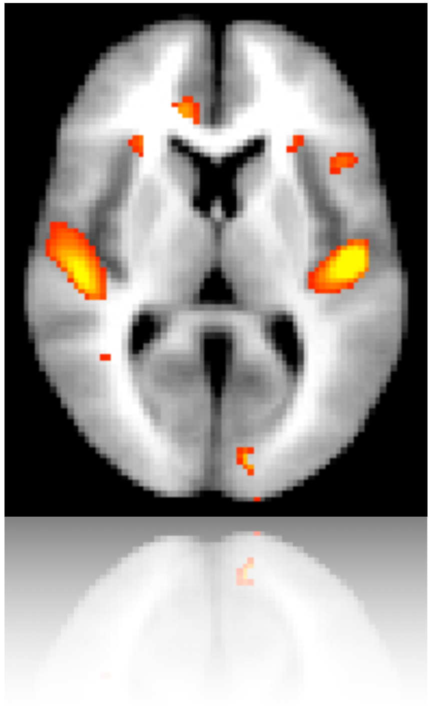
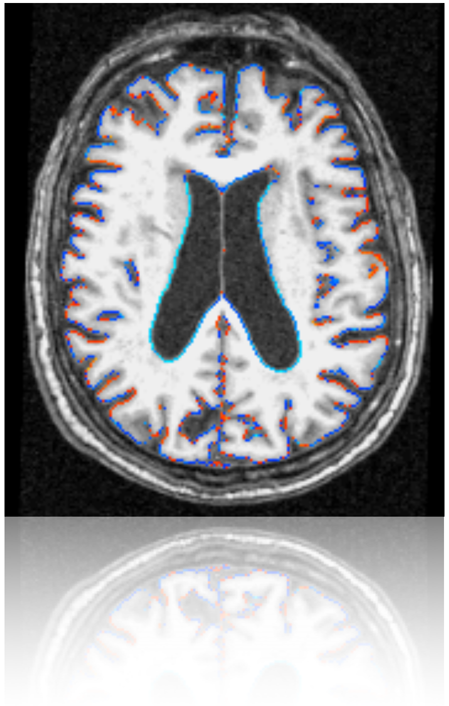
Structural Analysis

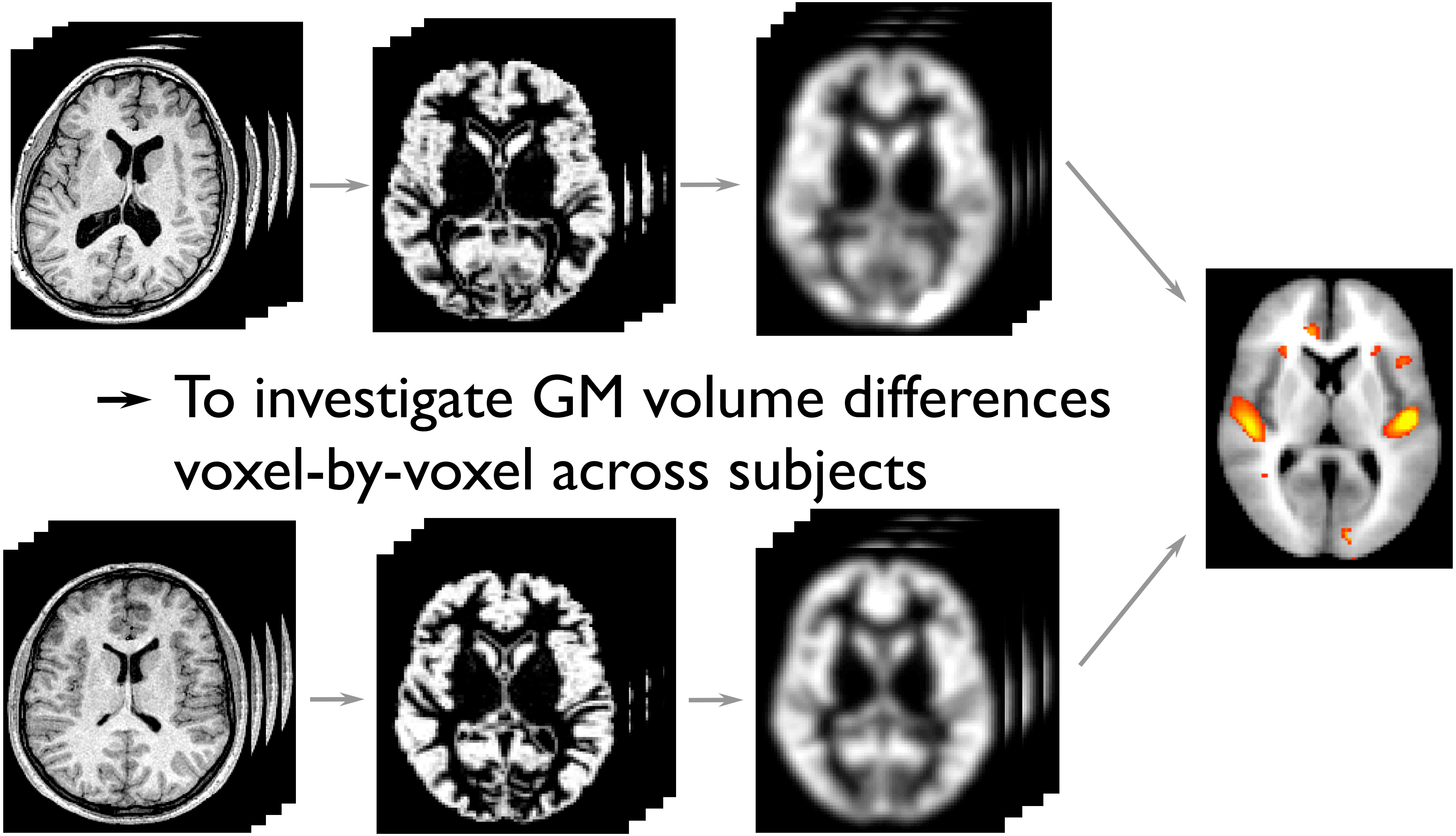
FSL-VBM voxelwise grey-matter density analysis
SIENA/SIENAX global atrophy estimation





FSL-VBM

Voxel-Based Morphometry with FSL tools



→ To investigate GM volume differences voxel-by-voxel across subjects

Voxel-based analysis of local GM volume

- Somewhat controversial approach
  (e.g. what exactly is it “looking at”?)

- BUT - it gives some clues for:
  - volume/gyrification differences between populations
  - correlations with (e.g.) clinical score
  - fMRI/PET results “caused” by structural changes

- Currently it is very widely used, although some other alternatives exist
  (e.g. surface-based thickness analysis,
  tensor/deformation-based morphometry)

Voxel-based analysis of local GM volume

- No a priori required = whole-brain unbiased analysis
- Automated = Reproducible intra/inter-rater
- Quick

- Localisation of the GM differences across subjects
  ⇒ non-linear registration

- Trade-off:
  - not enough non-linear = no correspondence
  - too much non-linear = no difference (in intensities)

Voxel-based analysis of local GM volume

- Optimised protocol (Good et al., 2001)
  1) Segmentation: BET then FAST to get GM partial volume estimate

Voxel-based analysis of local GM volume

- Optimised protocol (Good et al., 2001)

  2) Make a study-specific template

  & non-linearly register all images to it (FNIRT)

Make template by iteratively registering images together, starting with a standard template

Want equal numbers of patients and controls

X patients

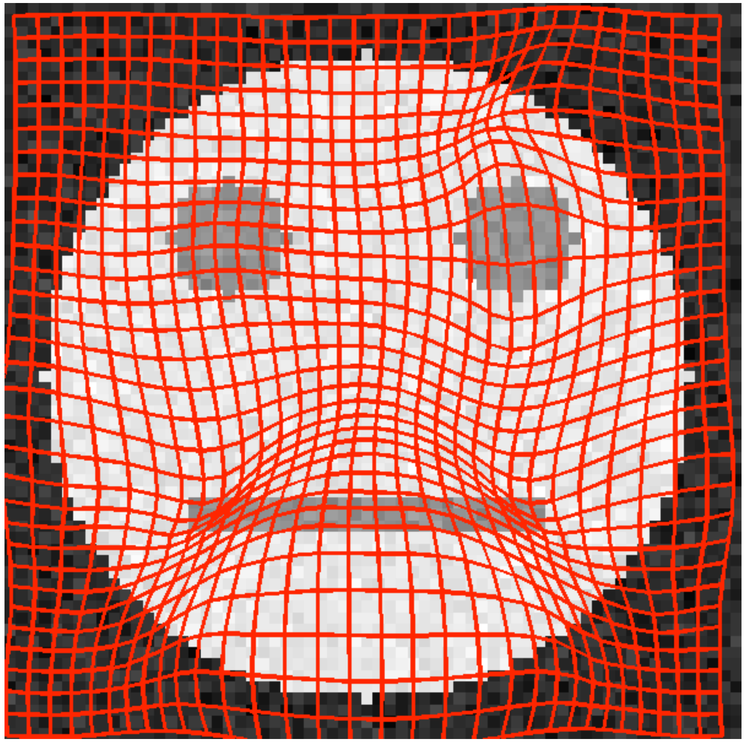
X controls

Voxel-based analysis of local GM volume

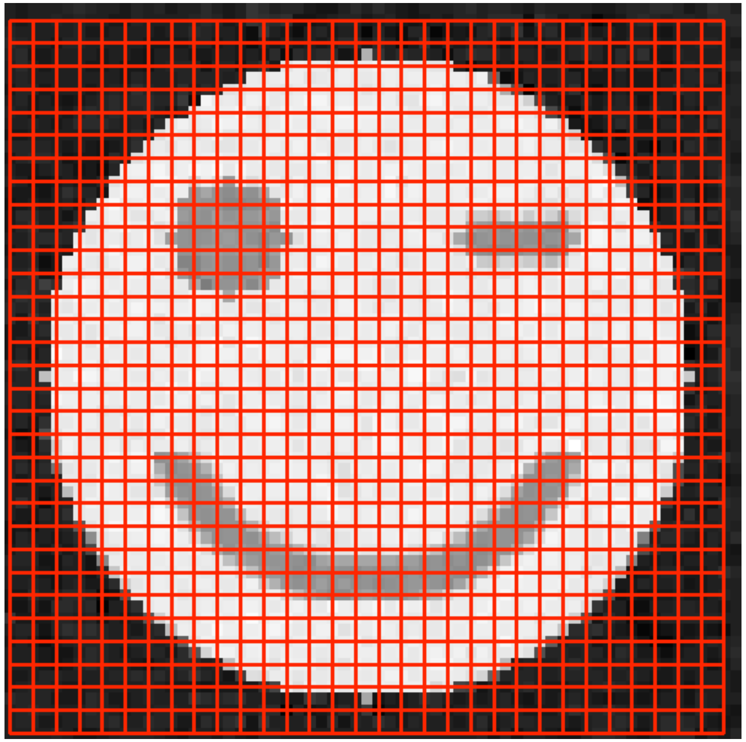
- Optimised protocol (Good et al., 2001)

3) “Modulation”: compensates tissue volume for the non-linear part of the registration (FNIRT)

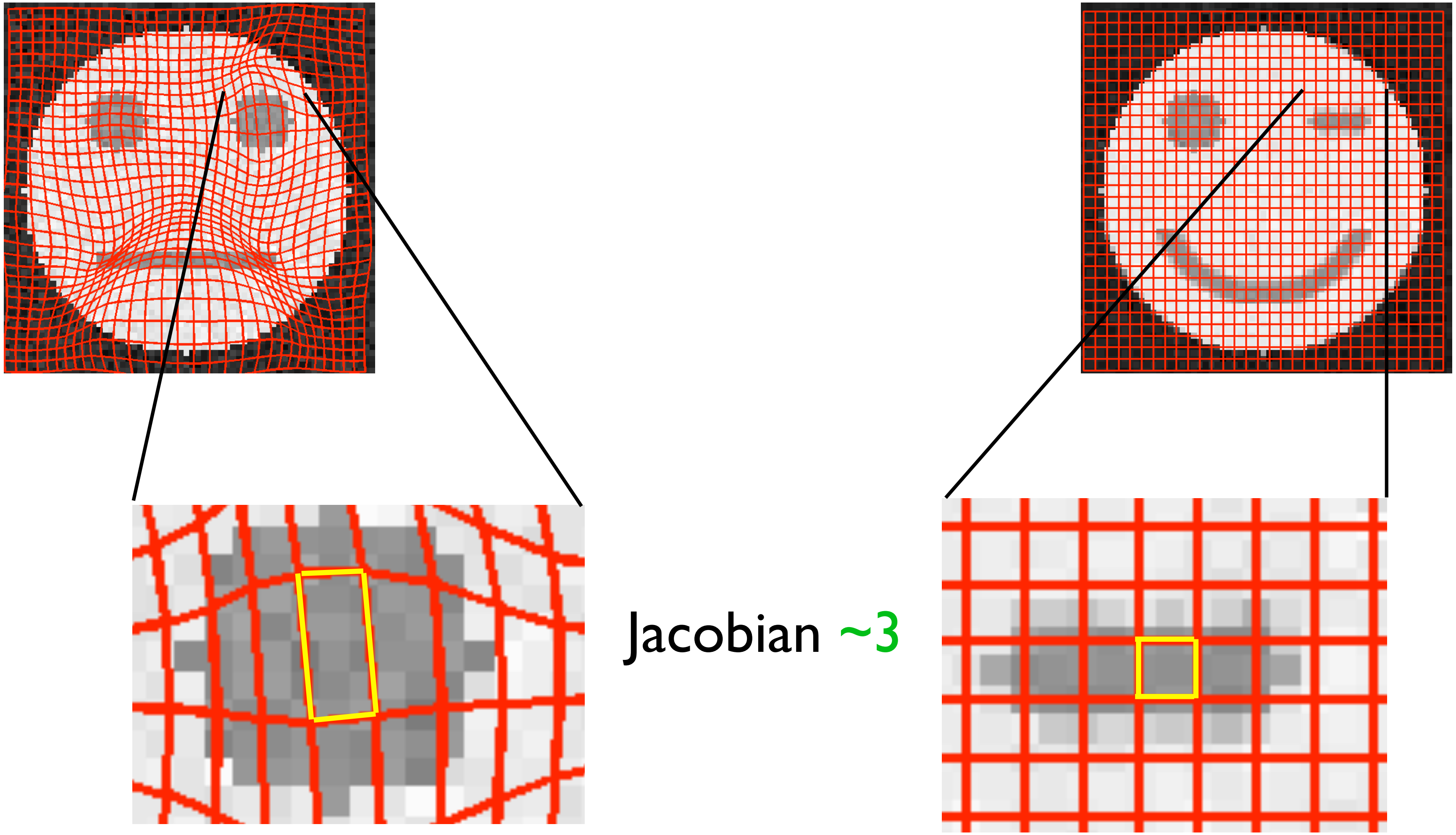
Jacobian modulation



Jacobian modulation



Jacobian modulation

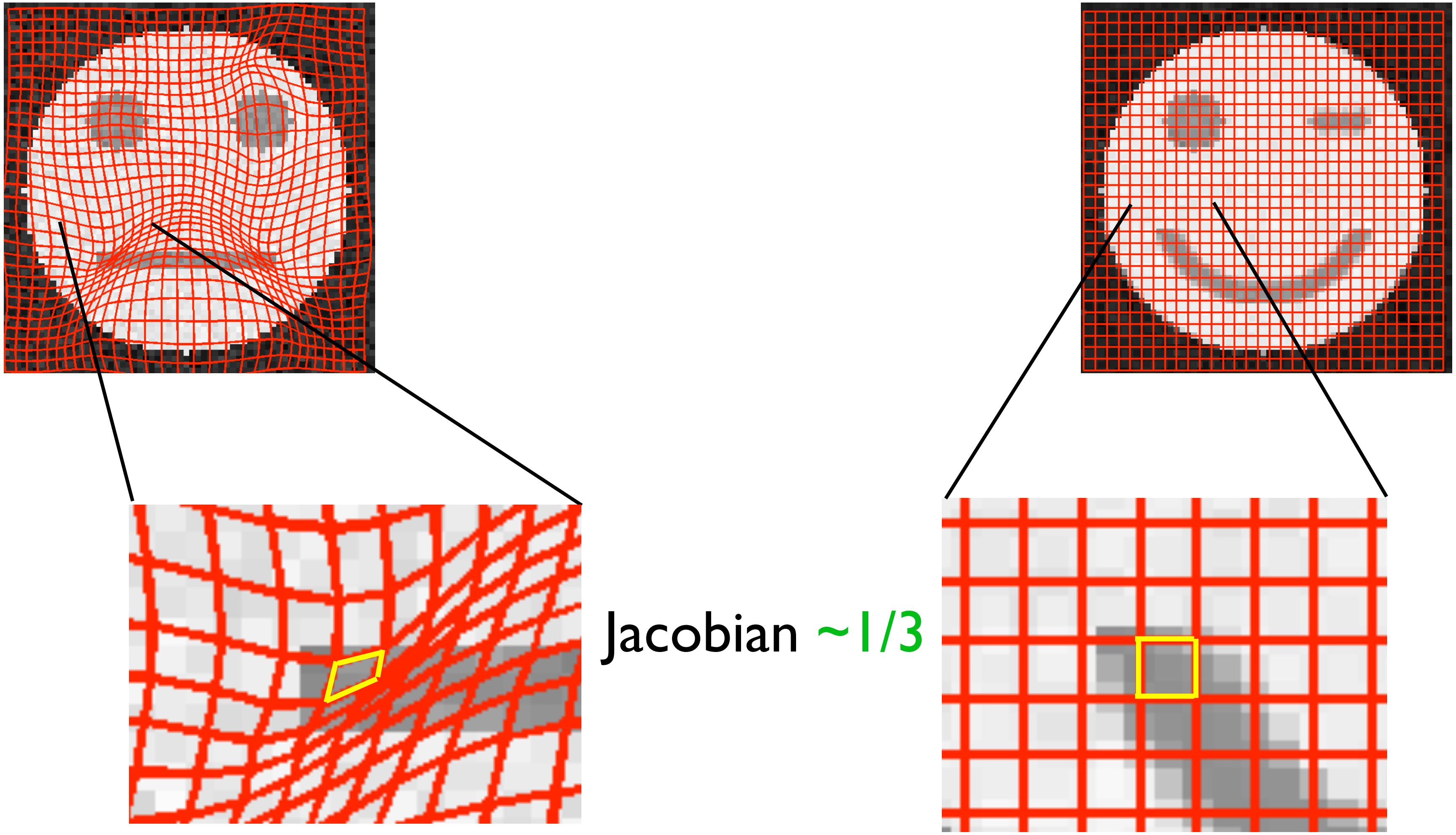


Jacobian ~3

~3mm^2 in original space

1mm^2 in warped space

Jacobian modulation

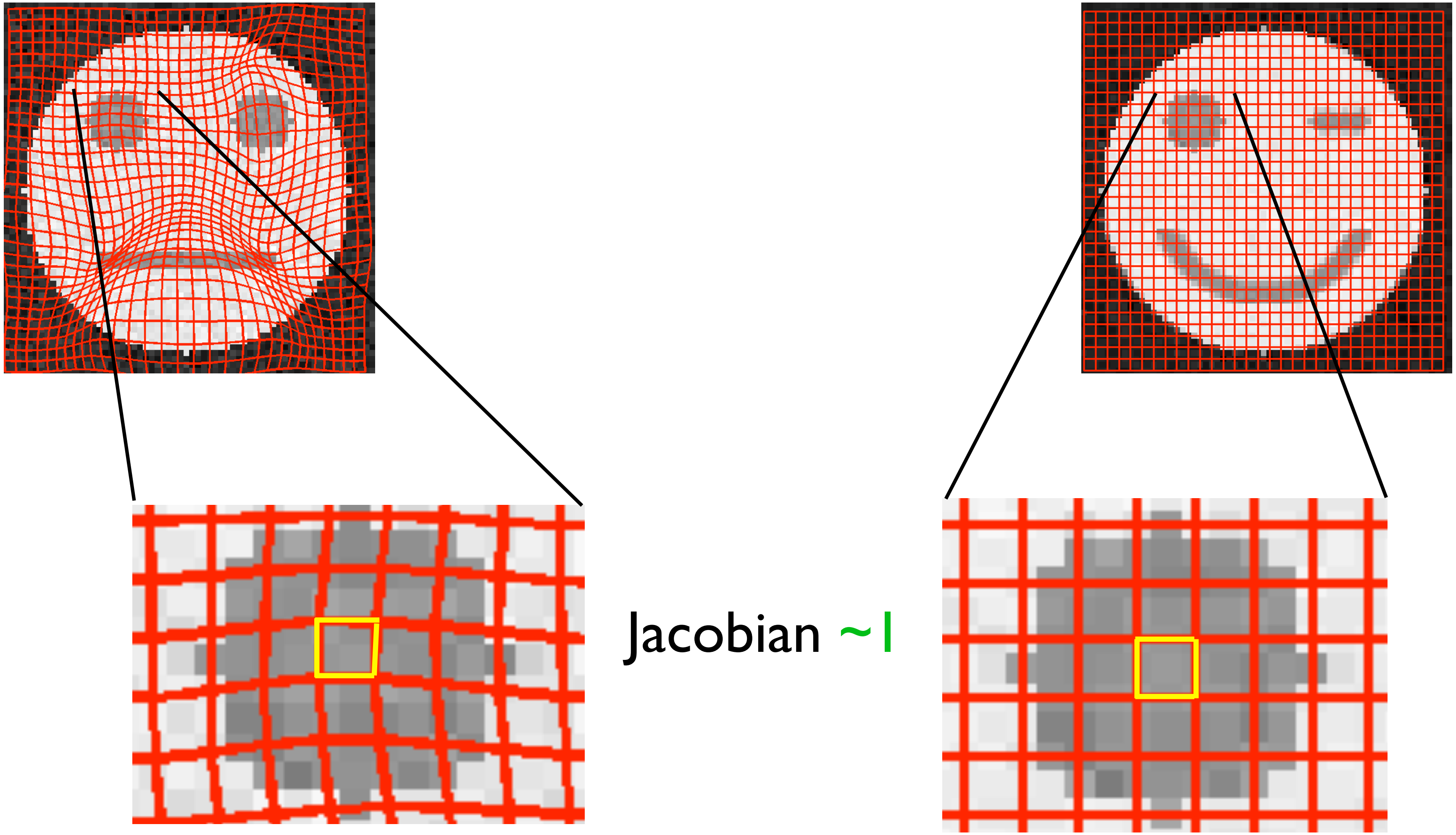


Jacobian ~1/3

~1/3mm^2 in original space

1mm^2 in warped space

Jacobian modulation

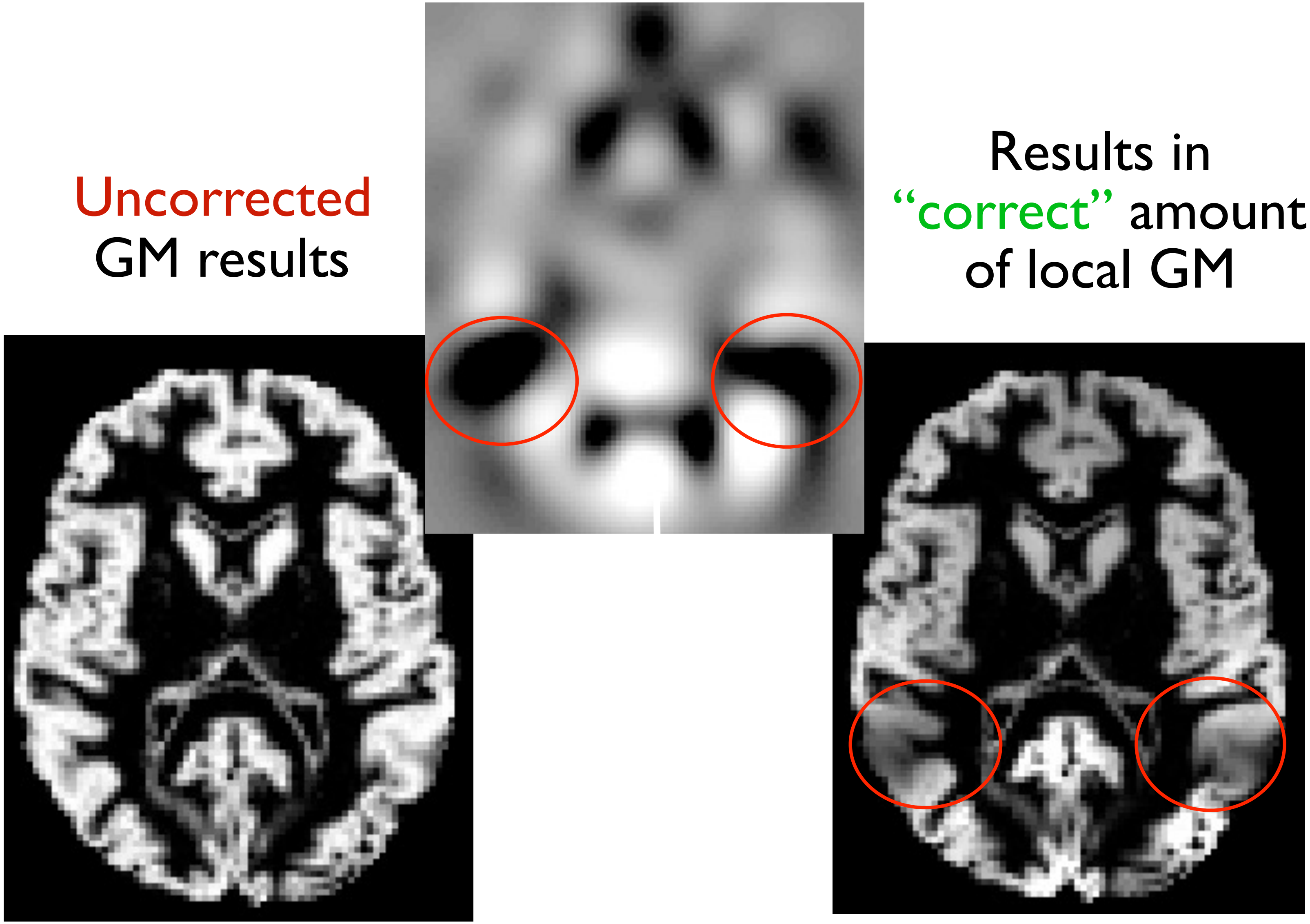


Jacobian ~1

~1mm^2 in original space

1mm^2 in warped space

Voxel-based analysis of local GM volume



Jacobian map: correction for
local expansion/contraction

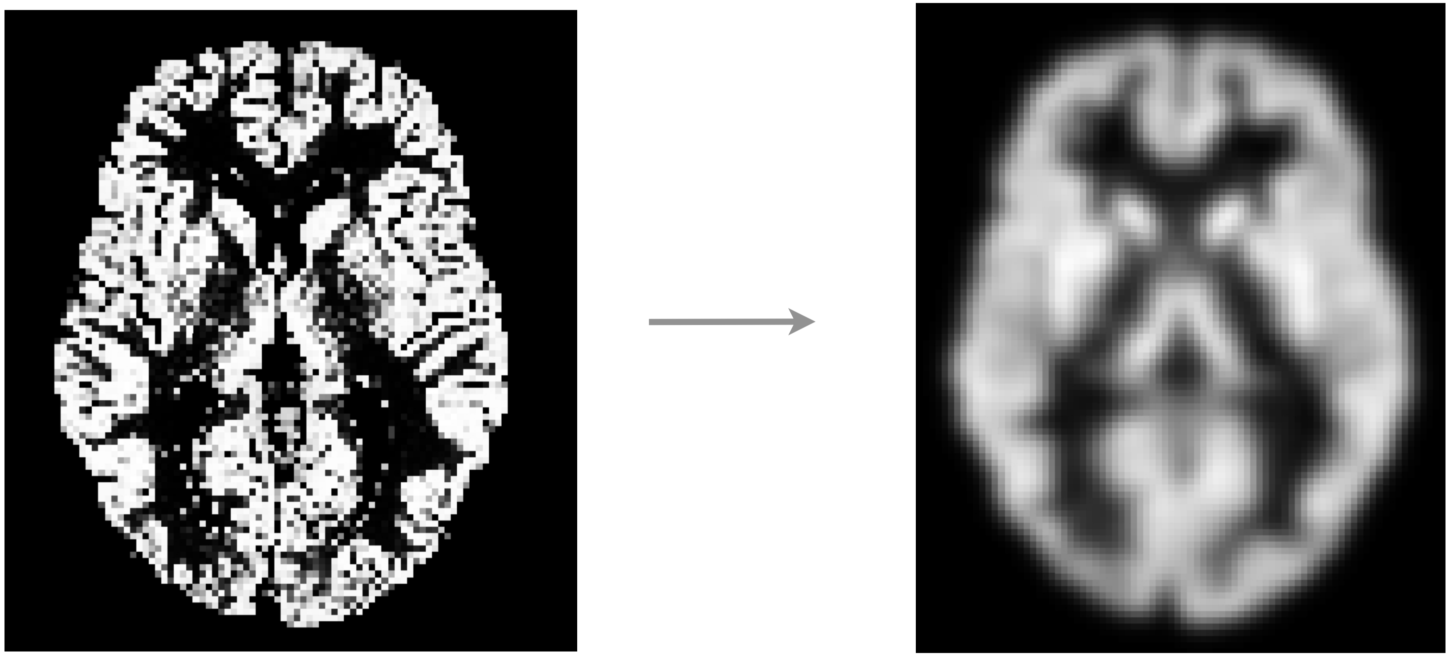
Uncorrected
GM results

Results in
"correct" amount
of local GM

Voxel-based analysis of local GM volume

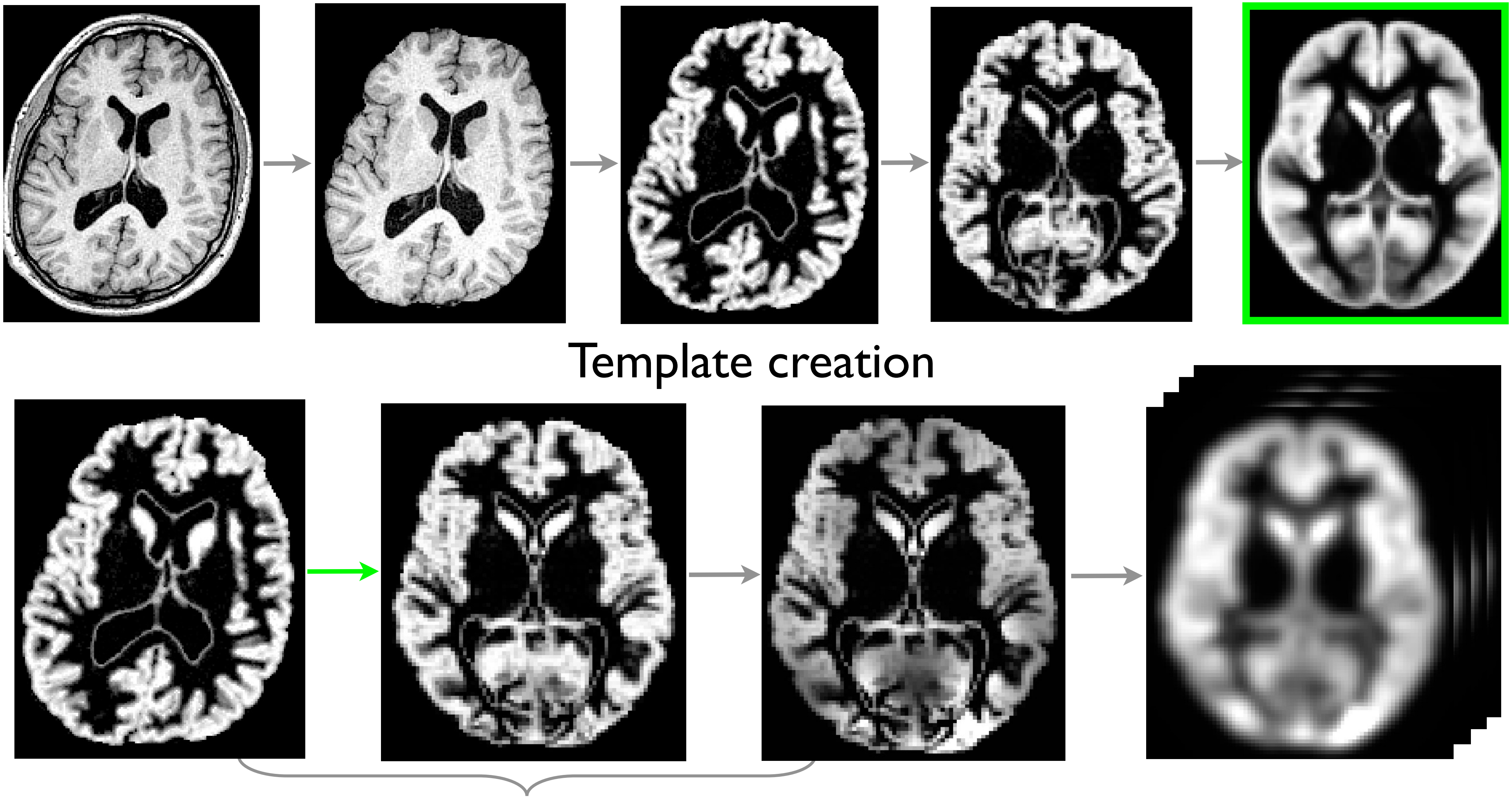
- Optimised protocol (Good et al., 2001)

4) Smooth with a Gaussian filter



Voxel-based analysis of local GM volume

- Optimised protocol (Good et al., 2001)

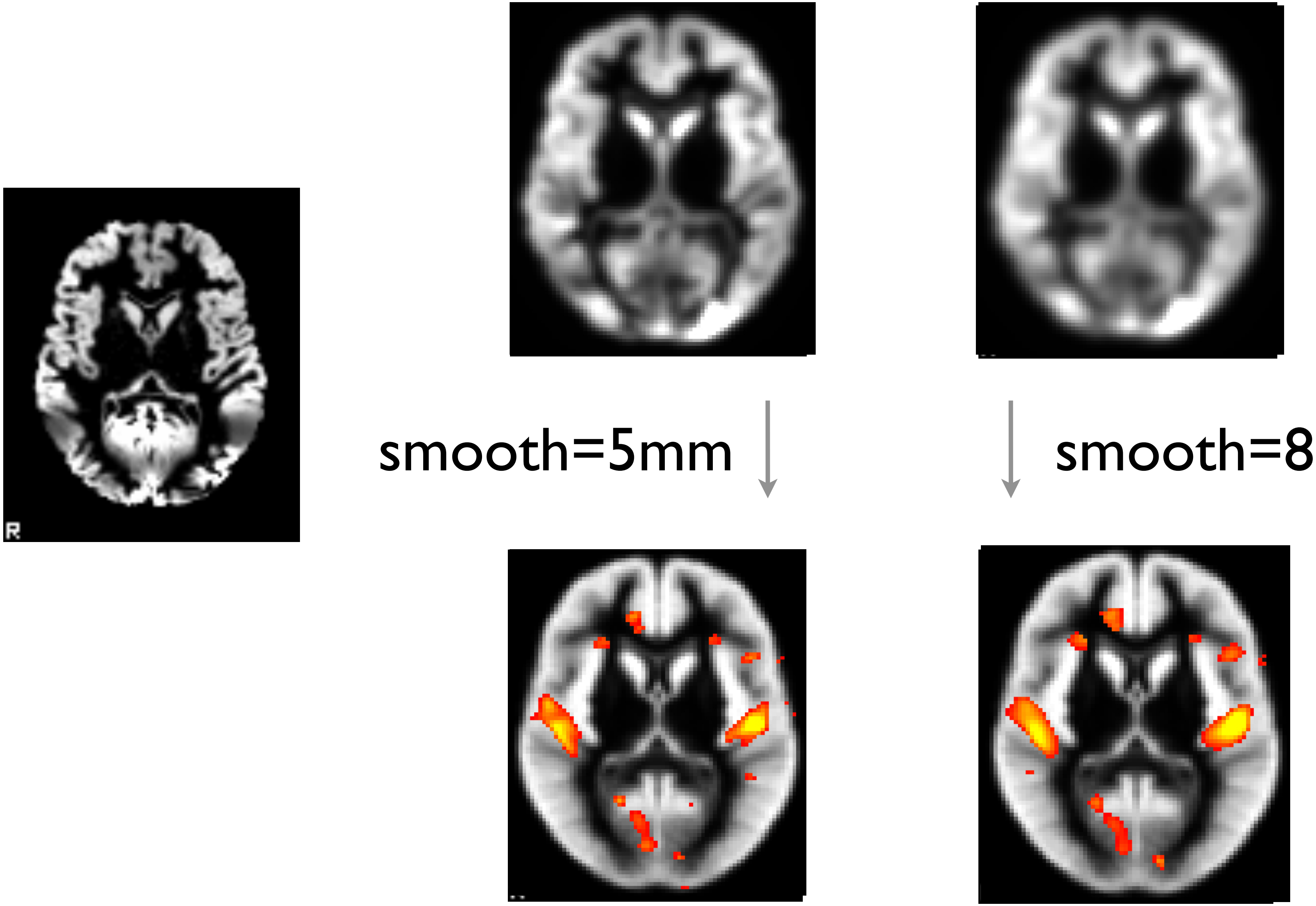


Template creation

Processing steps

Analysis

Voxel-based analysis of local GM volume



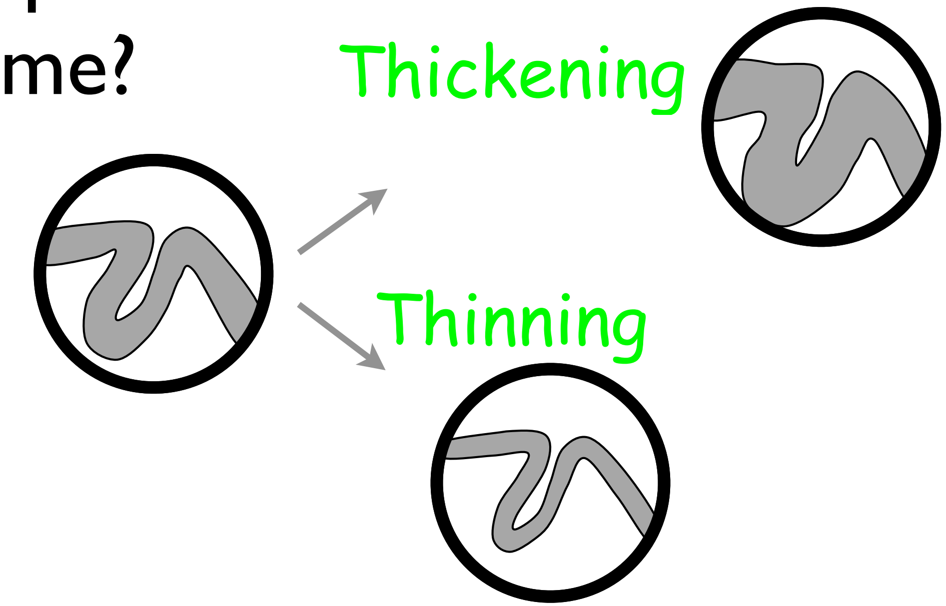
smooth=5mm

smooth=8mm

Voxel-based analysis of GM volume

- Controversial approach - back to the issues:

1) Interpretation of the results - real loss/increase of volume?

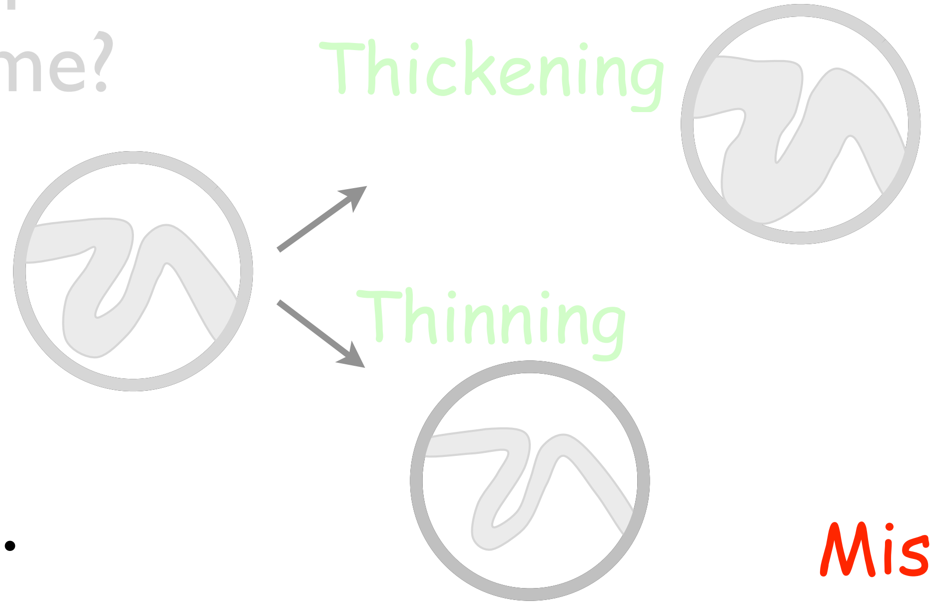


Illustrations courtesy of John Ashburner

Voxel-based analysis of GM volume

- Controversial approach - back to the issues:

I) Interpretation of the results - real loss/increase of volume?



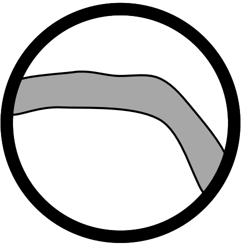
Or ...

- Difference in the contrast?

Mis-classify

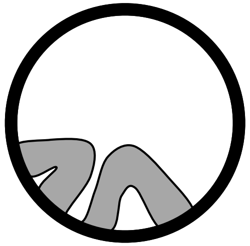
- Difference in gyrification pattern?

Folding



- Problem with registration?

Mis-register



Illustrations courtesy of John Ashburner

Voxel-based analysis of GM volume

- Controversial approach - back to the issues:

1) Interpretation of the results - real loss of volume?
  - Difference in the contrast?
  - Different in gyrification pattern (developmental)?
  - Problem with registration (Bookstein 2001)?

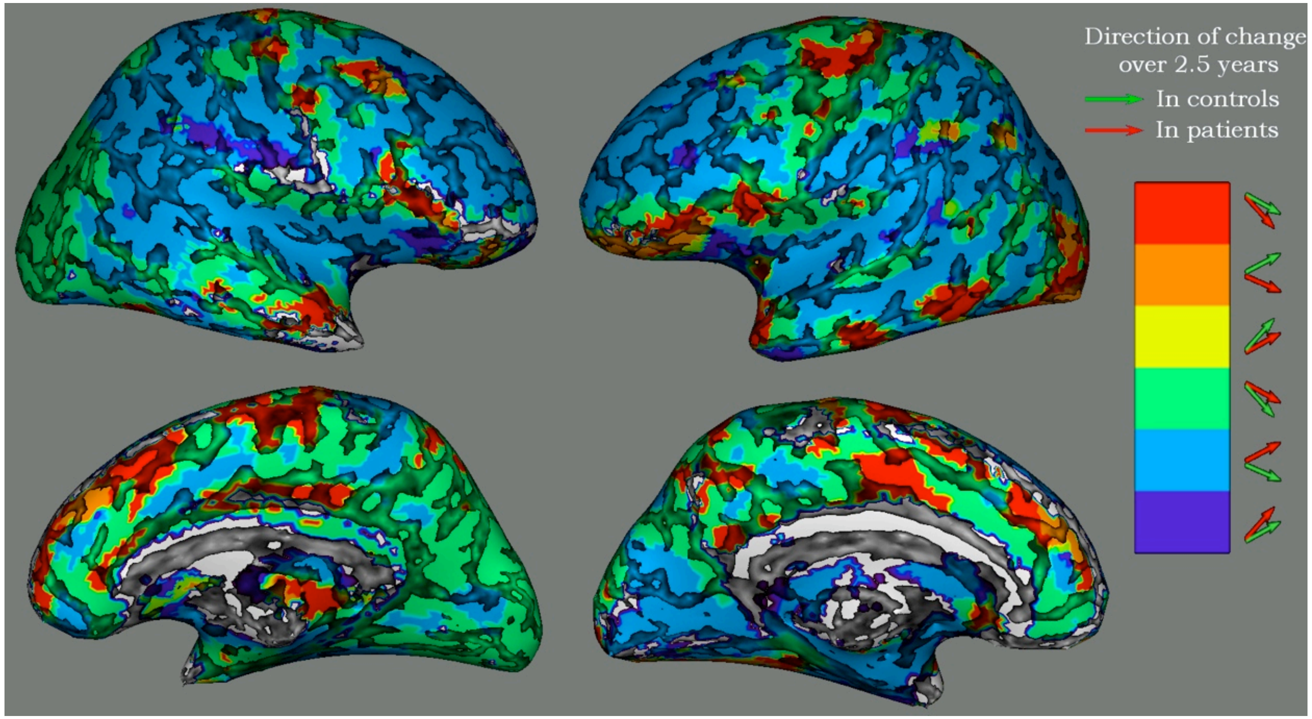
2) Continuum of results, depending on:
  - Smoothness (Jones 2005)
  - DOF of the nonlinear registration (Crum 2003)
  - Template?
  - Software?

⟶ See Ridgway et al., NeuroImage 2008 for best practice

Voxel-based analysis of GM volume

- Useful literature/examples:

  \- Longitudinal protocol in FSL: Douaud et al., Brain 2009



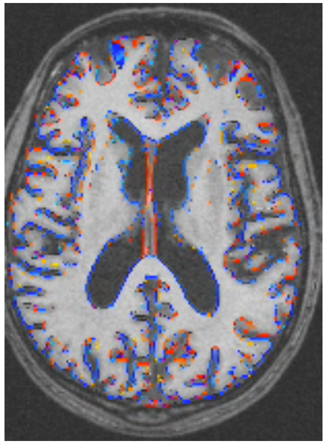
  \- Comparisons of longitudinal protocols and softwares:
  Thomas et al., NeuroImage 2009

SIENA

Structural Image Evaluation (with Normalisation) of Atrophy

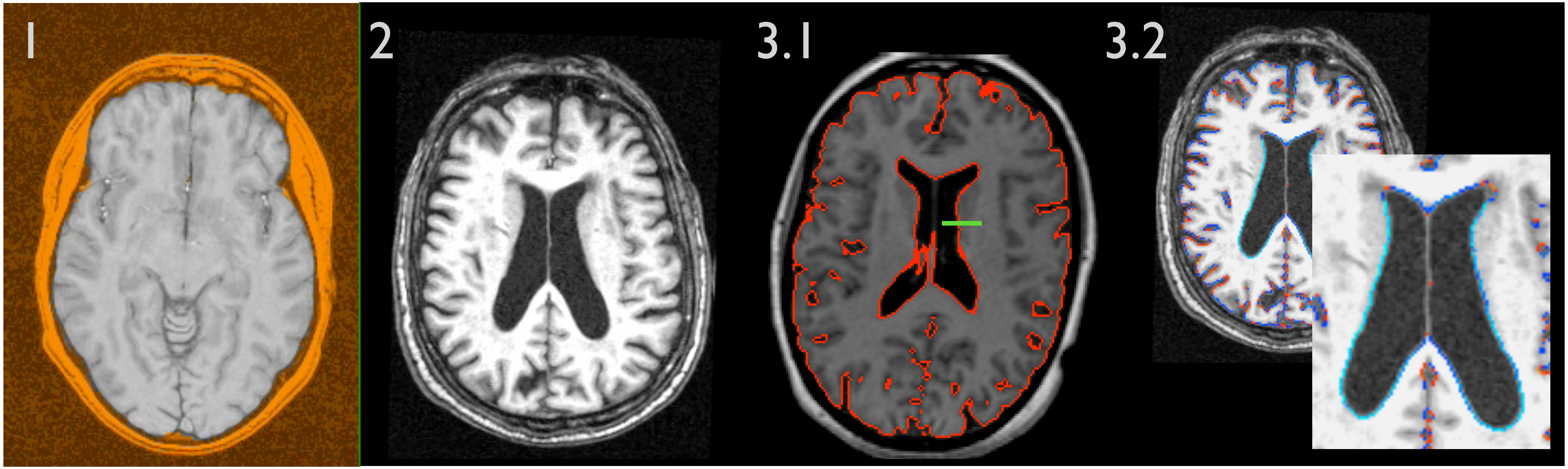
Multiple- and single-timepoint analysis of brain change

	original global-only estimation	voxelwise local-only estimation
two timepoints (atrophy *rate*)	SIENA	Longitudinal FSL-VBM
single timepoint (atrophy *state*)	SIENAX	FSL-VBM



SIENA Longitudinal atrophy estimation

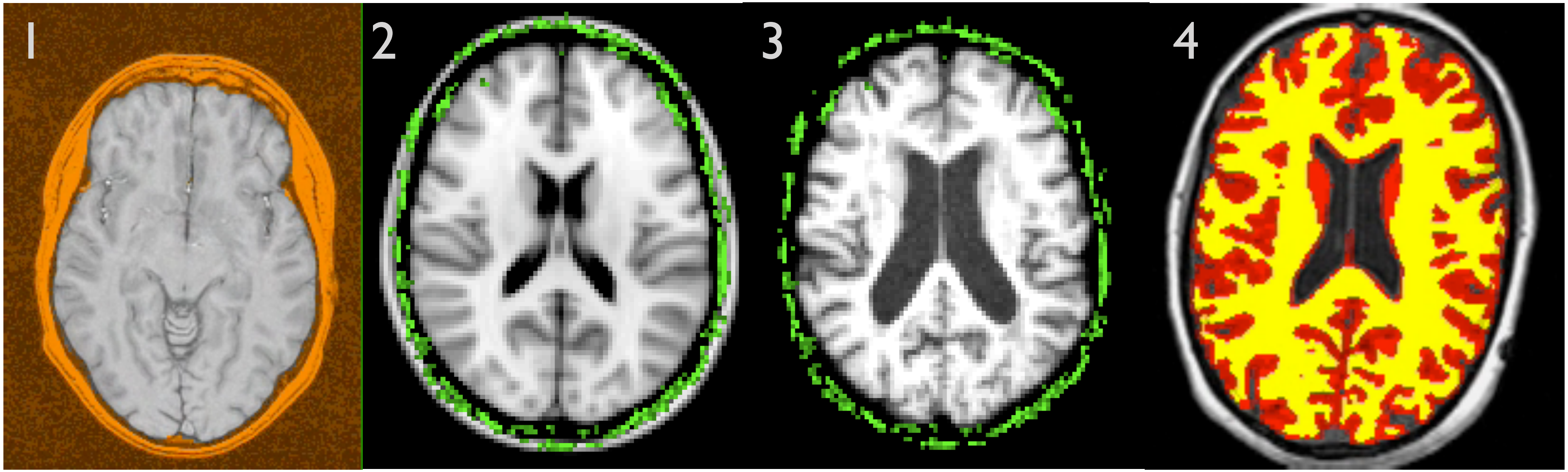
1. BET: find brain and skull - applied to both time points
2. FLIRT: register to half-way space (similar interpolation for 2 points)
3. Atrophy estimation using edge motion
   - 3.1. Run FAST, then sample normal profile of brain-non brain boundary
   - 3.2. Take derivative of both time points' profiles and calculate shift for each boundary point: blue=atrophy, red="growth"
4. Average over all edge points and conversion to % brain volume change (PBVC)



SIENAX Cross-sectional atrophy estimation

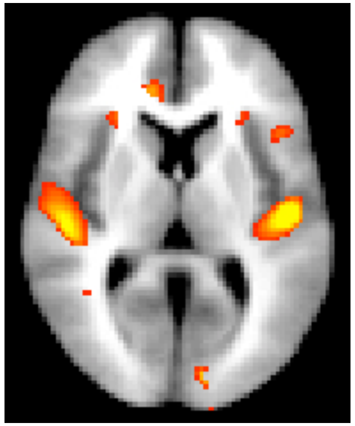
1. BET : find brain and skull
2. FLIRT : register to standard space using skull for scaling
3. Use standard-space masking to remove residual eyes/optic nerve
4. FAST : partial volume segmentation of tissues
5. Output : normalised brain volume (NBV)

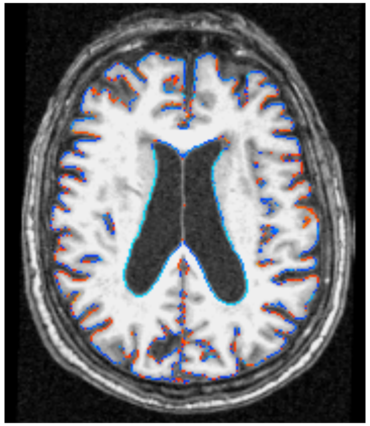
Note: NBV is useful for including as a *head/brain-size covariate* in other structural analyses (e.g. FIRST, VBM, etc.)



Structural Segmentation

FSL-VBM voxelwise grey-matter density analysis
SIENA/SIENAX global atrophy estimation





Summary

- VBM combines registration and segmentation
- Provides *voxelwise* maps of changes in GM
- It creates a study-specific template
  - Need to balance groups for template only
- Spatial smoothing helps with stats but makes interpretation more difficult
  - Arbitrary choice on amount of smoothing
- Need to check that all stages work
- Alternatives (e.g. cortical thickness) also used
- Longitudinal version has separate pipeline
- SIENA/SIENAX provide *global* estimates of GM changes, for longitudinal and cross-sectional studies