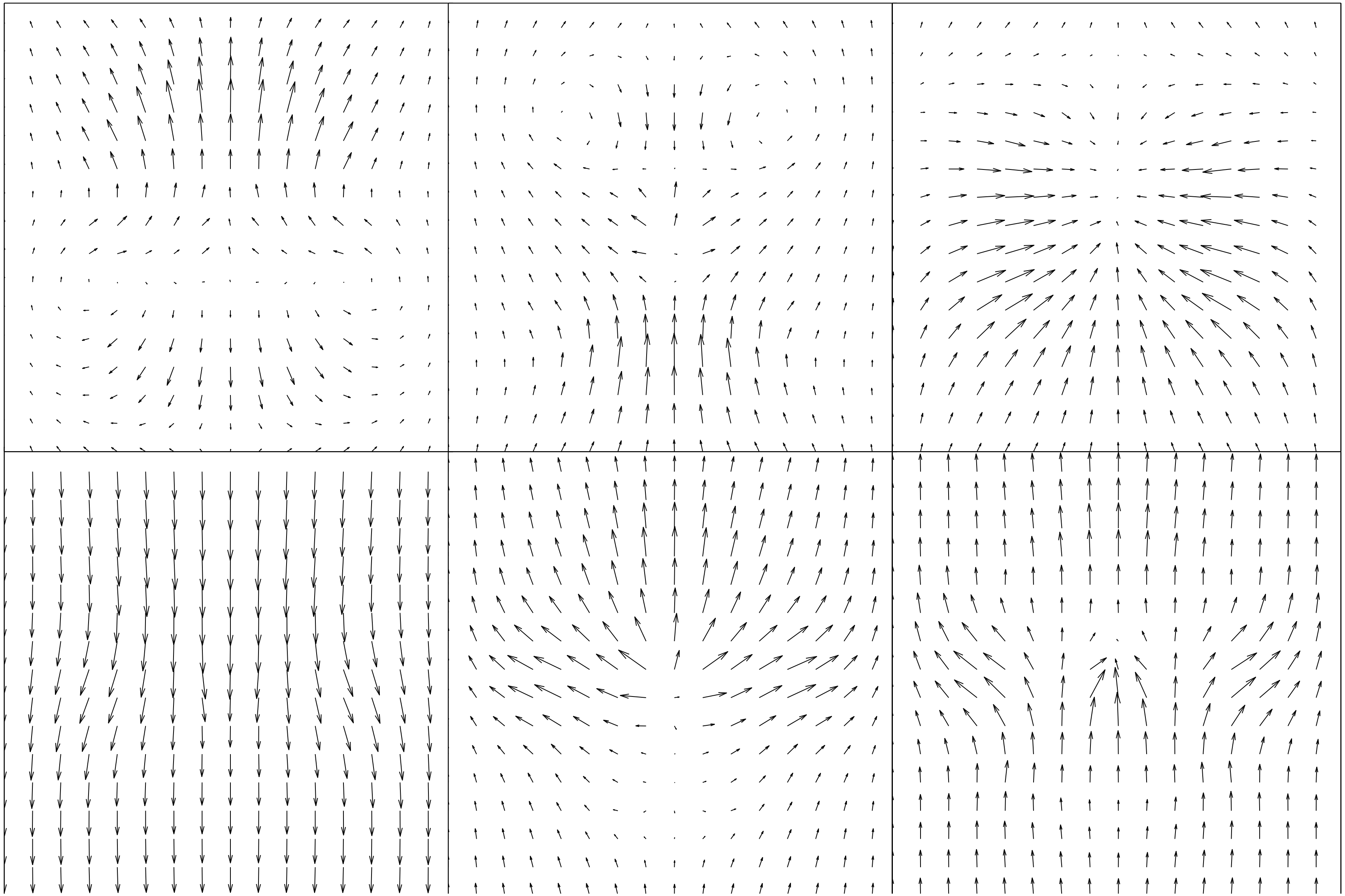
Inverses of the deformations



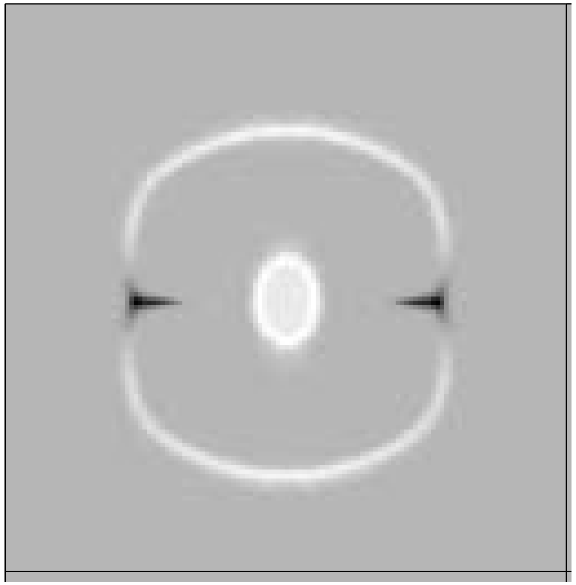
and their Jacobian determinants



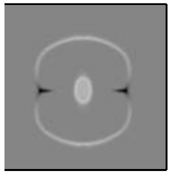
Initial velocity – analogous to logarithms of deformations



These + template encode the original shapes



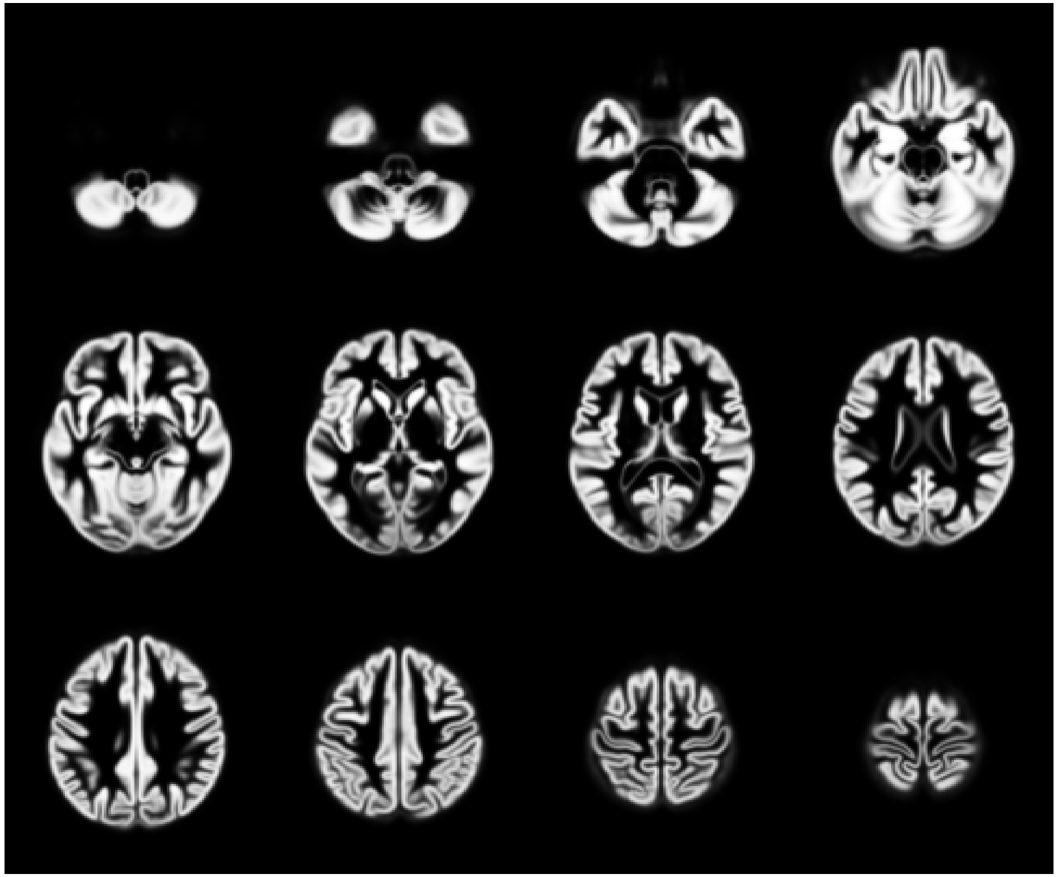
Residuals



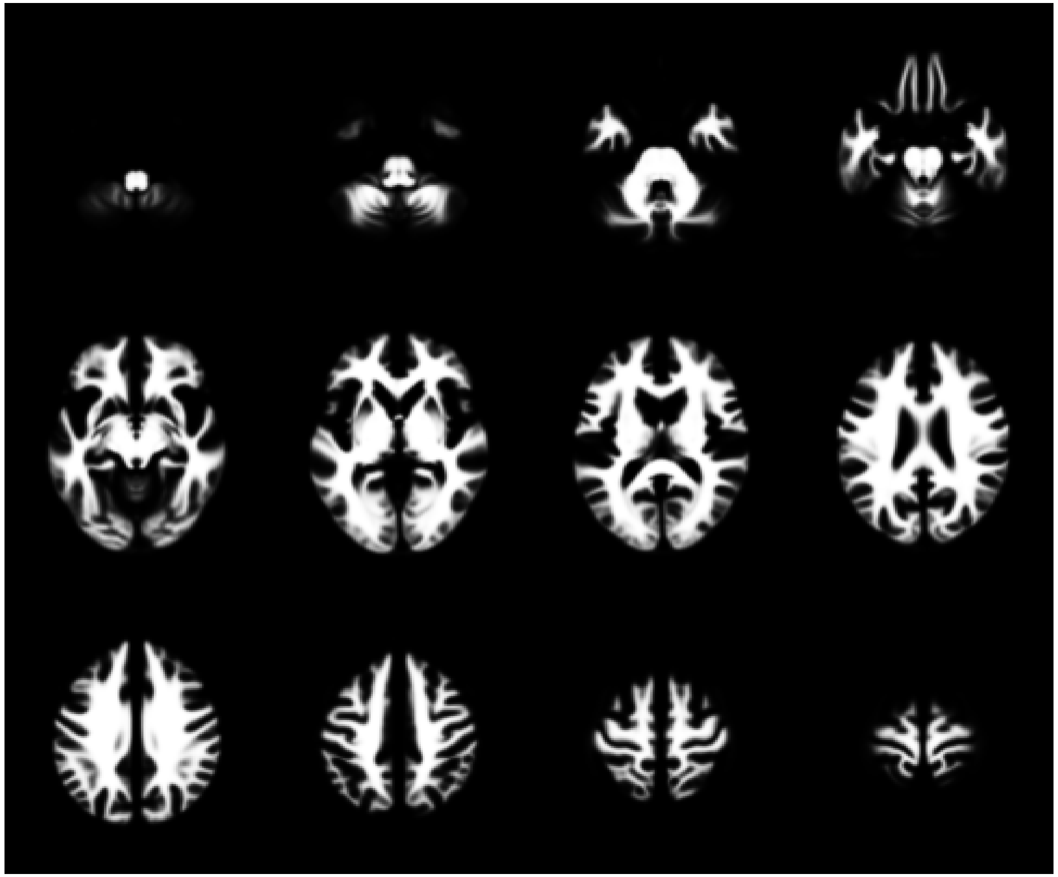
A 3D Example

- Used 550 T1-wighted scans from the **IXI** dataset.
  - A freely available dataset, whose web pages keep changing.
  - More data sharing will happen.
  - Freedom of information requests.
- Iteratively aligned all images to their common average template, using a diffeomorphic approach.
- Modelled anatomical differences using multivariate pattern recognition.

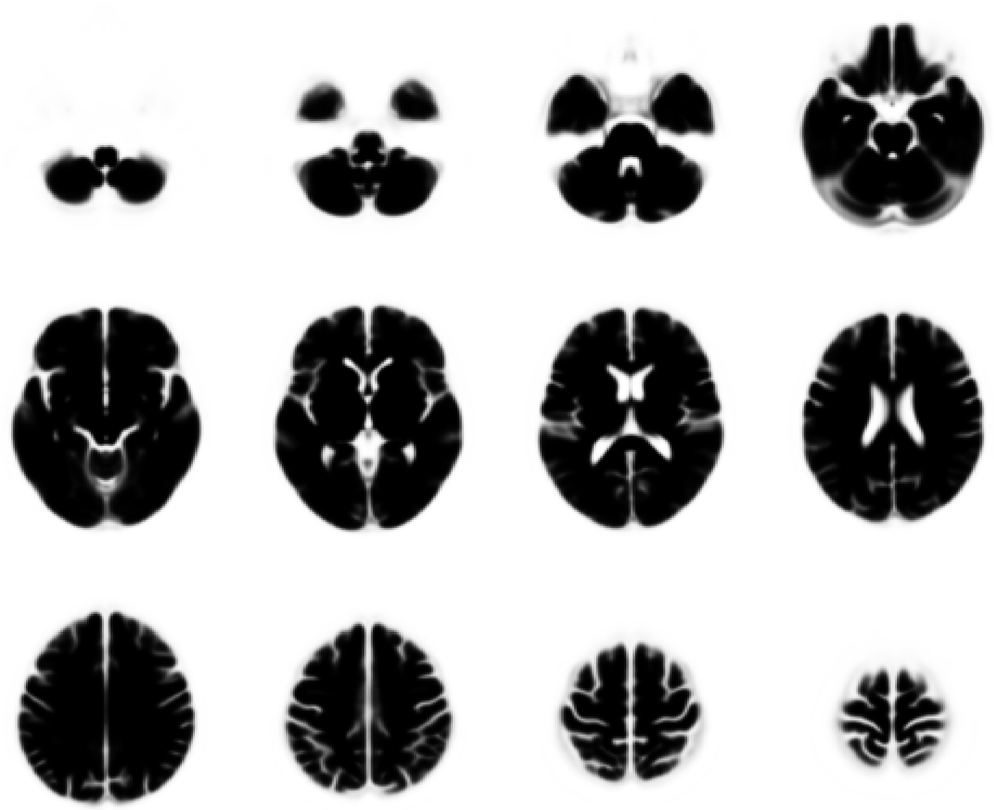
Template: Grey Matter



Template: White Matter



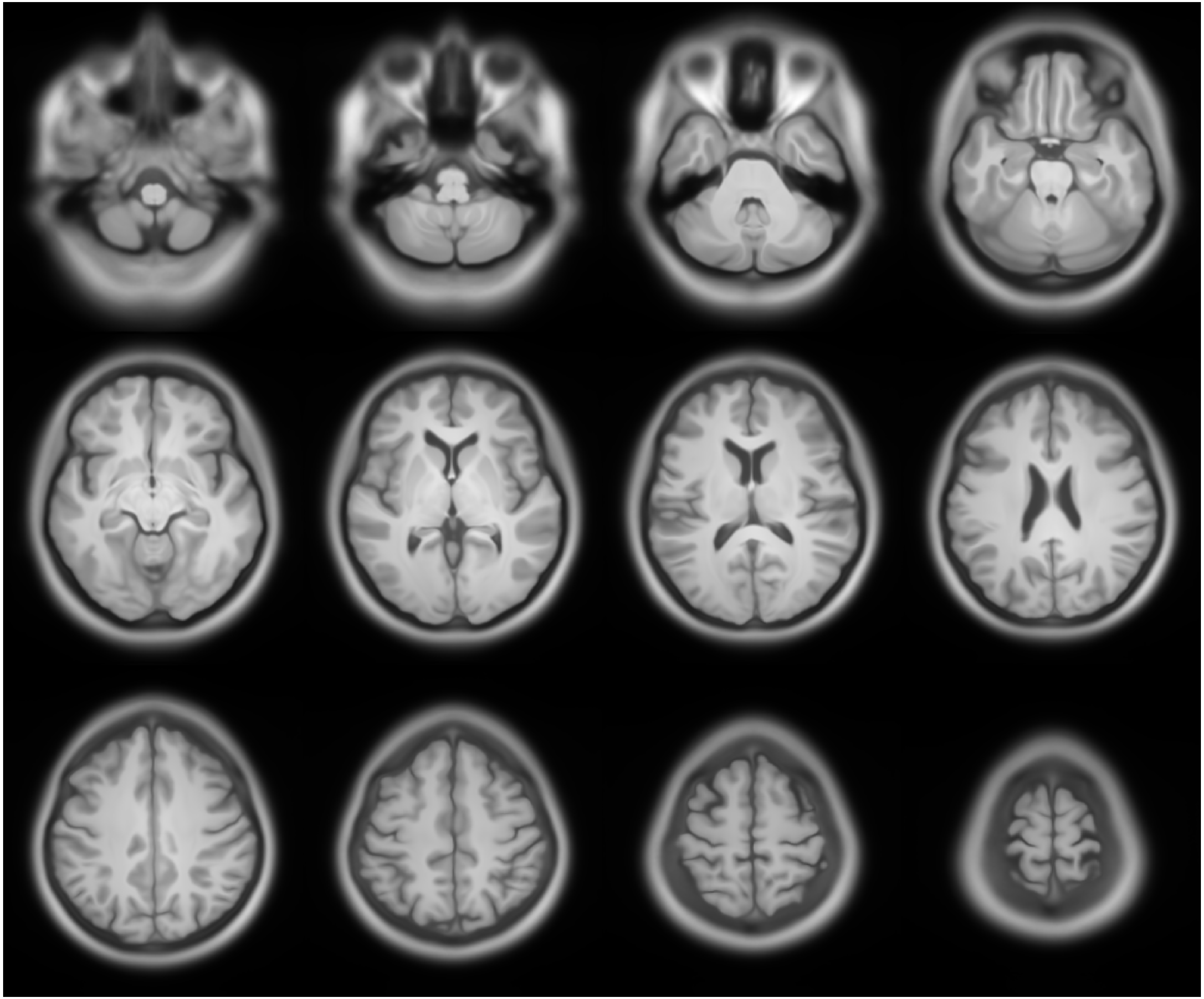
Template: Other

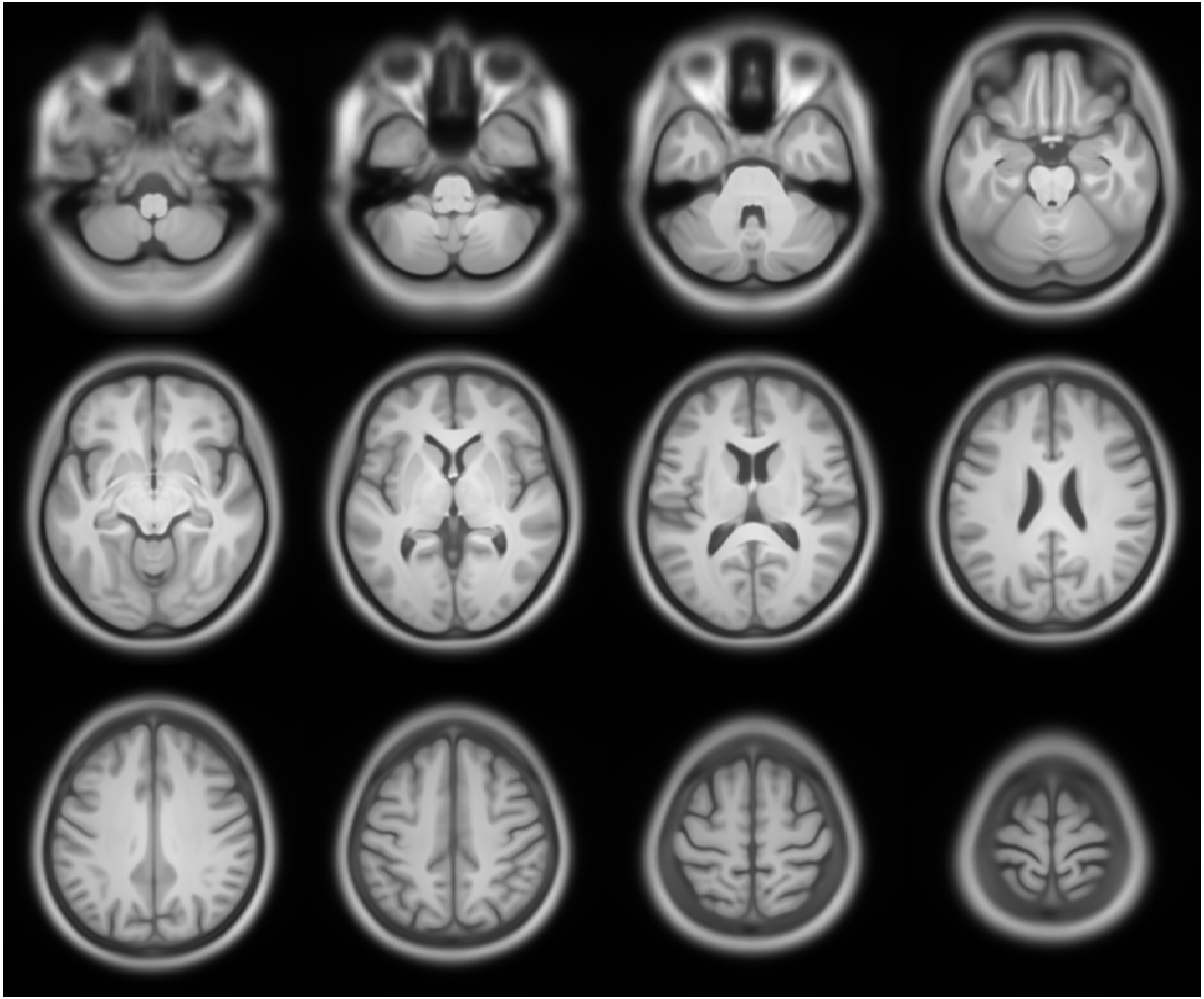


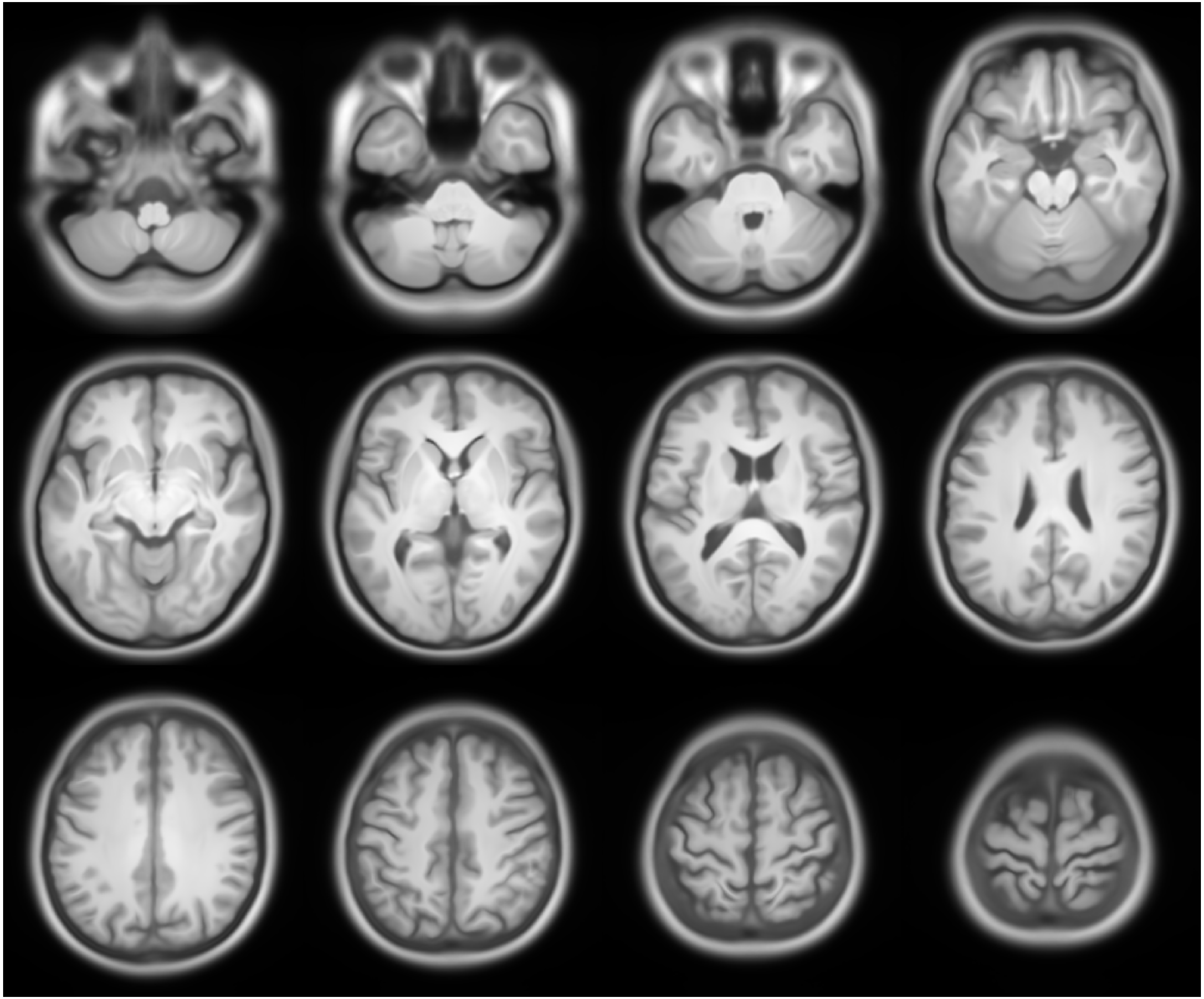
Caricatured Differences

- Used multivariate logistic regression to determine the initial velocity that best separates male from female brains.
  - Similar principles to Gaussian Process Classification, but with kernel matrix related to that of:

  Wang, L., Beg, M., Ratnanather, J., Ceritoglu, C., Younes, L., Morris, J.C., Csernansky, J.G. & Miller, M.I. *Large deformation diffeomorphism and momentum based hippocampal shape discrimination in dementia of the Alzheimer type*. IEEE Transactions on Medical Imaging 26(4):462 (2007).
- Diffeomorphic shooting to obtain exaggerated deformations.
- Average brain deformed using these exaggerated deformations.

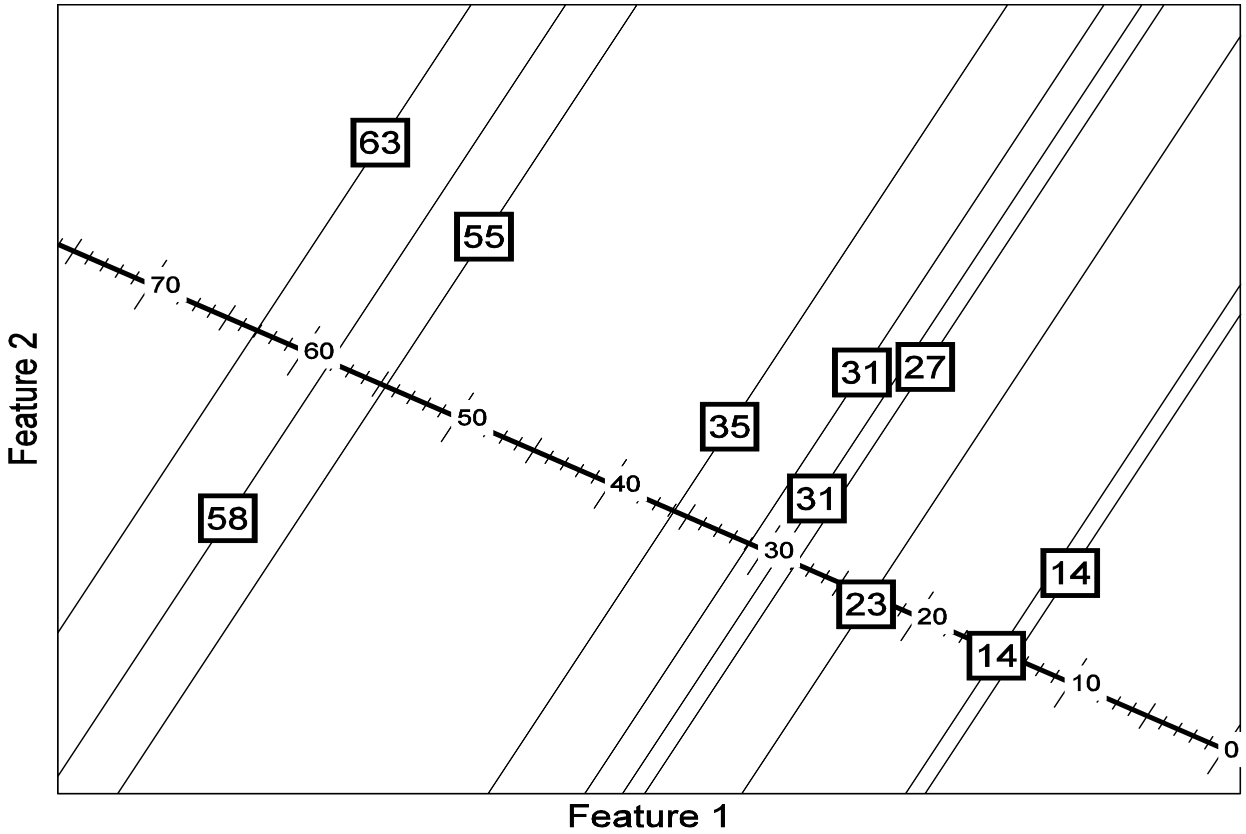


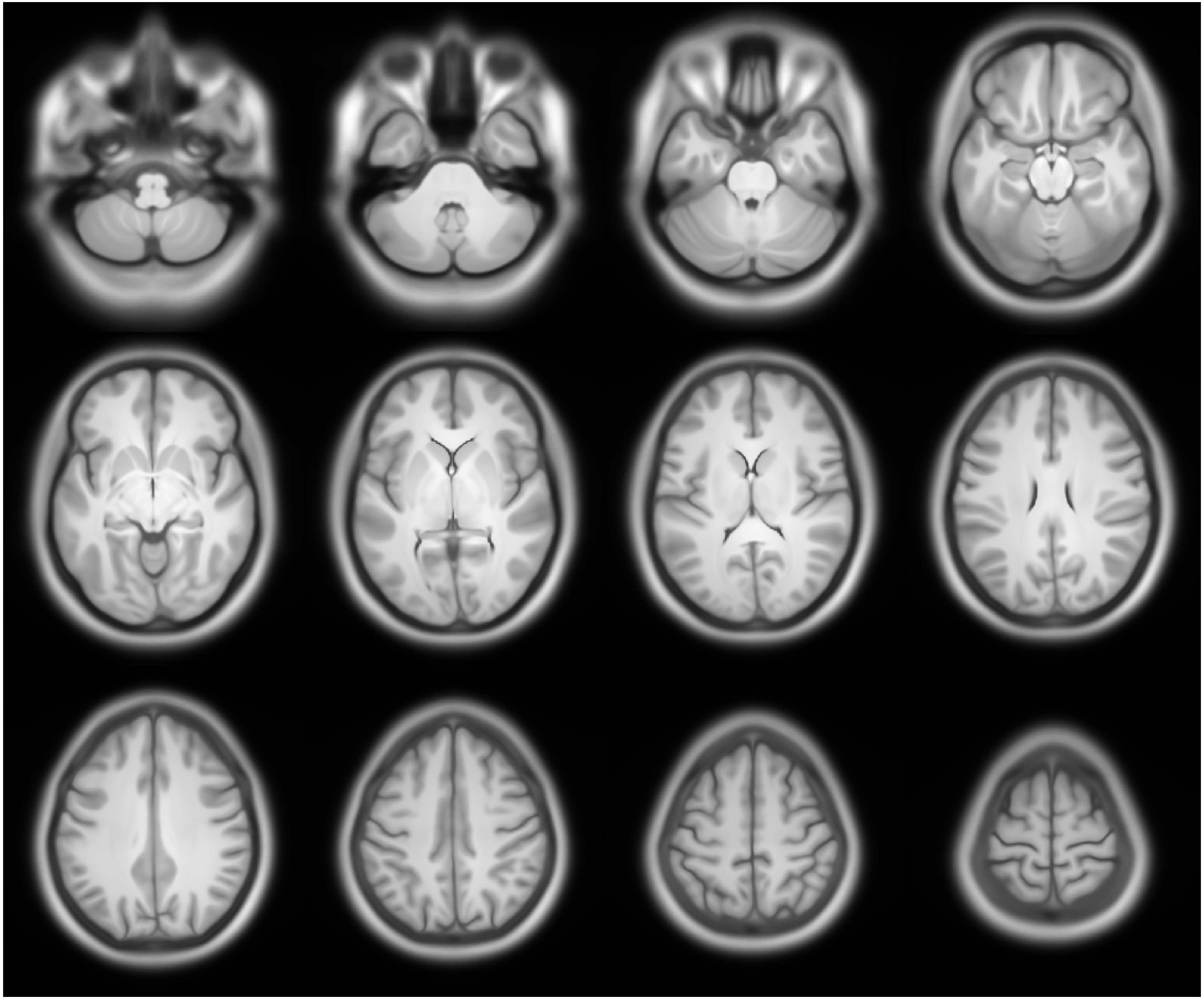


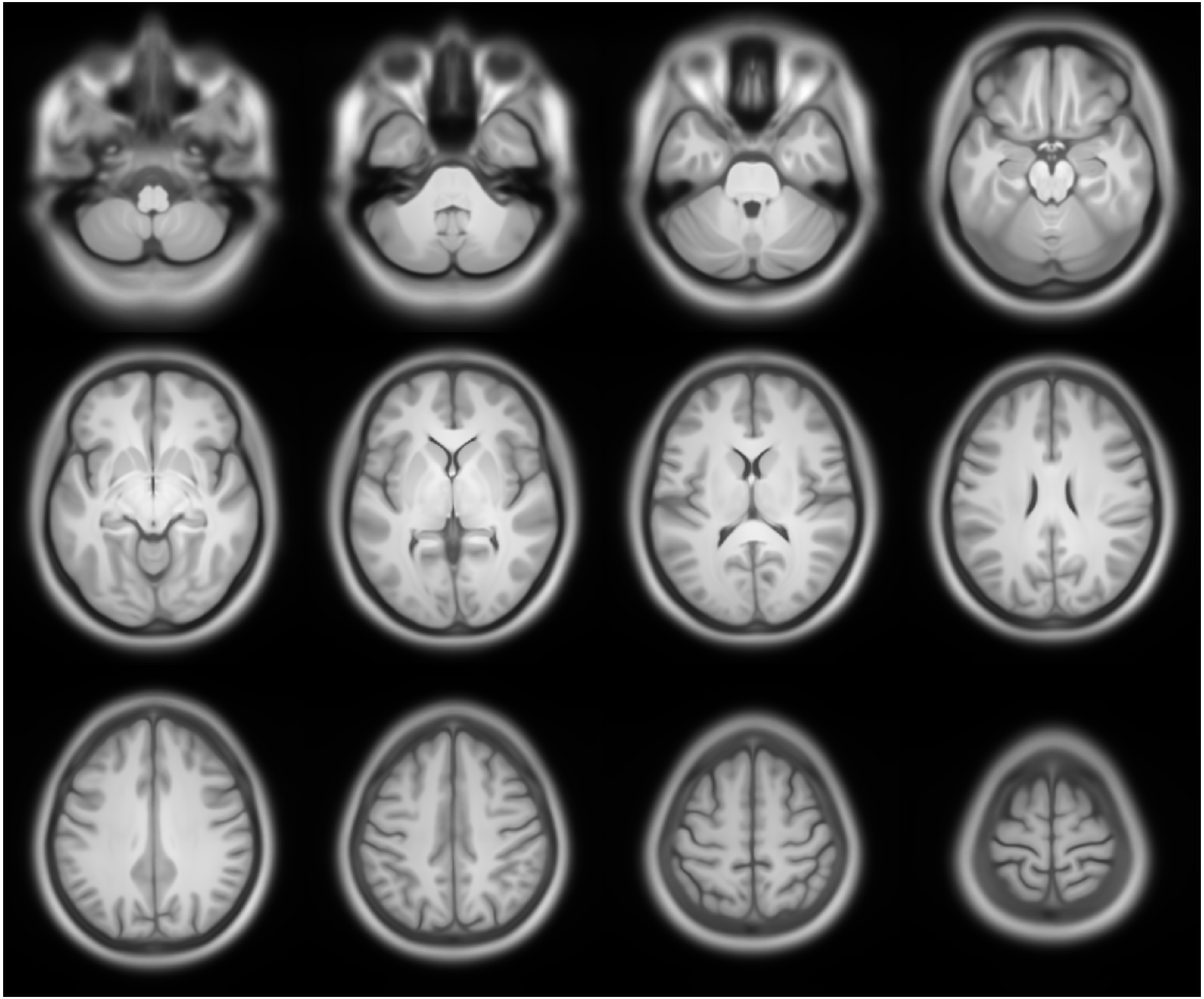


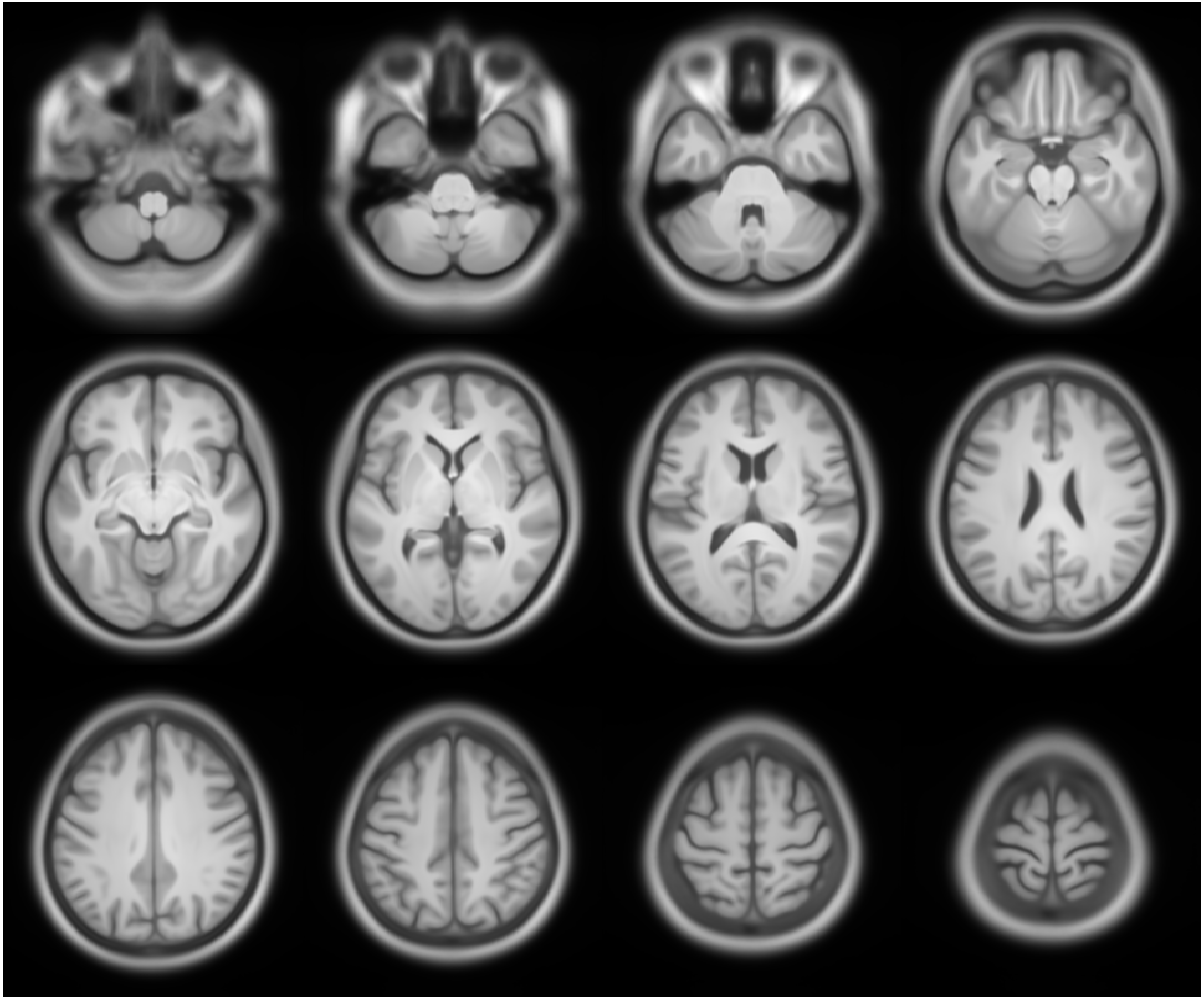
Another example

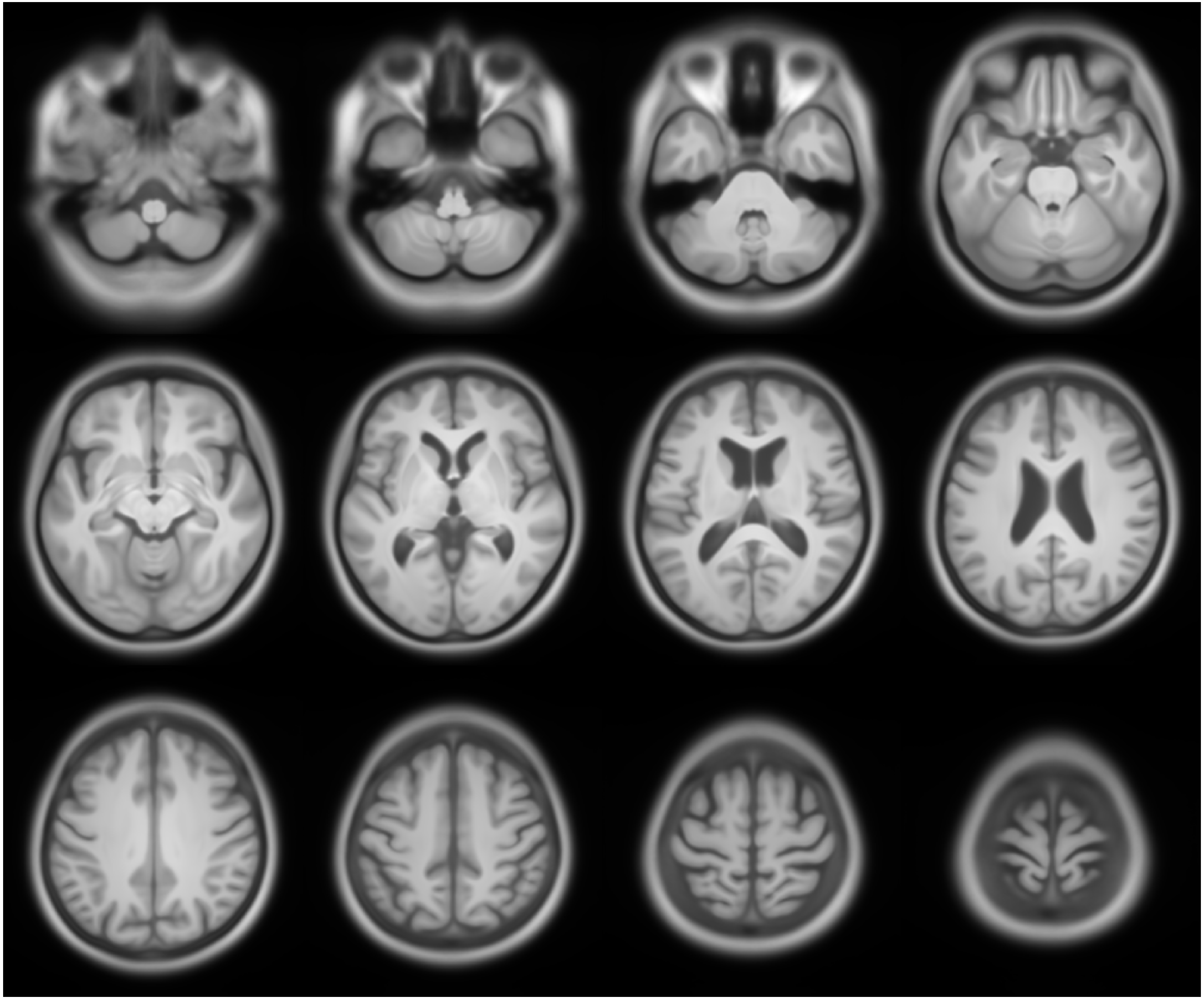
- Predicting the logarithm of the brain/CSF ratio.
- Used a Gaussian Process Regression approach.
- Deformed average, from a brain with very little CSF, to one with a lot.

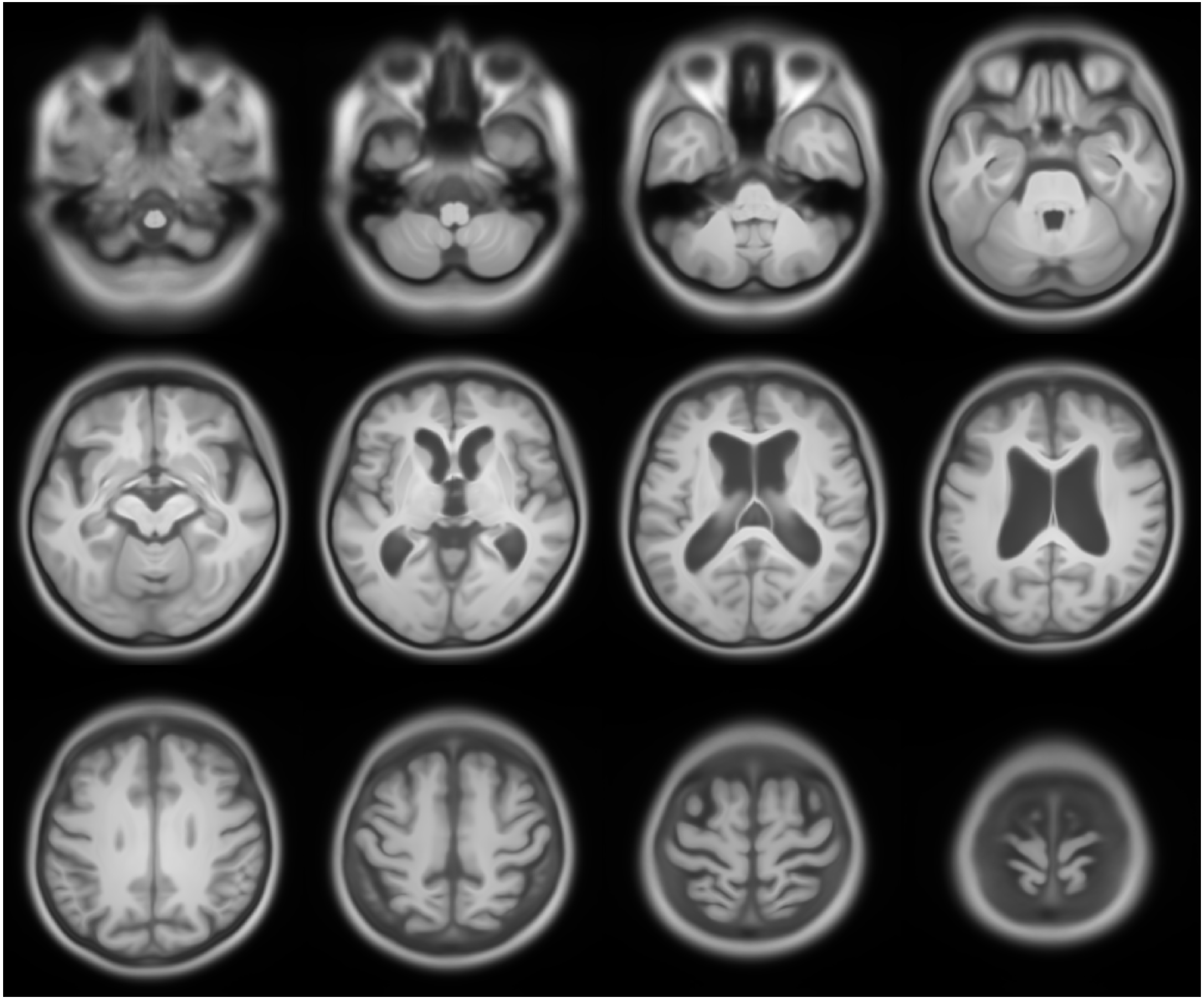












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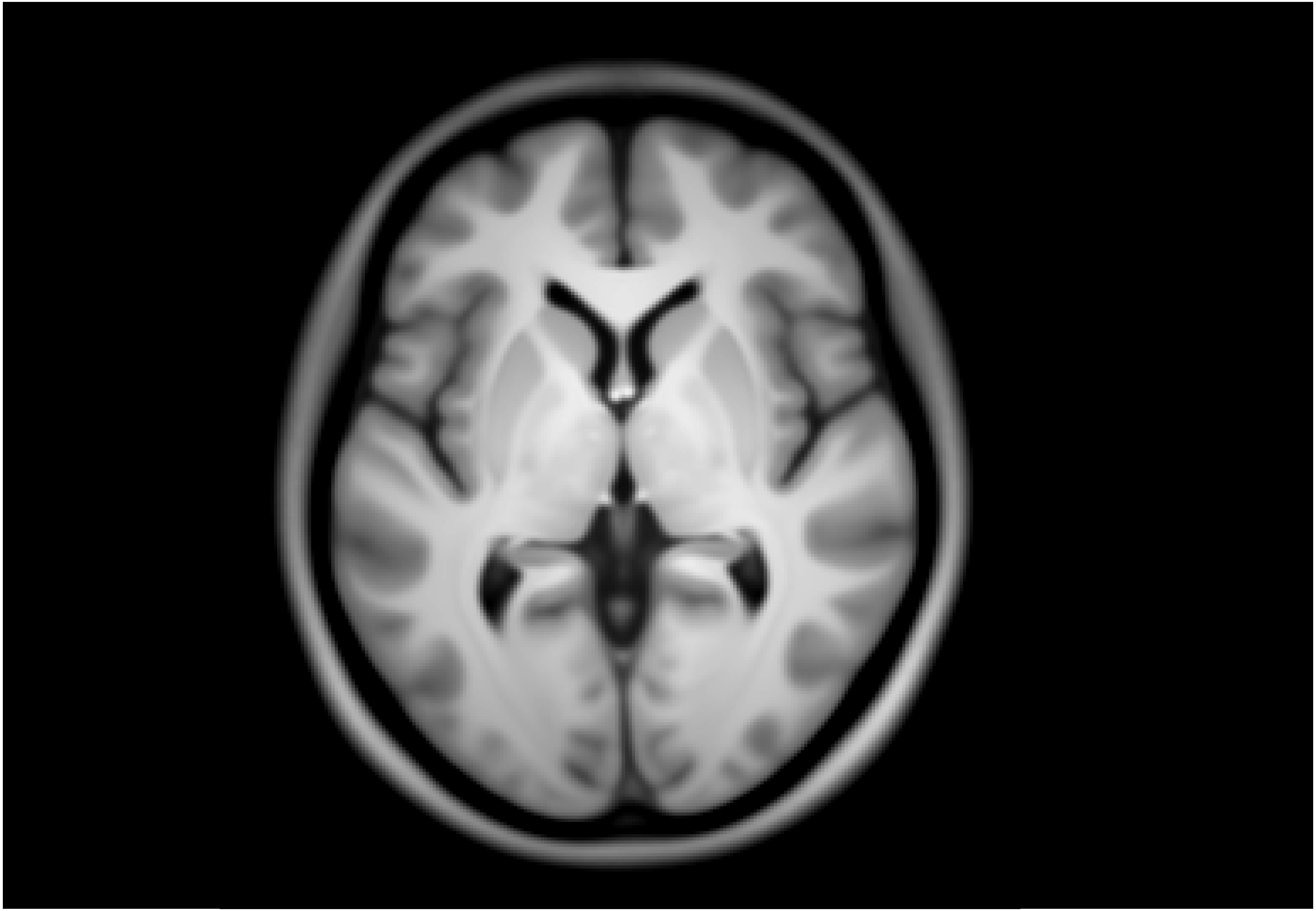


Principle of Stationary Action

Lagrangian = Kinetic Energy – Potential Energy

$$L(\underset{\text{Position}}{q}, \underset{\text{Velocity}}{\dot{q}}, t) = T - V$$

Principle of stationary action:

$$\delta \int_a^b L(q, \dot{q}, t)\,dt = 0$$

LDDMM formulation only uses kinetic energy.

Hamiltonian Mechanics

Introduce momentum:
$$p_i = \frac{\partial L}{\partial \dot{q}_i}$$

The Hamiltonian formalism gives

$$H(q,p,t) = \sum_j p_j \dot{q}_j - L(q,\dot{q},t)$$

The dynamical system equations are then

$$\frac{dq_i}{dt} = \frac{\partial H}{\partial p_i} \quad \text{and} \quad \frac{dp_i}{dt} = -\frac{\partial H}{\partial q_i}$$

Hamiltonian for diffeomorphisms

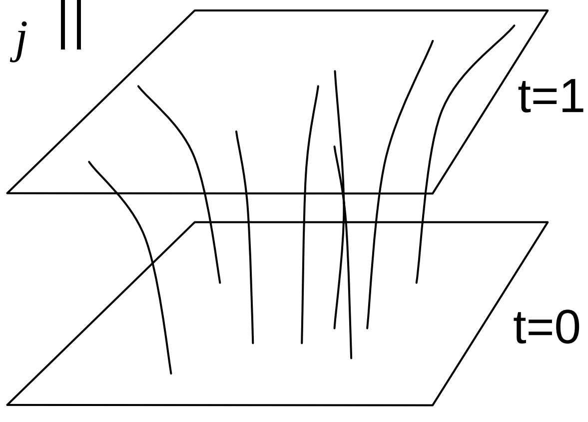
In the landmark-based framework

$$H = \frac{1}{2}\sum_{ij} p_i . p_j G(\| q_i - q_j \|) = \frac{1}{2}\sum_{ij} p_i . \dot{q}_j$$

So update equations are

$$\dot{p}_i = \sum_j p_i . p_j G'(\| q_i - q_j \|) \frac{q_i - q_j}{\| q_i - q_j \|}$$

$$\dot{q}_i = \sum_n G(\| q_i - q_j \|) p_j$$



See e.g. the work of Steve Marsland et al

Aging effects