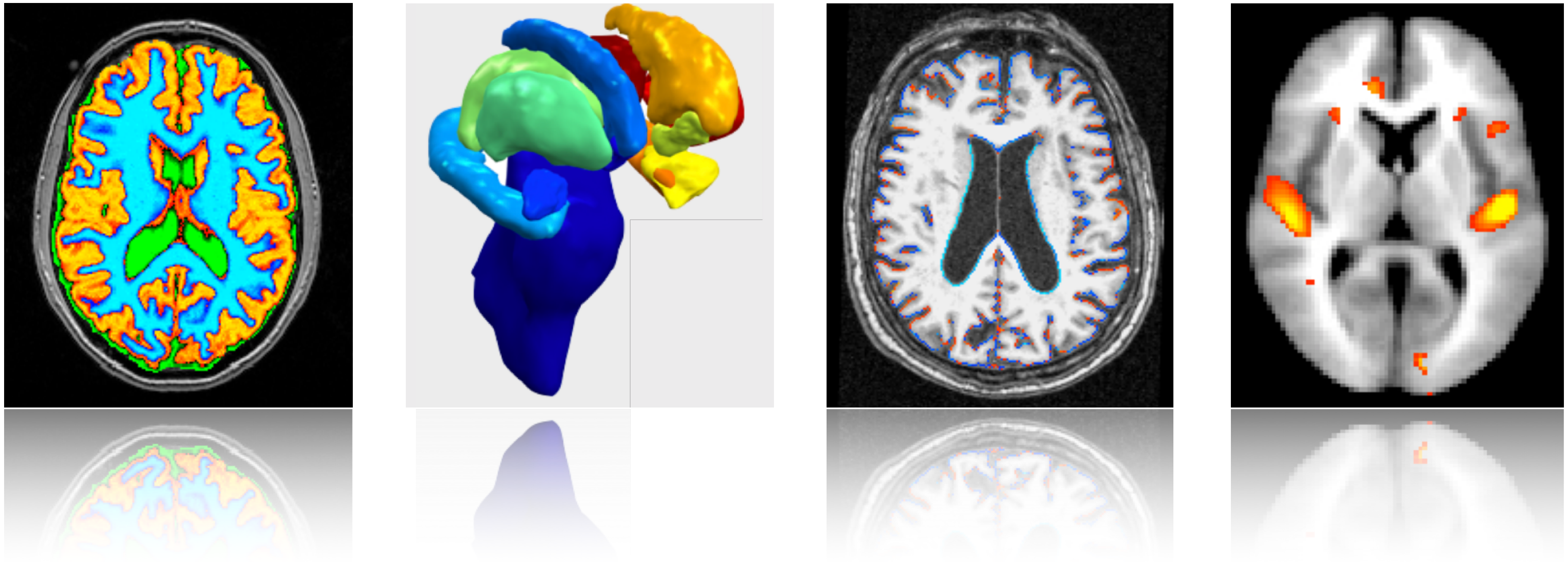
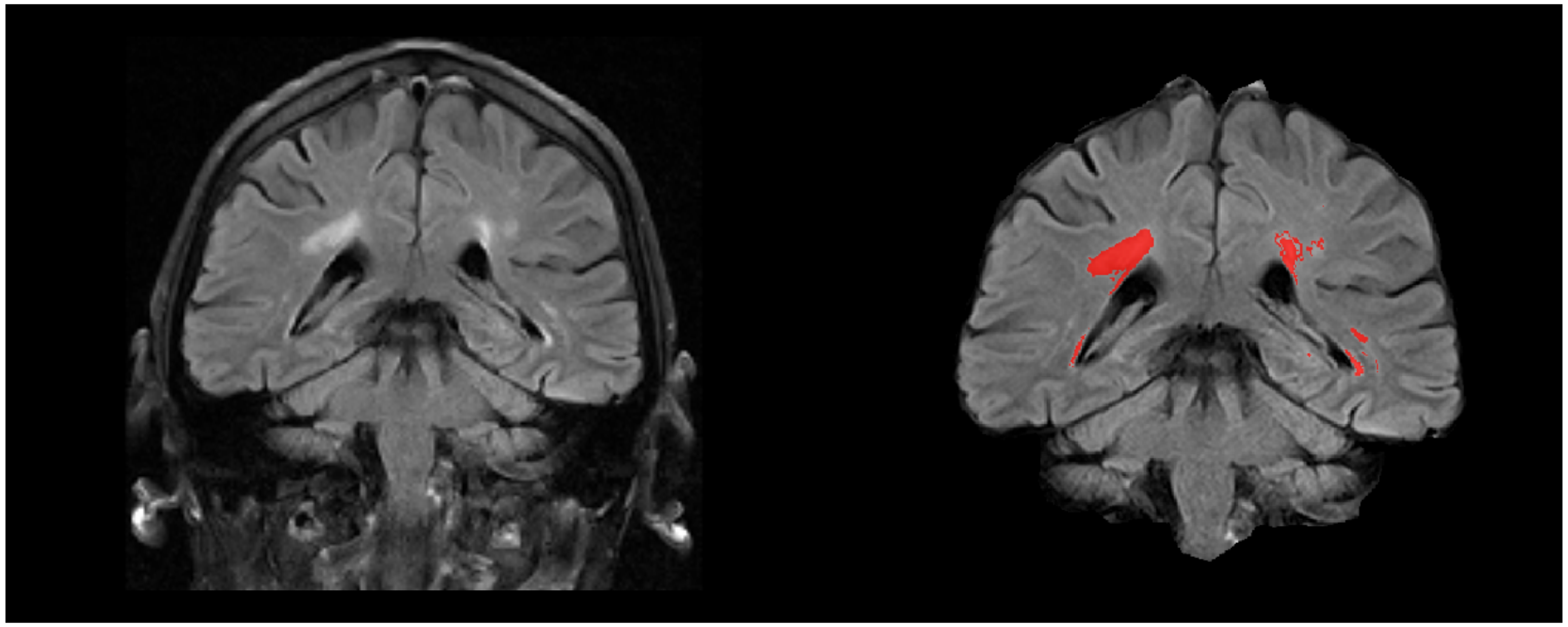
Structural Segmentation



- FAST tissue-type segmentation
- FIRST sub-cortical structure segmentation
- BIANCA segmentation of white matter lesions
- FSL-VBM voxelwise grey-matter density analysis
- SIENA/SIENAX global atrophy estimation

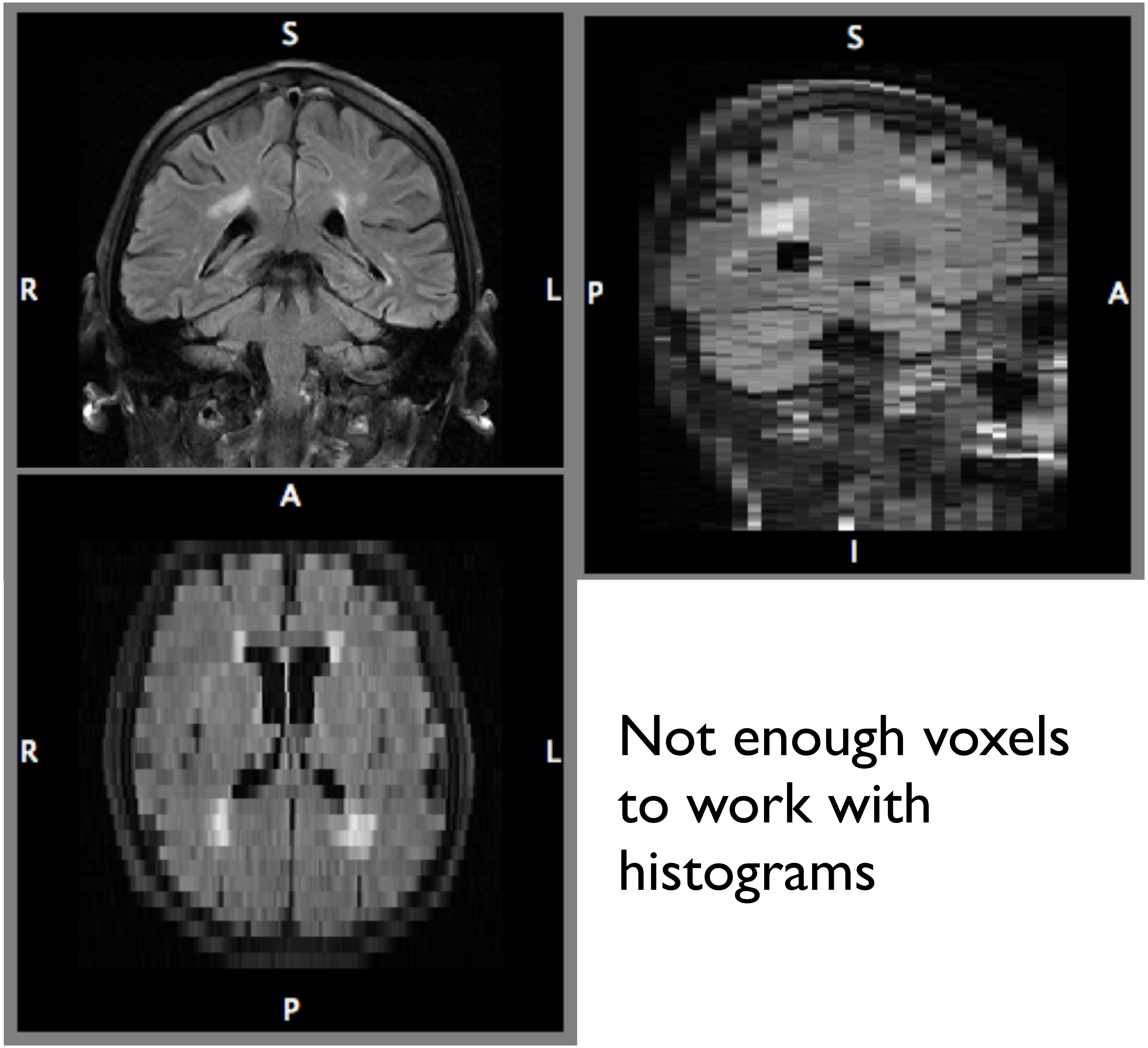
BIANCA

Segmentation of White Matter Hyperintensities / Lesions

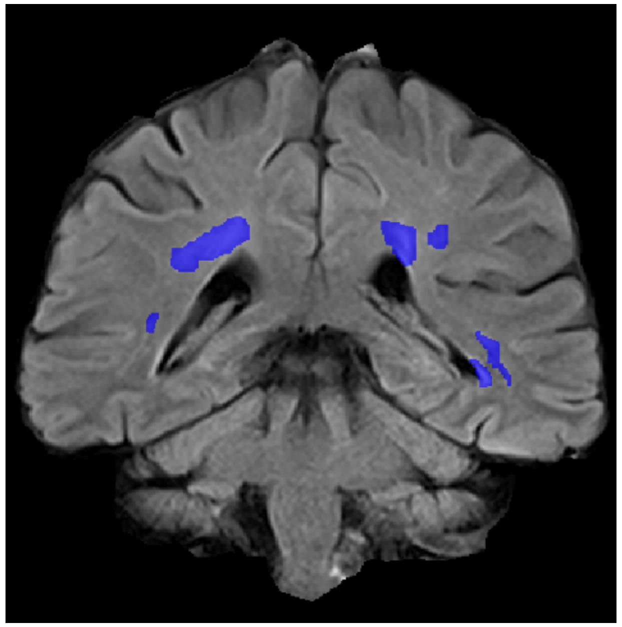


Lesion/WMH Segmentation

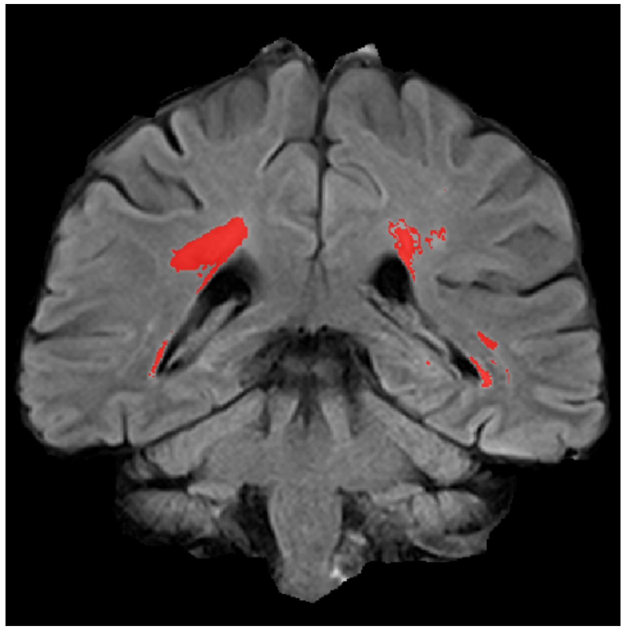
WMH = White Matter Hyperintensities (leukoaraiosis)



Not enough voxels to work with histograms



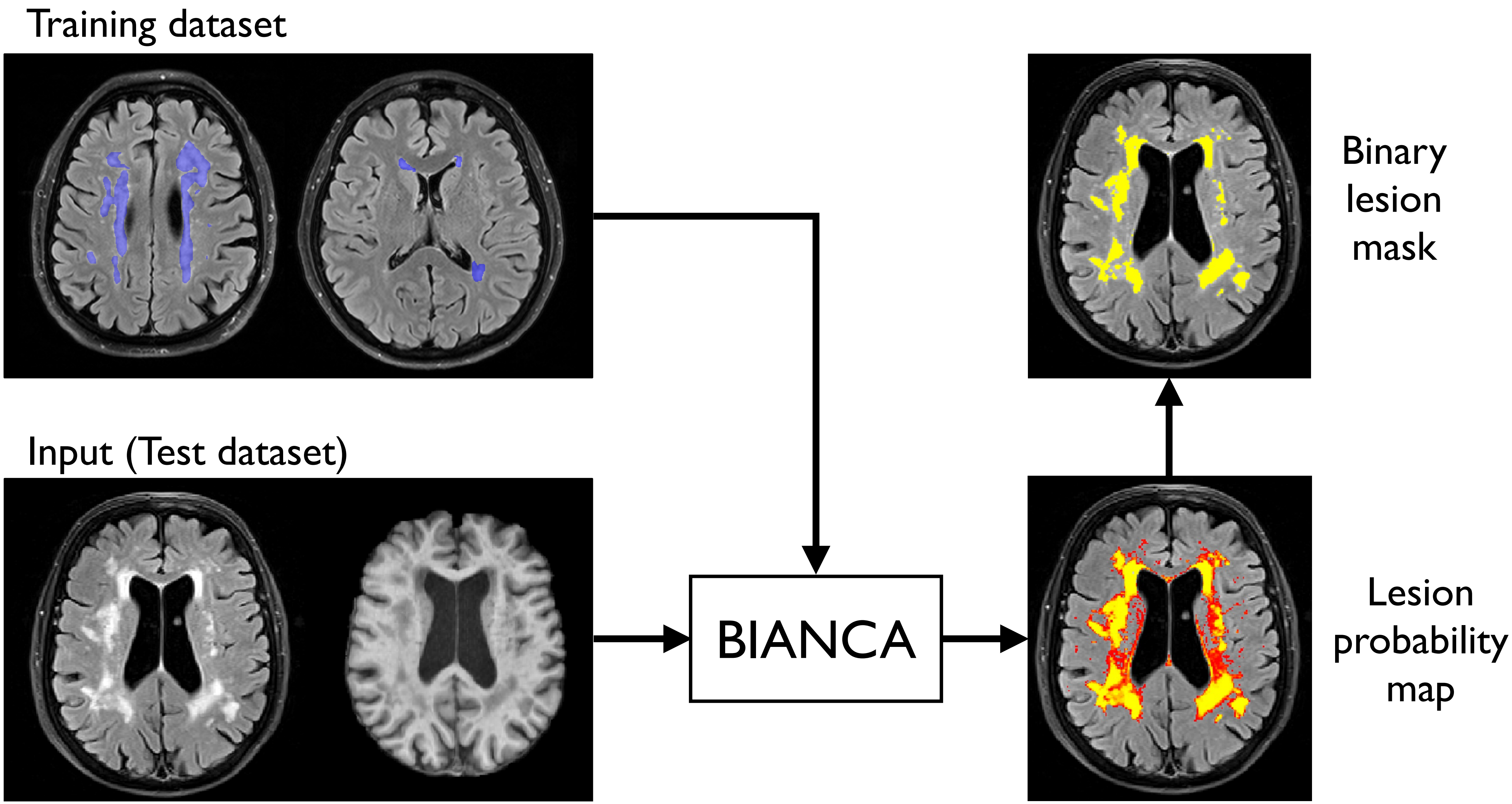
manual



automated

Lesion/WMH Segmentation

Brain Intensity AbNormalities Classification Algorithm (BIANCA)



Training dataset

Input (Test dataset)

BIANCA

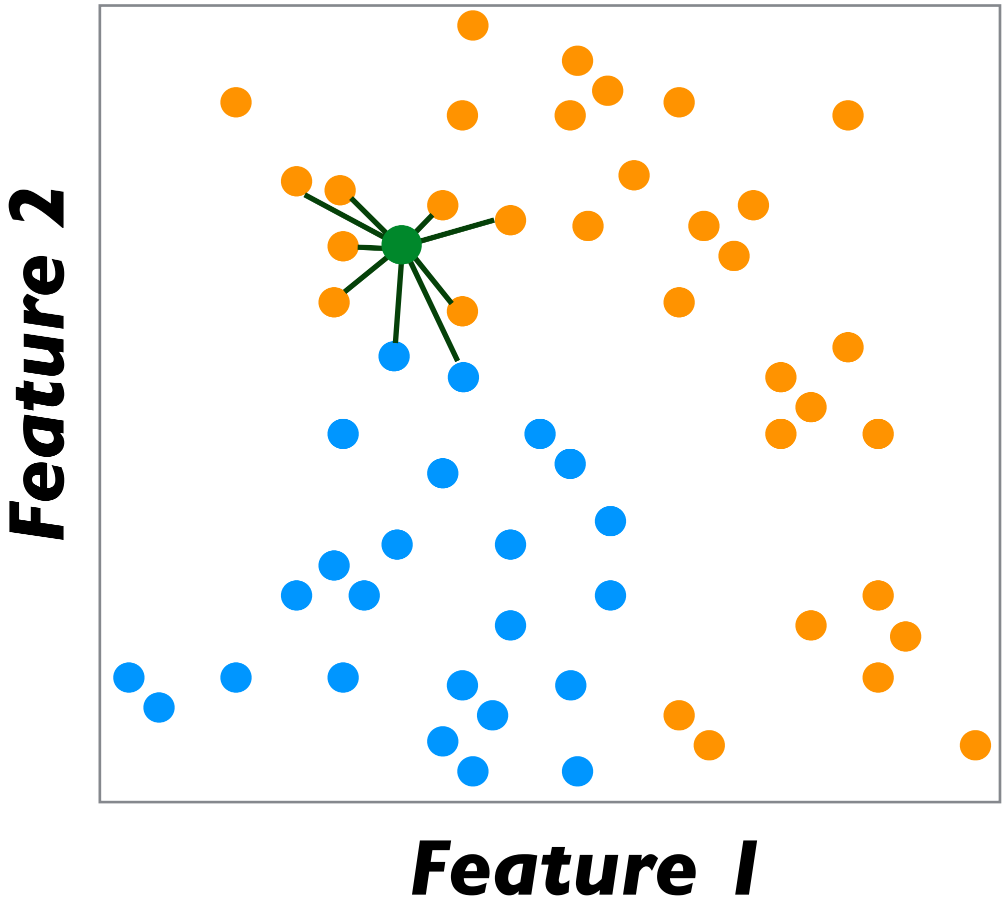
Lesion probability map

Binary lesion mask

Griffanti, et al., NeuroImage 2016

Methodology

- kNN method
  - Anbeek et al, 2004, 2008
  - Steenwijk et al, 2013
- Each point is from one voxel in a training image (labelled lesion or non-lesion)
- Data at each point comprises intensities, coordinates, local averages, etc. (***features***)

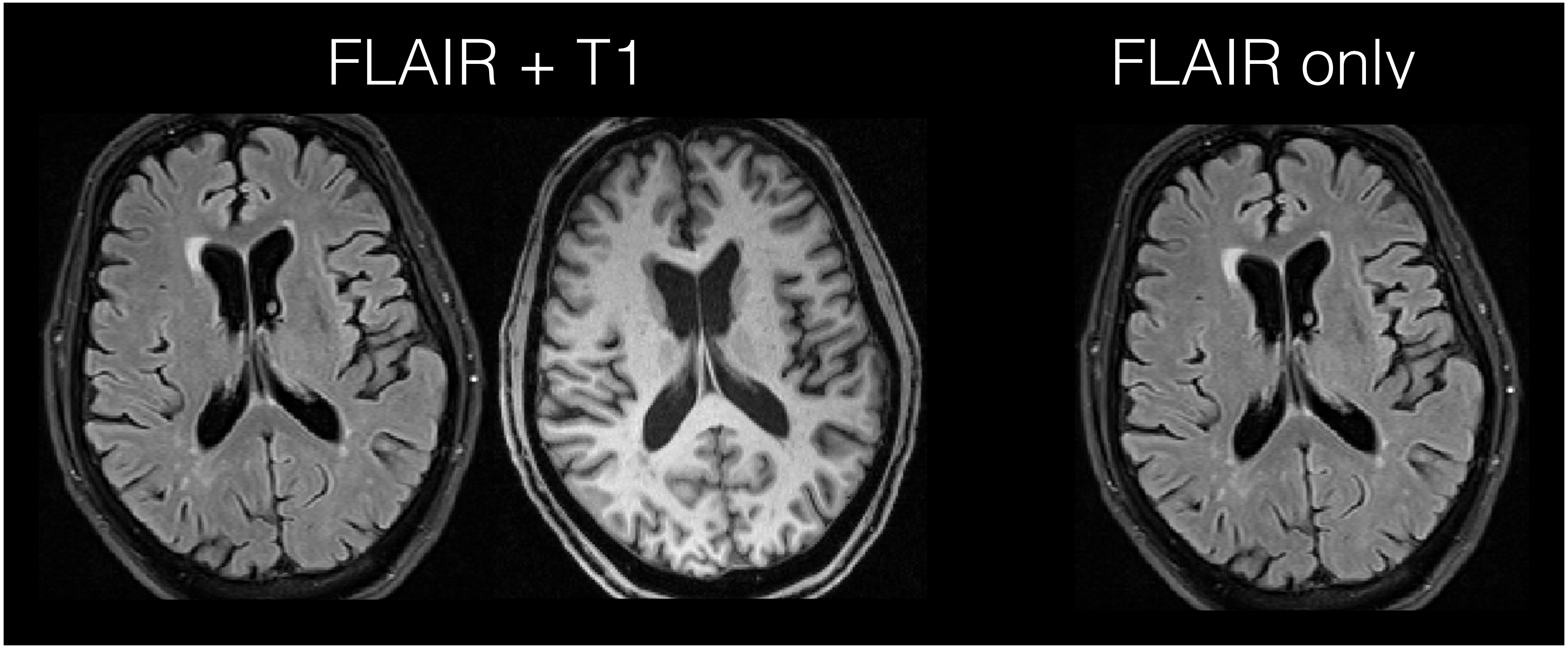


k=9; p(lesion)=7/9=0.78

- New data point: kNN picks k nearest neighbours for a voxel of interest and calculates the ratio between those labelled as lesion and non-lesion ➜ **probability** of being lesion

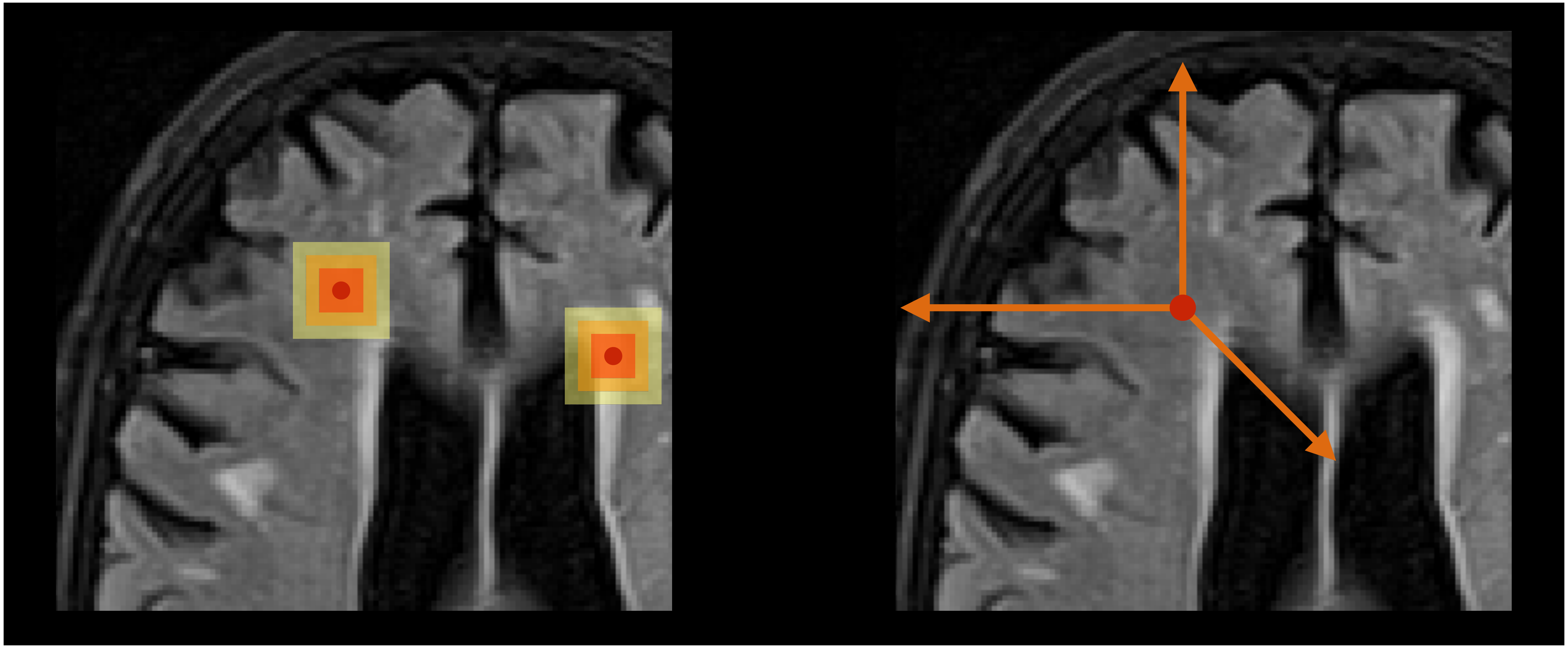
Methodology - options

- Many options exist:
    - **modalities** (e.g. FLAIR, T2w, T1w)



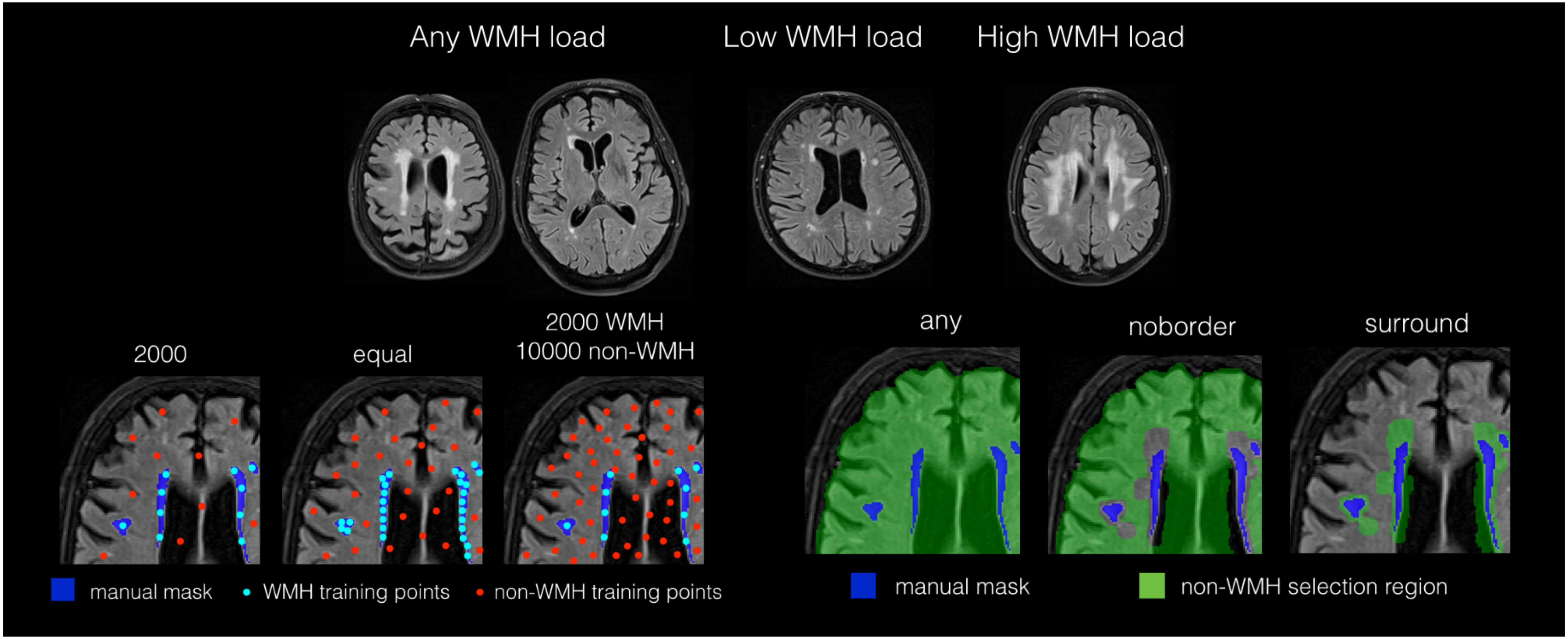
Methodology - options

- Many options exist:
  - modalities (e.g. FLAIR, T2w, T1w)
  - **features** (e.g. local averages, MNI coordinates)



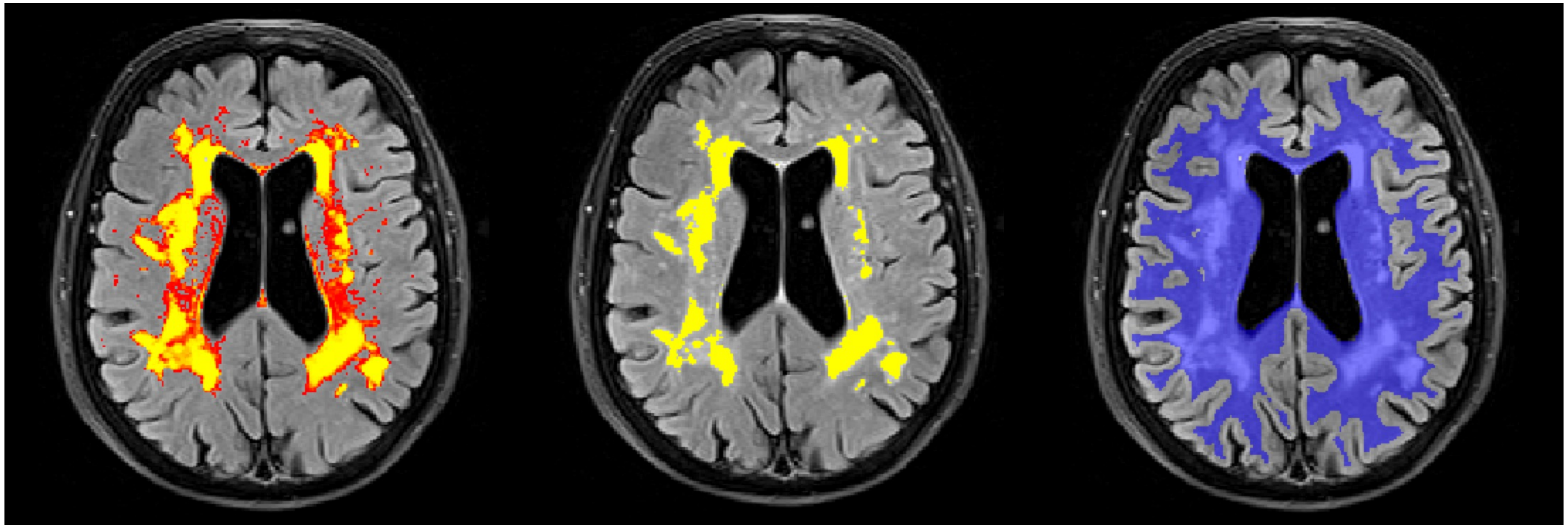
Methodology - options

- Many options exist:
  - modalities (e.g. FLAIR, T2w, T1w)
  - features (e.g. local averages, MNI coordinates)
  - **training** (e.g. type of scans, no. voxels, locations sampled)

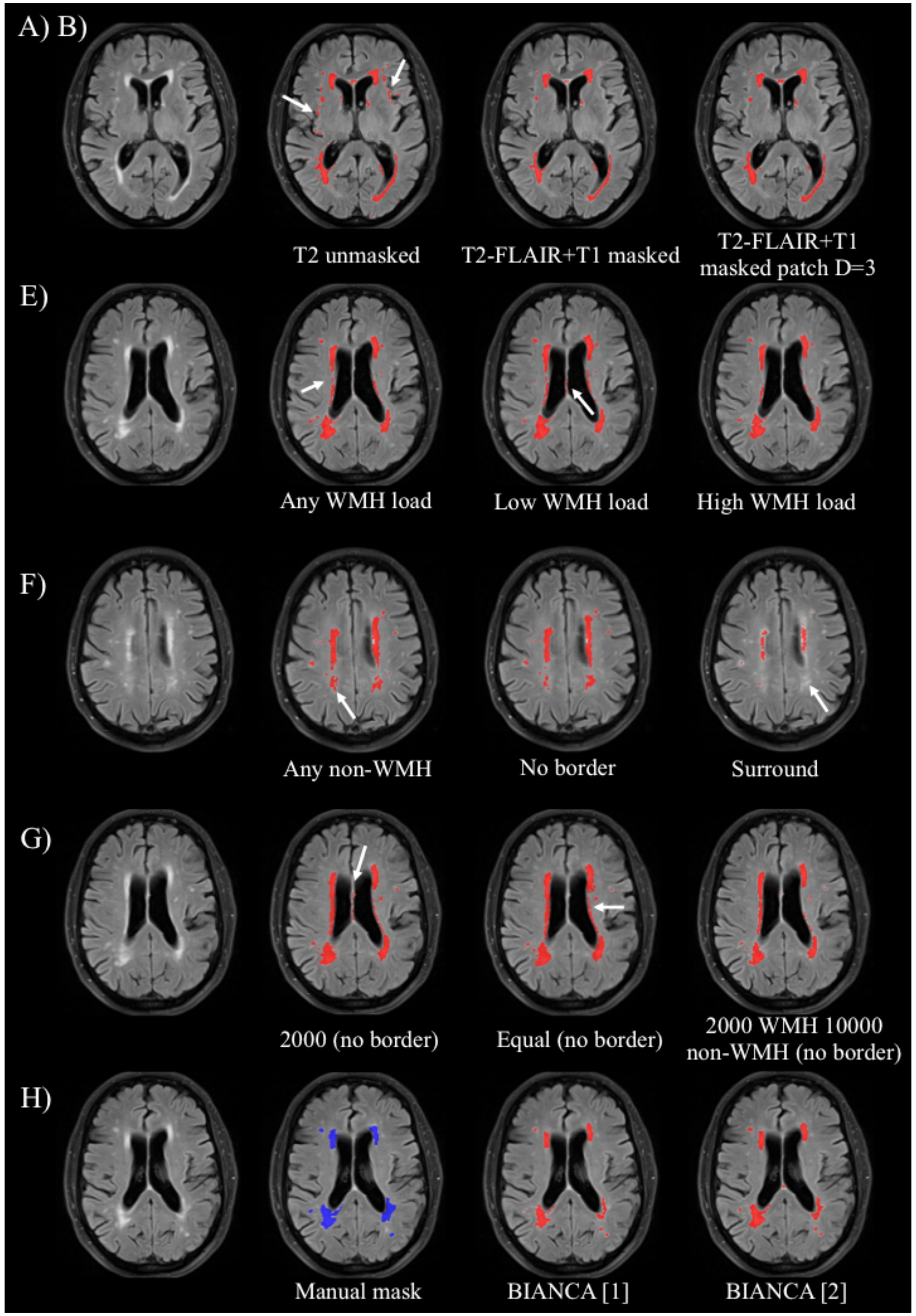


Methodology - options

- Many options exist:
  - modalities (e.g. FLAIR, T2w, T1w)
  - features (e.g. local averages, MNI coordinates)
  - training (e.g. type of scans, no. voxels, locations sampled)
  - **post-processing** (Thresholding and Masking: cerebellum, thalamus, inferior deep GM and cortex masked out)

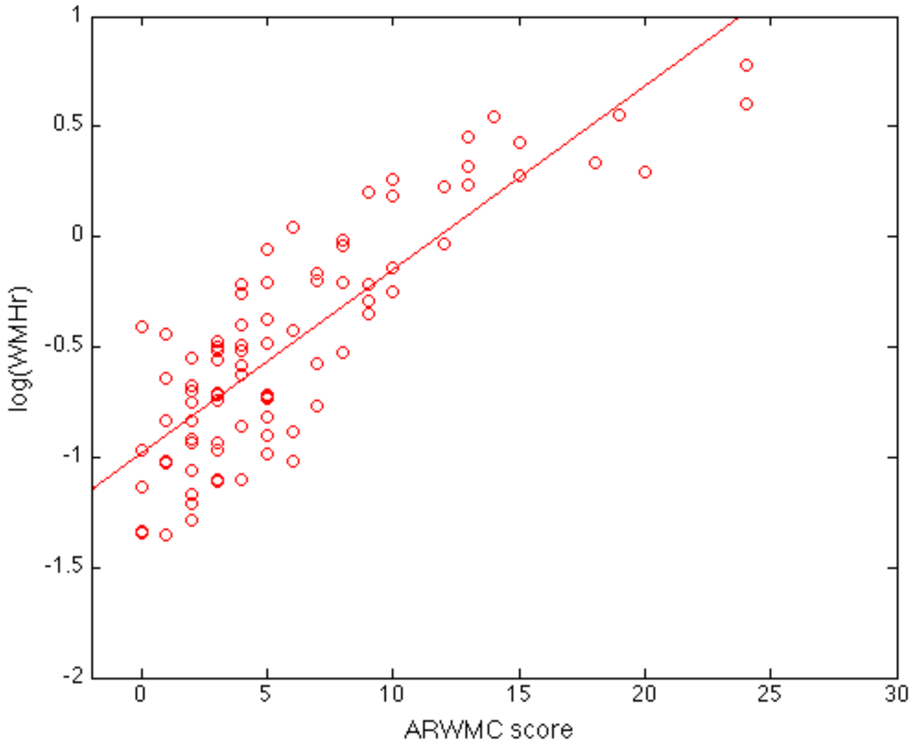


Performance evaluation

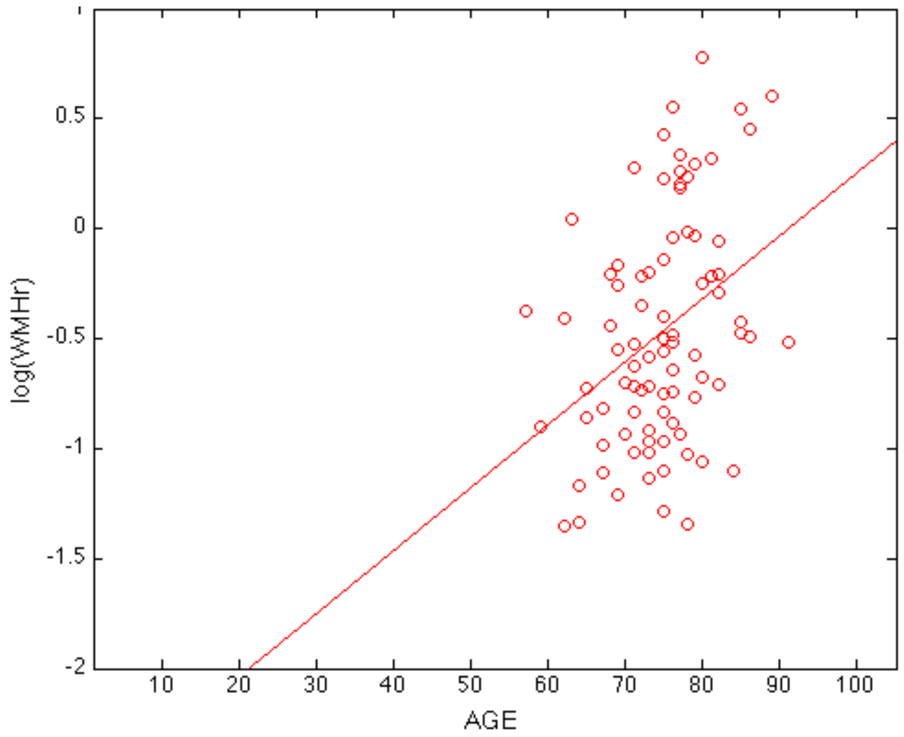


Algorithm optimisation SI = 0.76 ICC = 0.99

Correlation with visual ratings



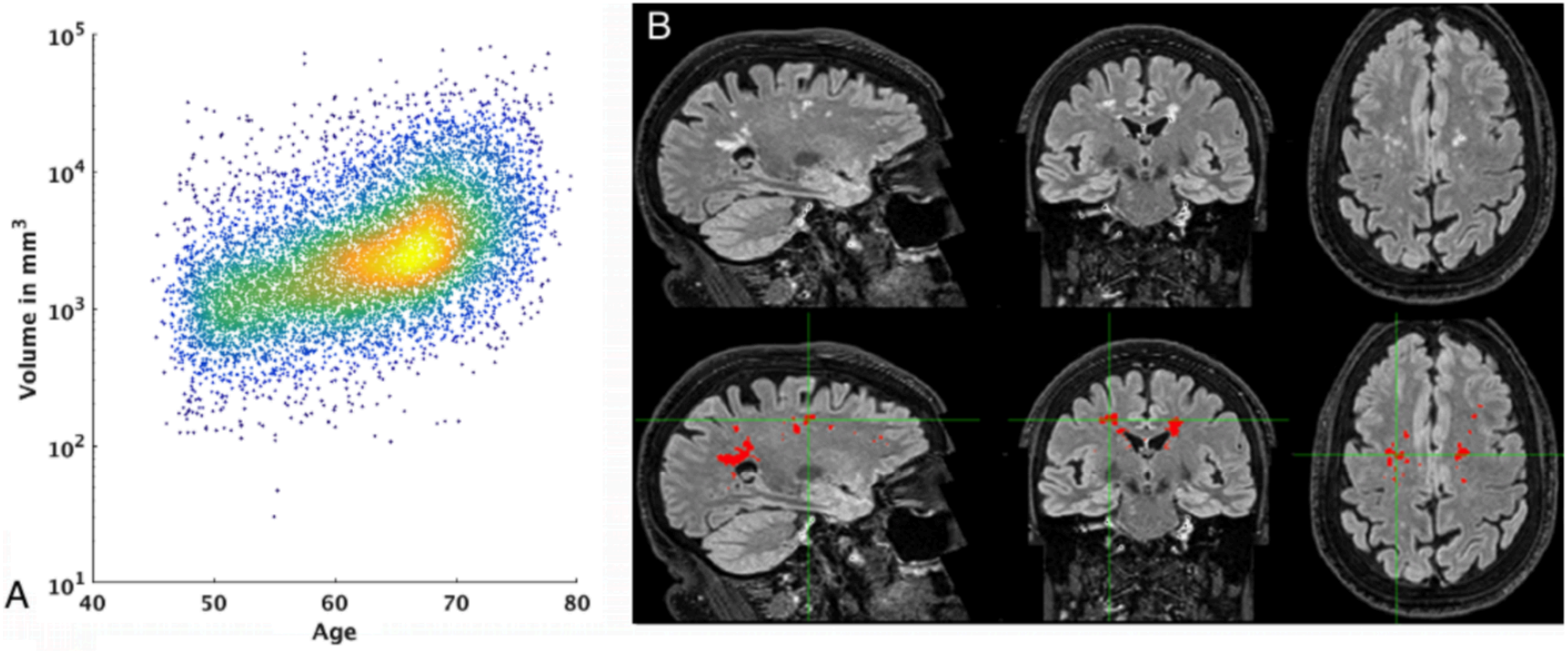
Correlation with age



Griffanti, et al., NeuroImage 2016

Applications

UK Biobank - 10,000 subjects



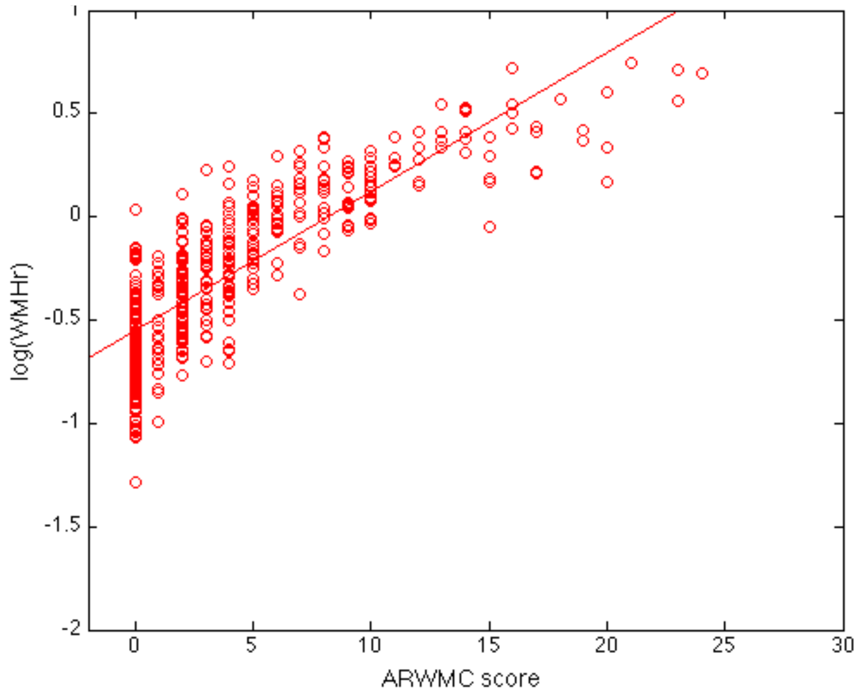
Significant correlations with:

- systolic blood pressure ($r=0.13, p<10^{-20}$)
- diastolic blood pressure ($r=0.11, p<10^{-15}$)

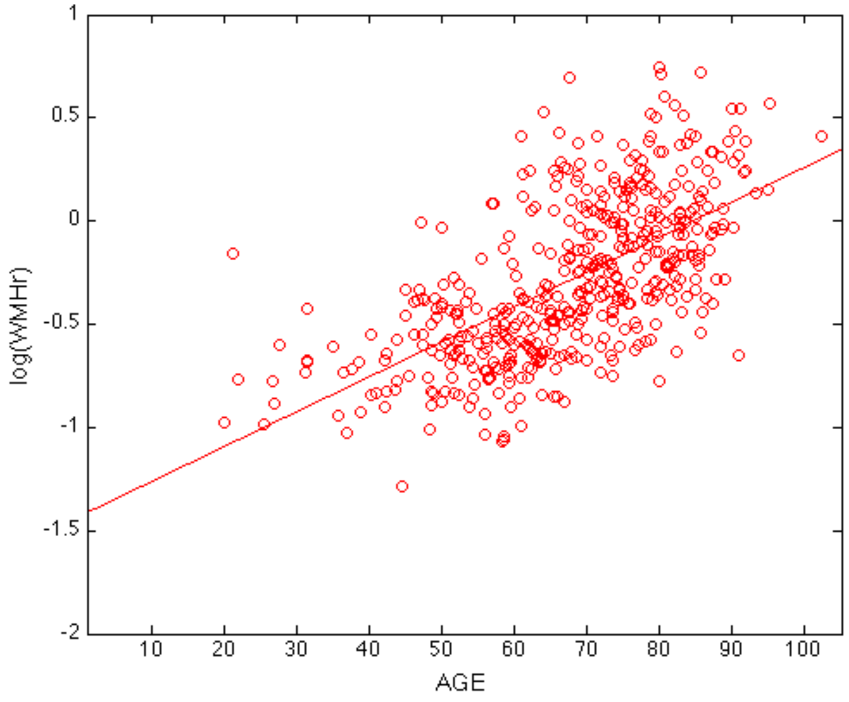
Alfaro-Almagro, et al., NeuroImage 2017

Applications

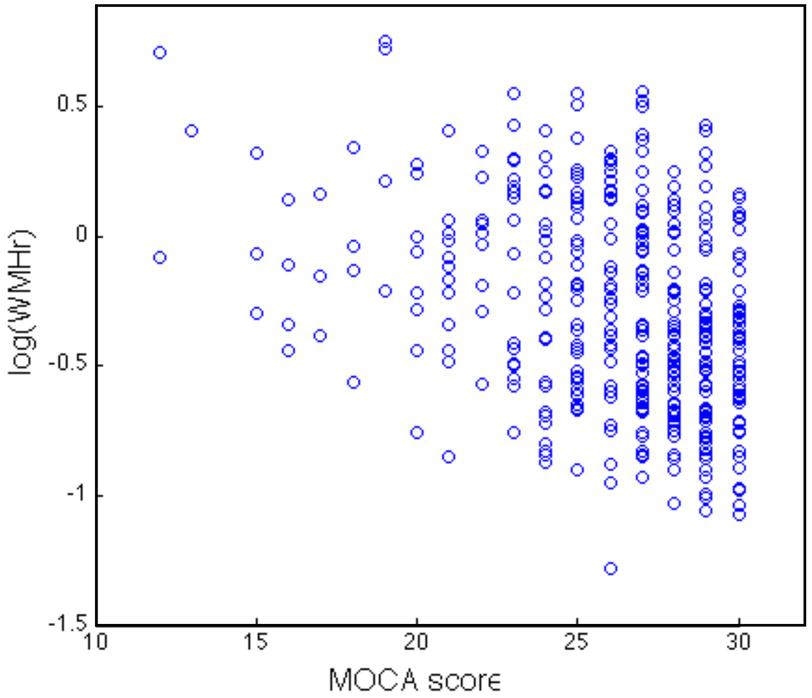
Correlation with visual ratings



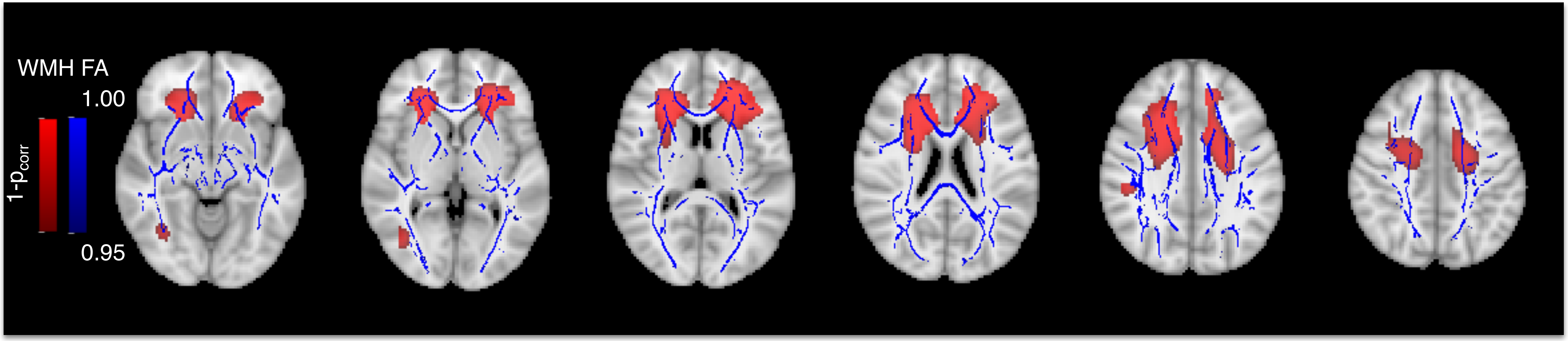
Correlation with age



Correlation with cognitive score



VOXEL-WISE ANALYSIS



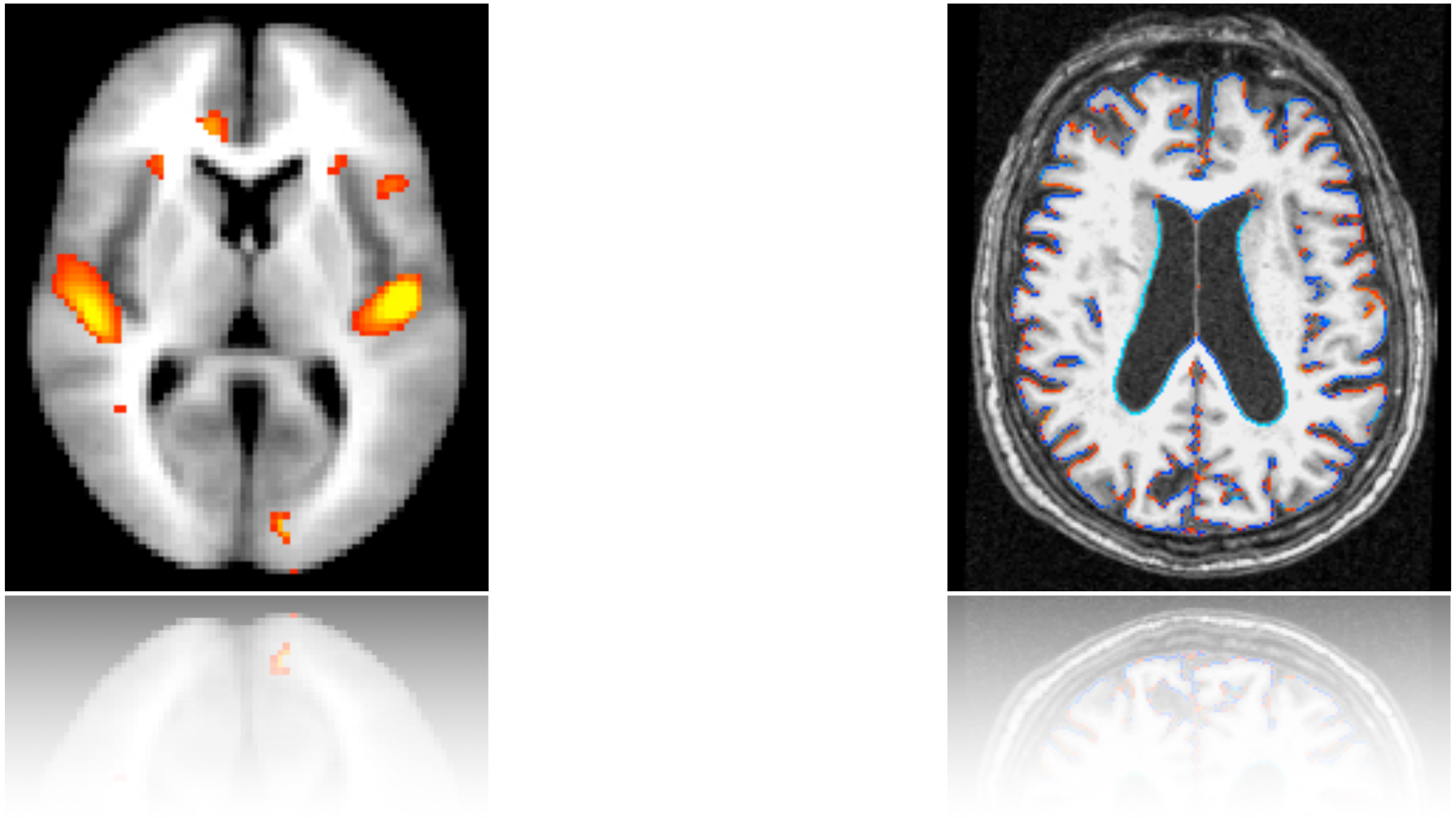
Vascular cohort - Higher WMH and lower FA in subjects with cognitive impairment (CI) according to both MMSE and MoCA vs subjects with no CI.

Zamboni, et al., Stroke 2017

Structural Analysis

FSL-VBM voxelwise grey-matter density analysis

SIENA/SIENAX global atrophy estimation

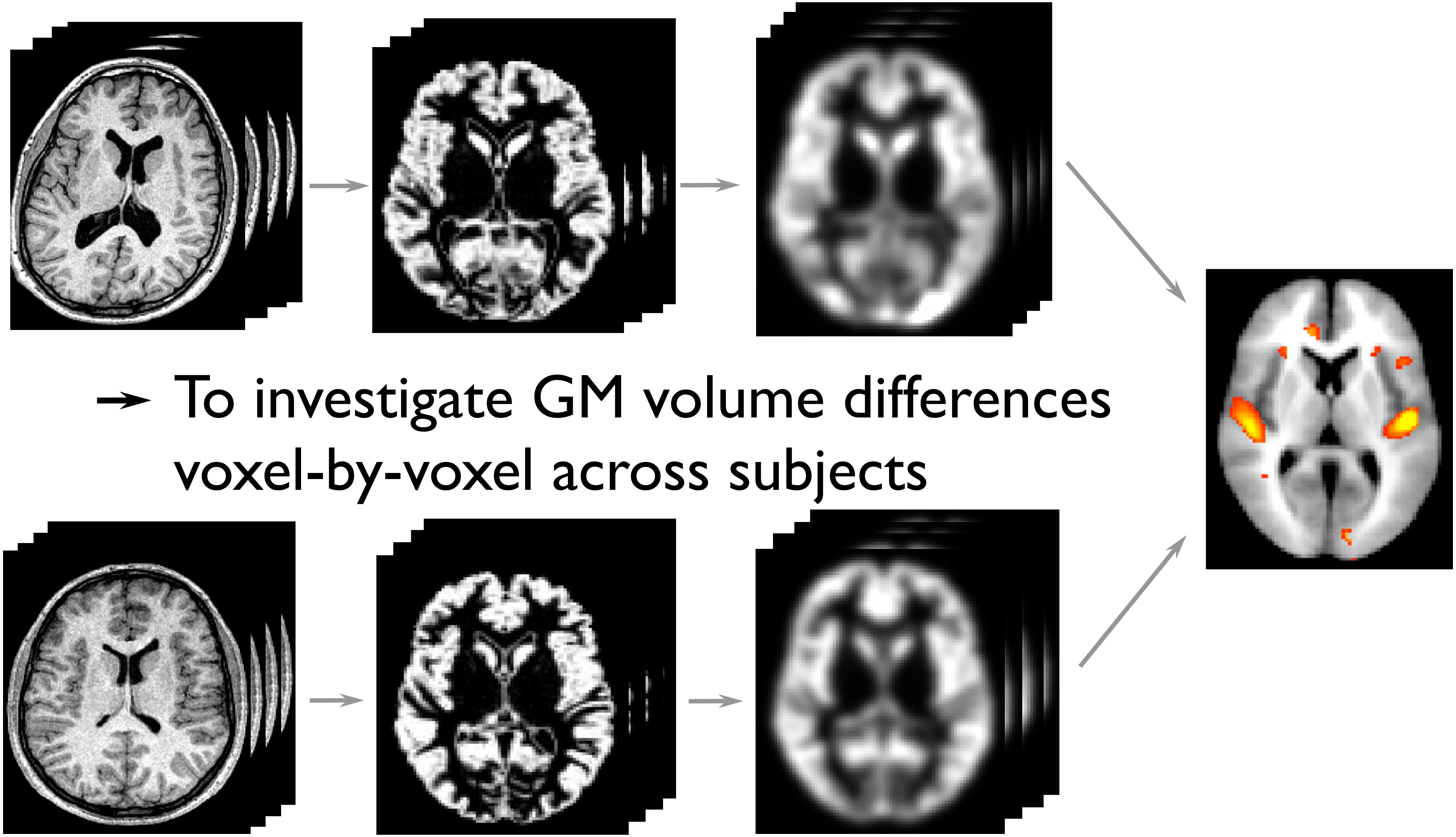


Multiple- and single-timepoint analysis of brain change

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

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
  ⇒ segmentation + 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

X patients

X controls

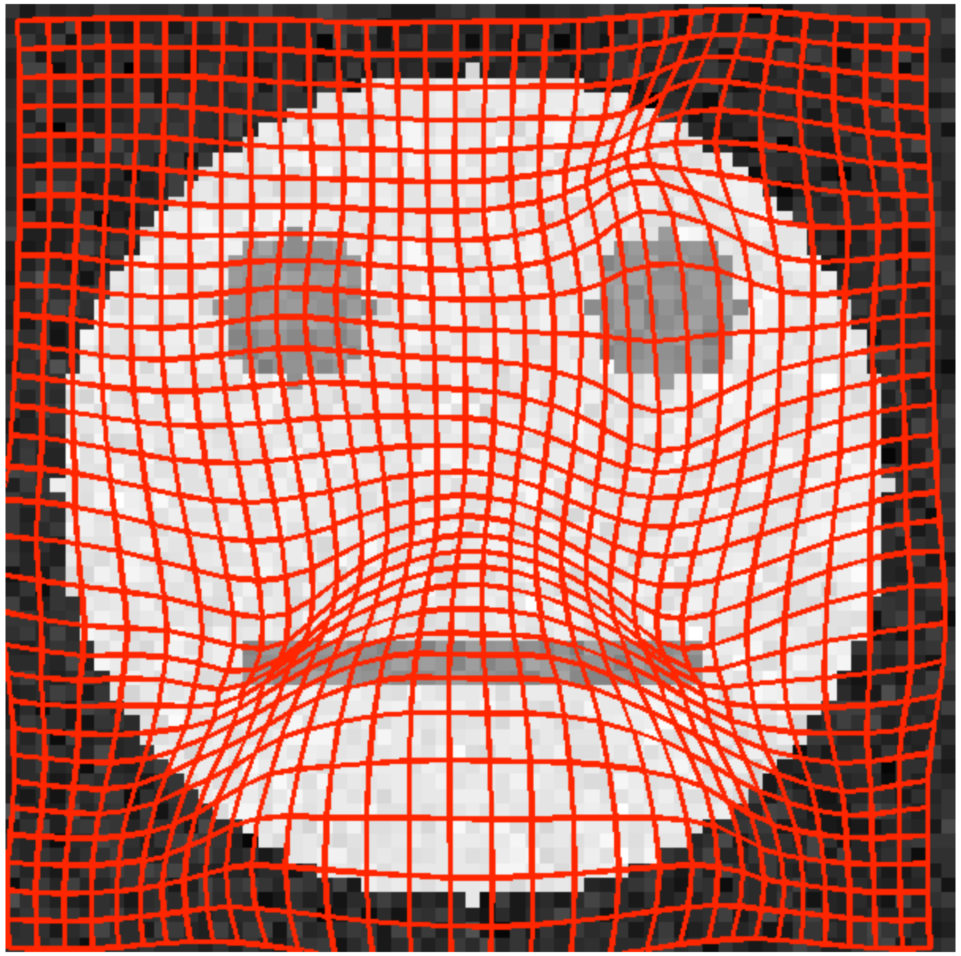
Want equal numbers of patients and controls

Voxel-based analysis of local GM volume

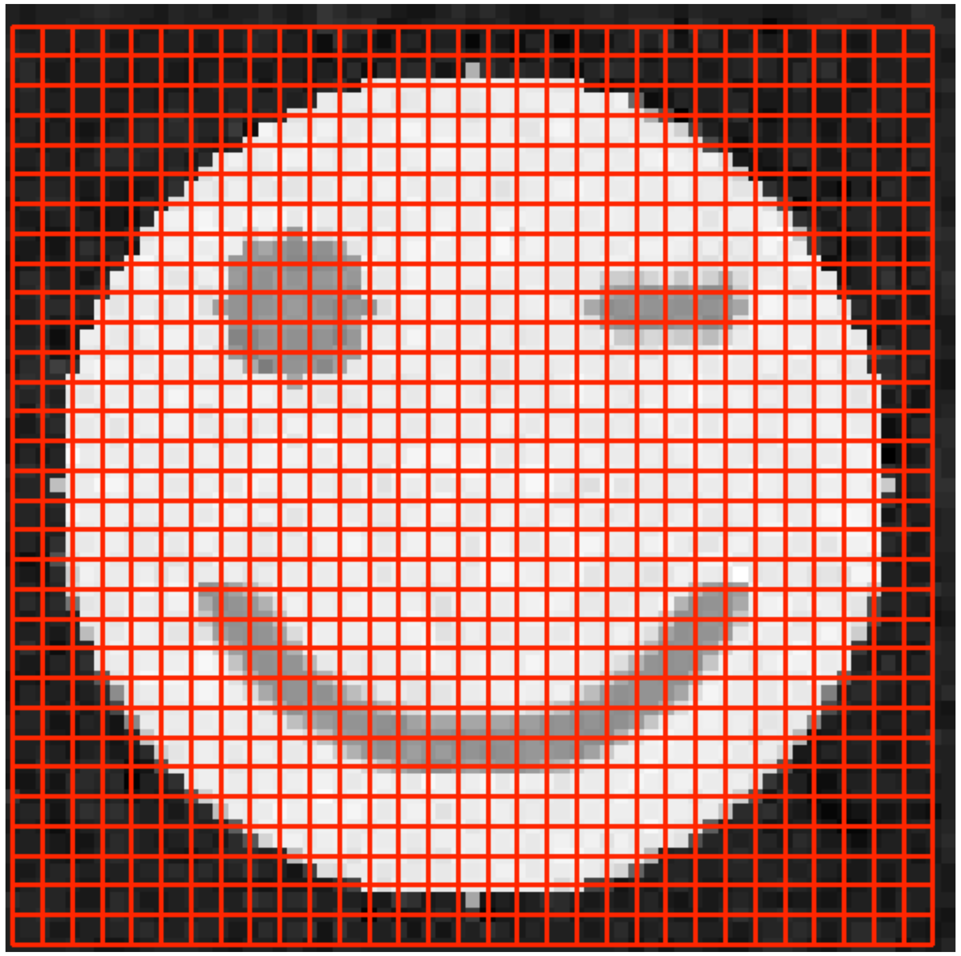
- Optimised protocol (Good et al., 2001)

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

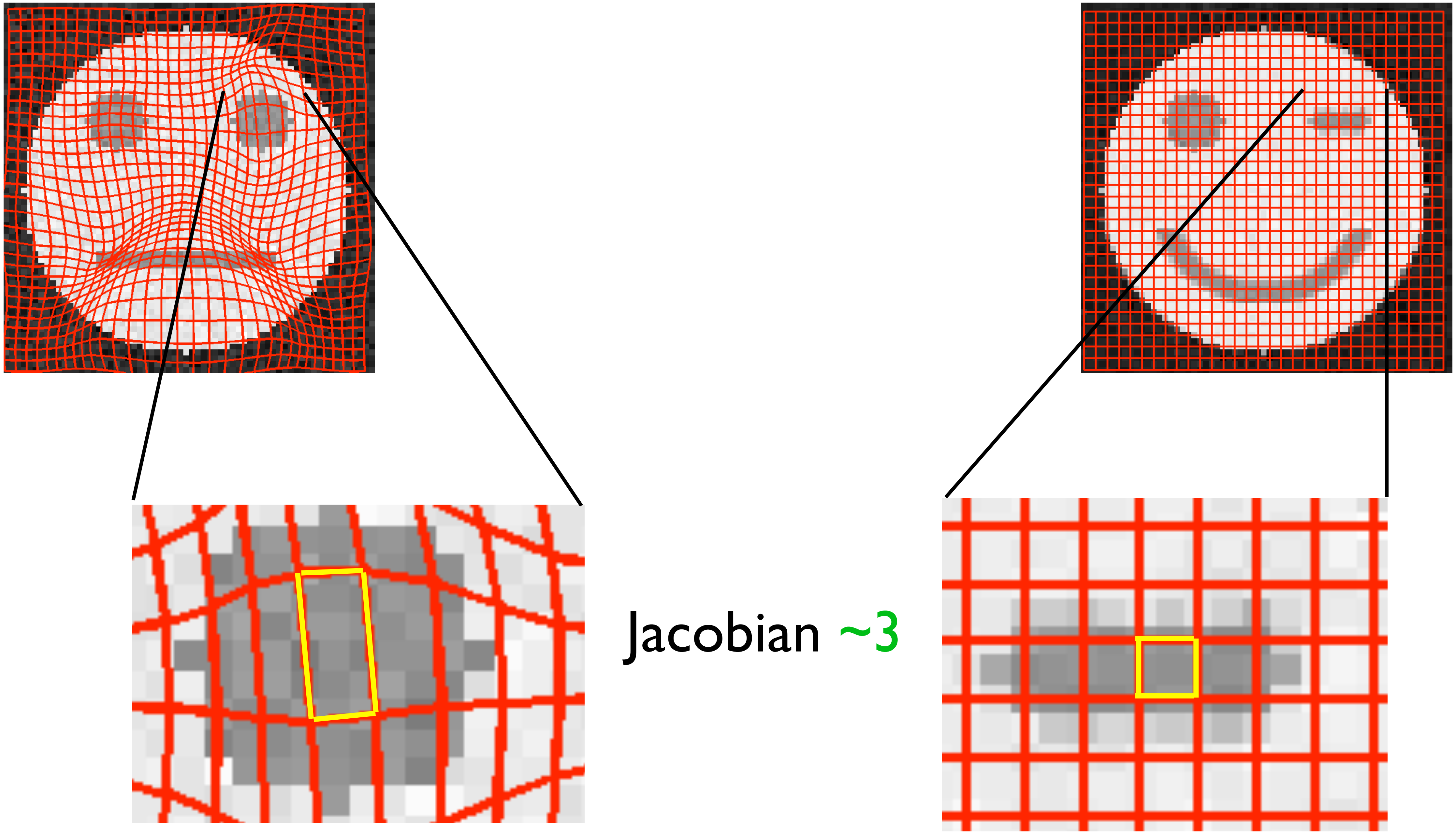
Jacobian modulation



Jacobian modulation



Jacobian modulation

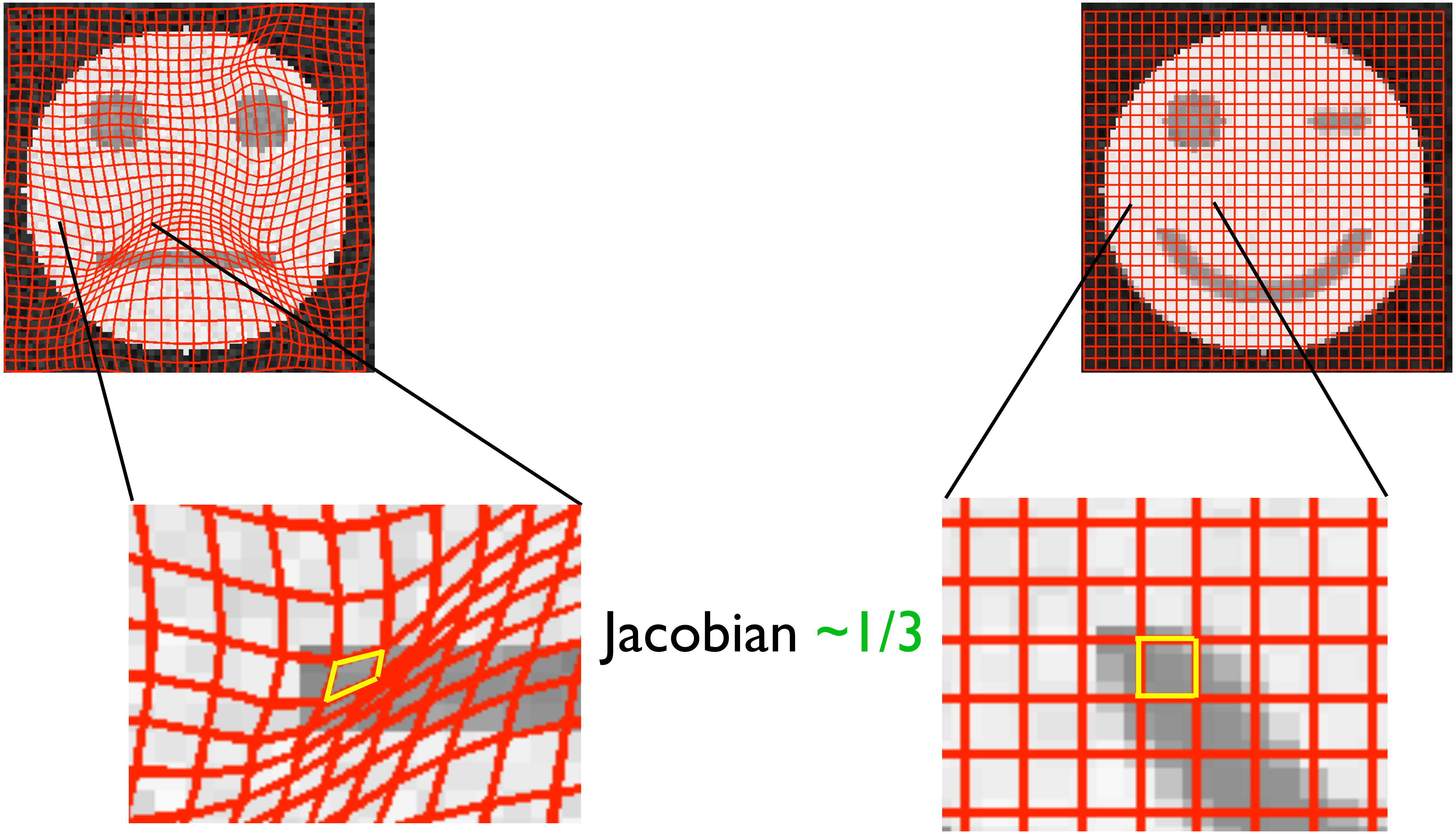


Jacobian ~3

~3mm^2 in original space

1mm^2 in warped space

Jacobian modulation

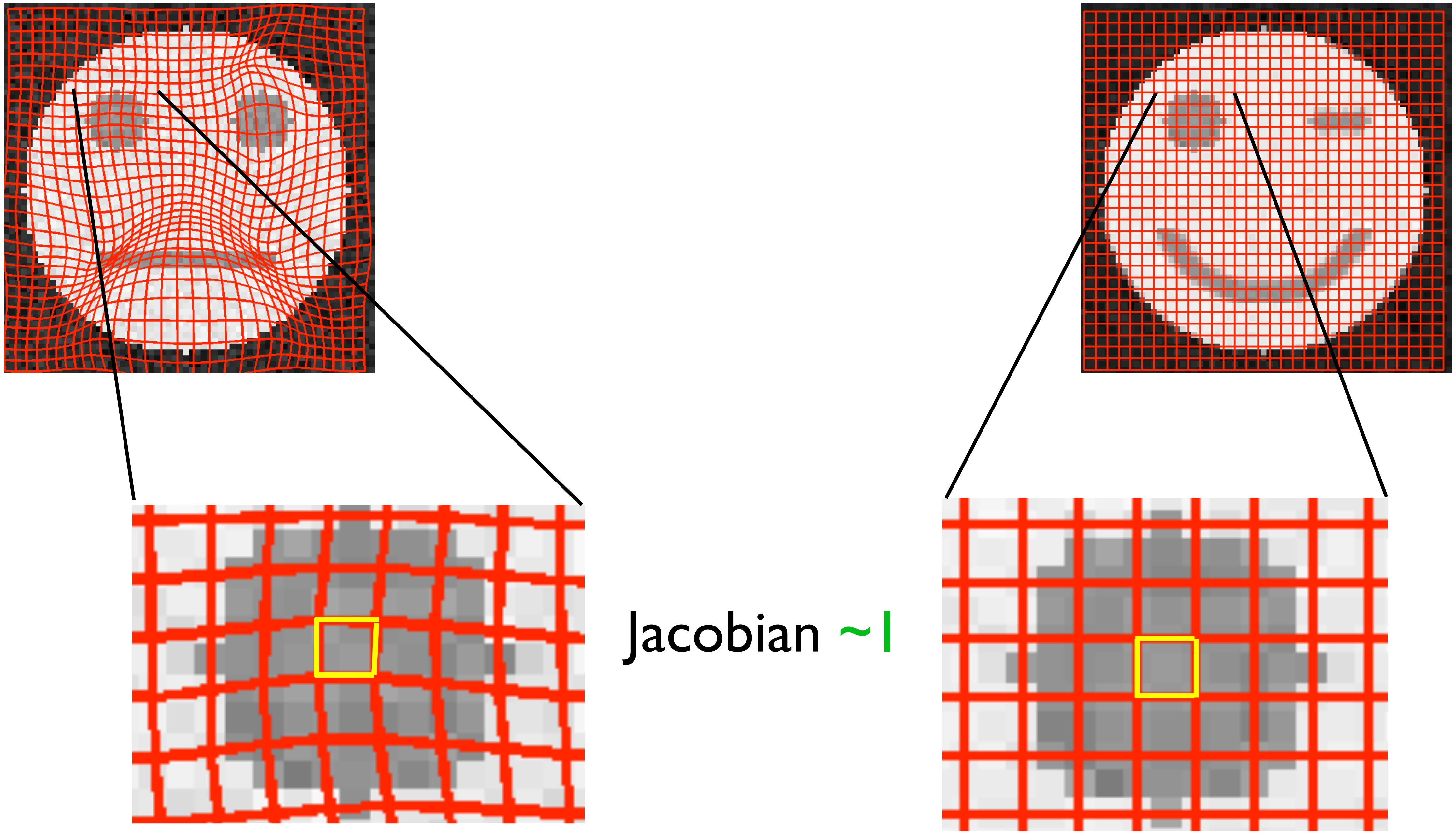


Jacobian ~1/3

~1/3mm^2 in original space

1mm^2 in warped space

Jacobian modulation

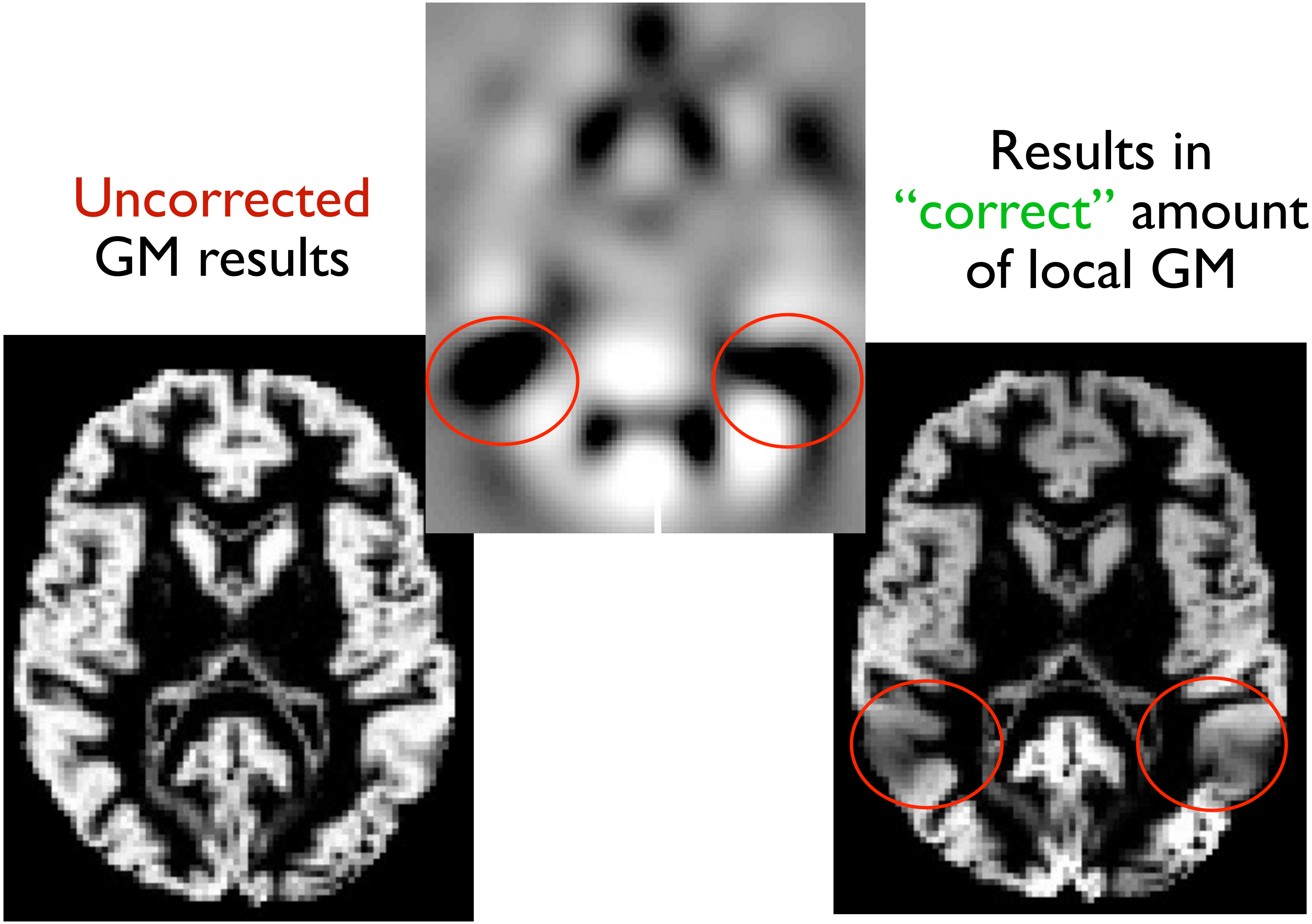


Jacobian ~1

~1mm^2 in original space

1mm^2 in warped space

Voxel-based analysis of local GM volume



Jacobian map: correction for local expansion/contraction

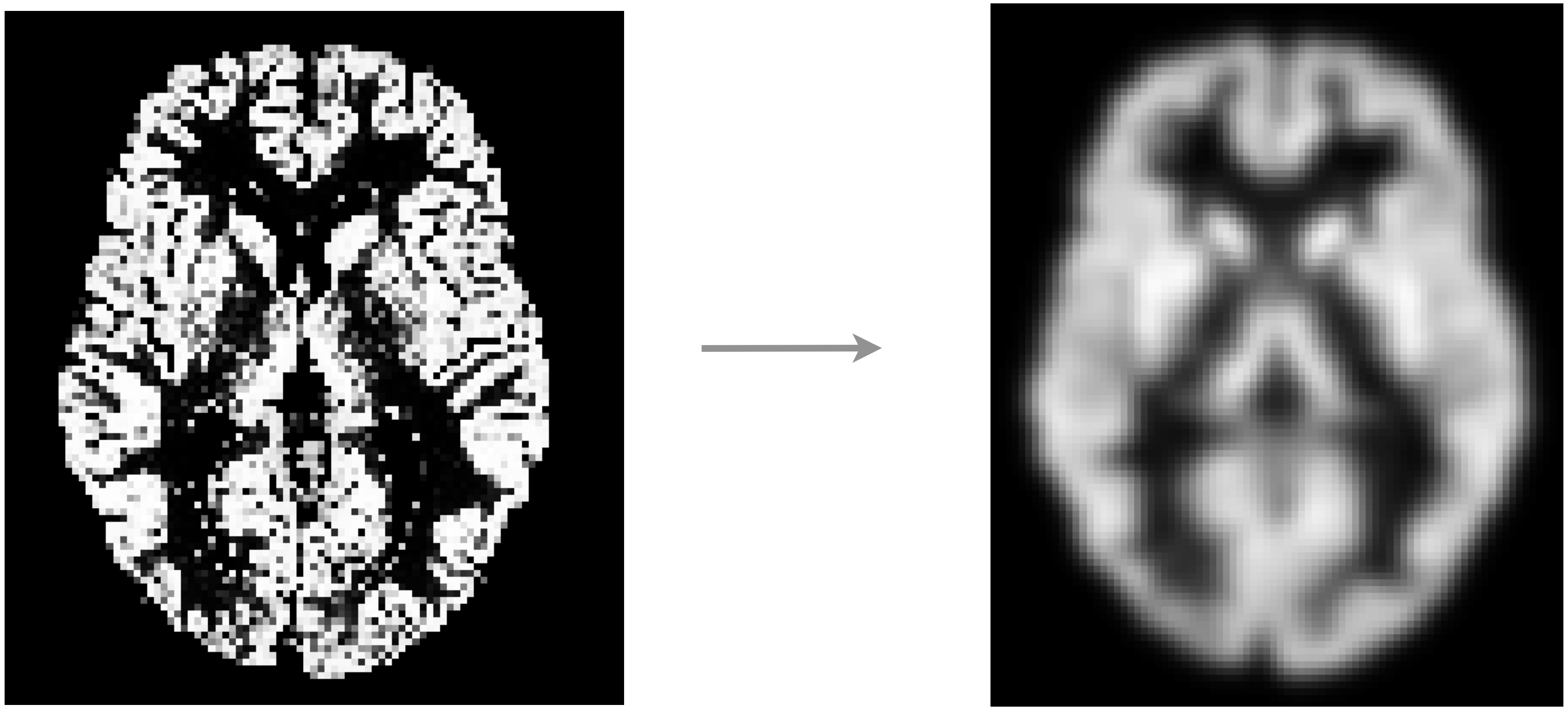
Uncorrected GM results

Results in "correct" amount of local GM

Voxel-based analysis of local GM volume

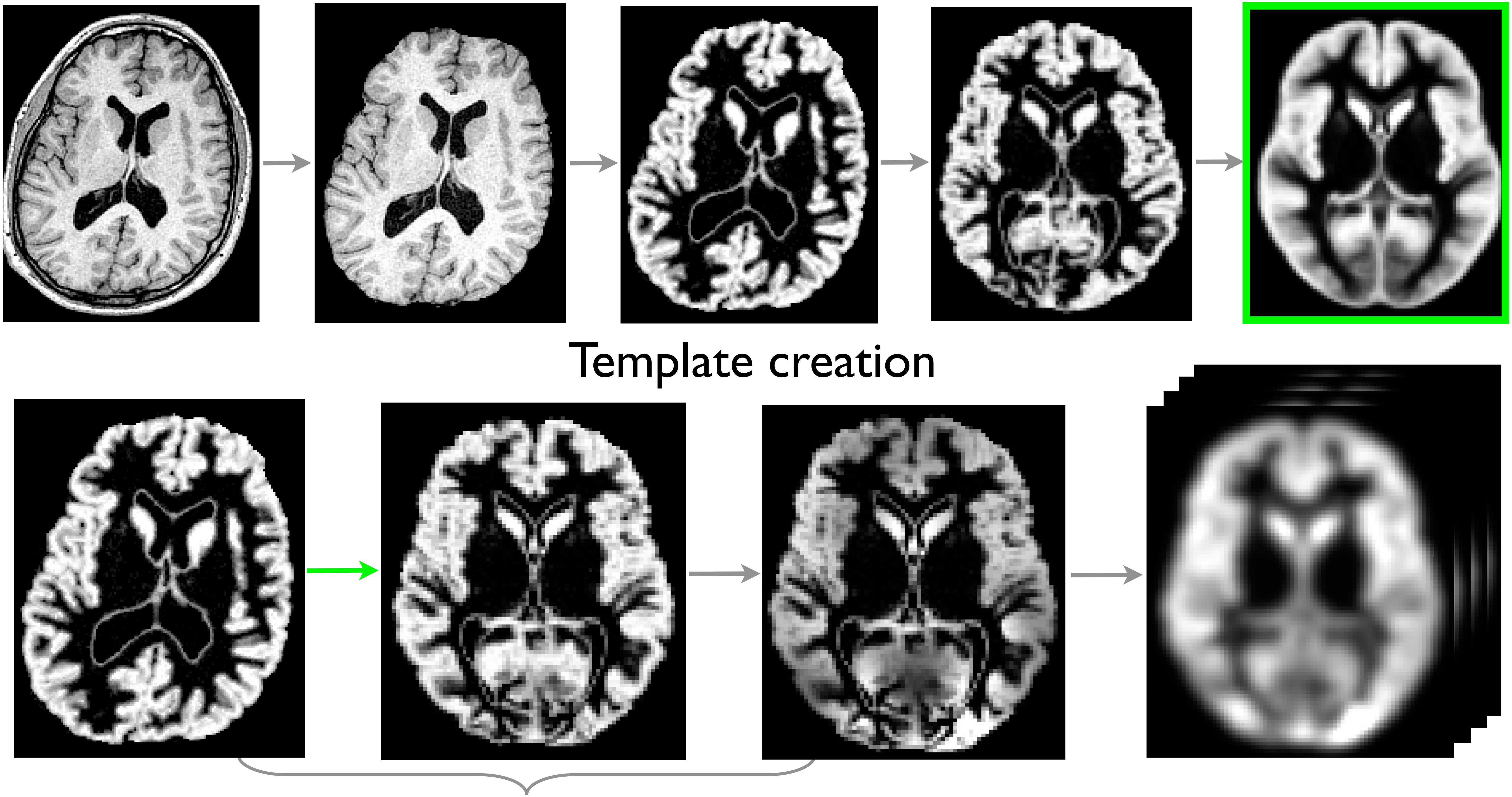
- Optimised protocol (Good et al., 2001)

4) Smooth with a Gaussian filter



Voxel-based analysis of local GM volume

- Optimised protocol (Good et al., 2001)

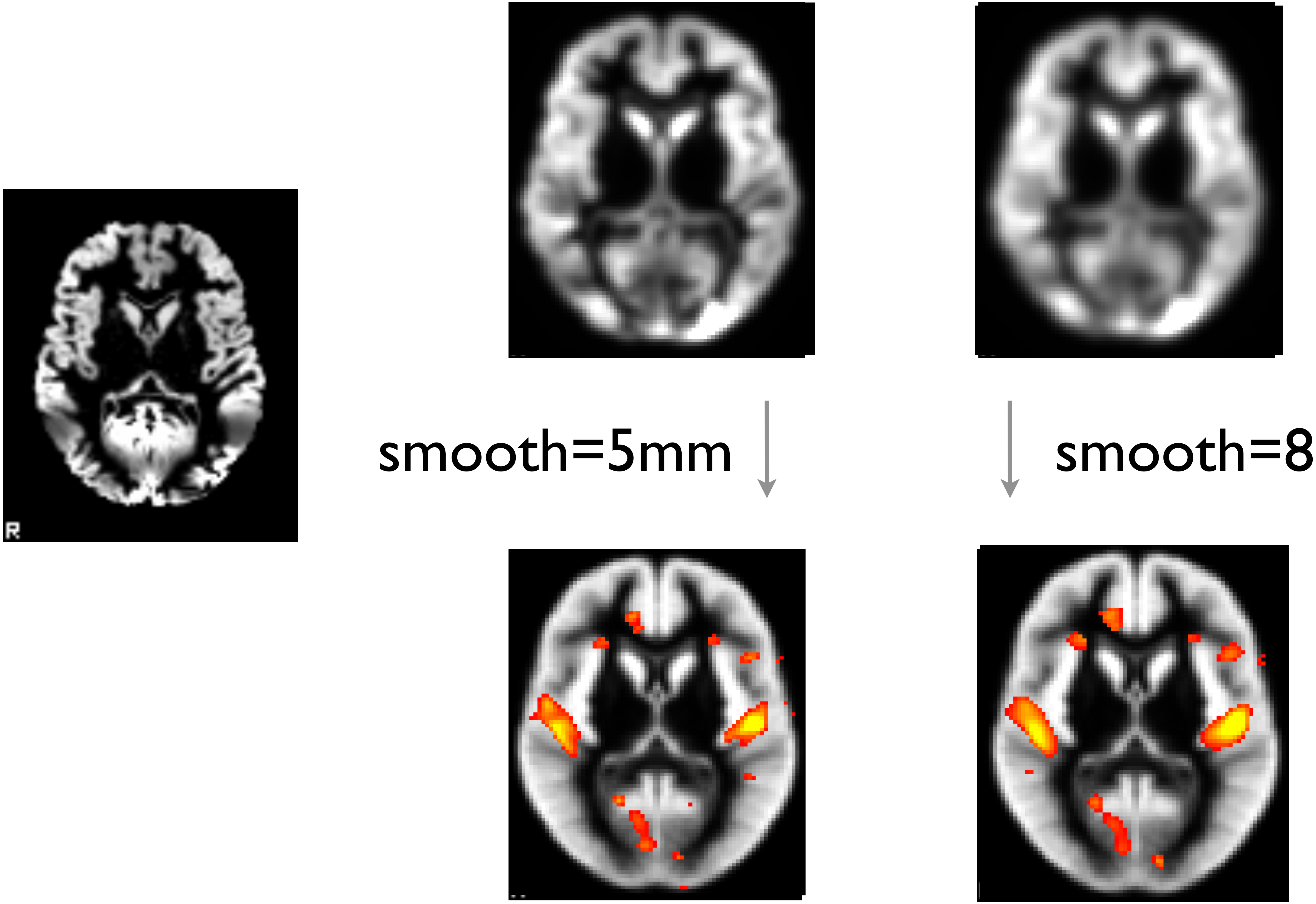


Template creation

Processing steps

Analysis

Voxel-based analysis of local GM volume



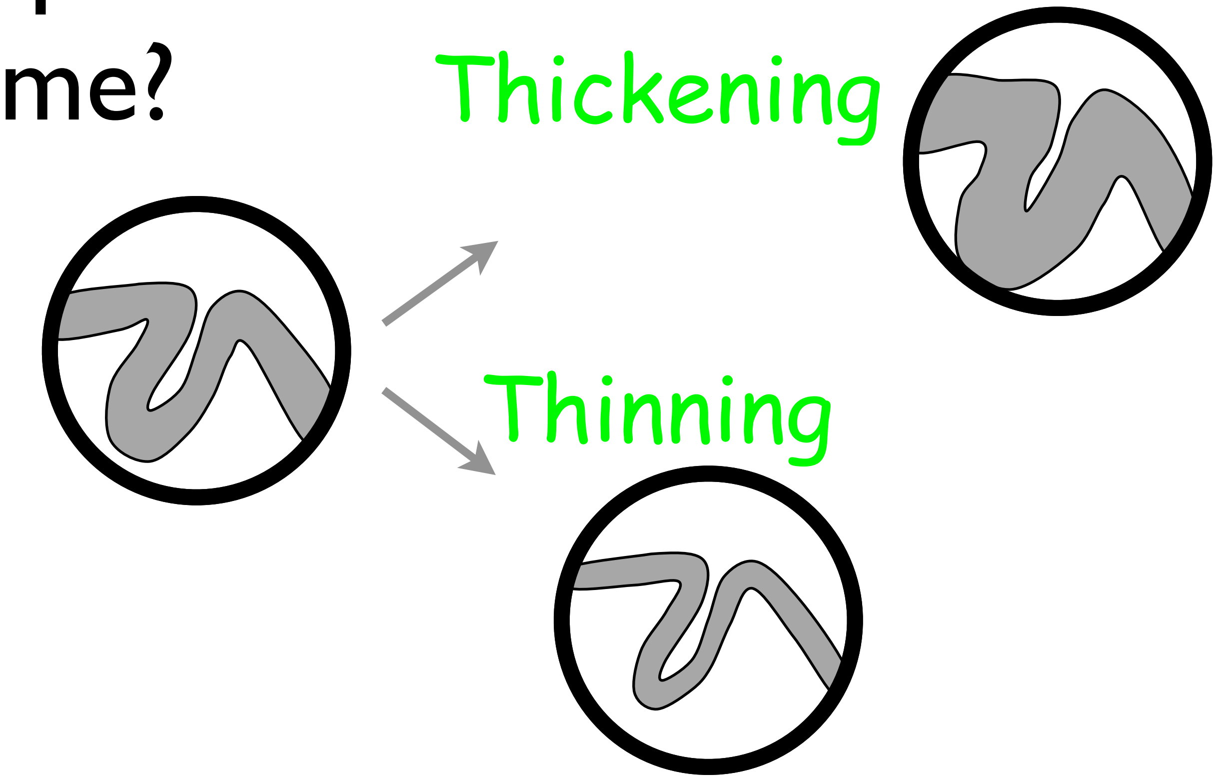
smooth=5mm

smooth=8mm

Voxel-based analysis of GM volume

- Controversial approach - back to the issues:

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

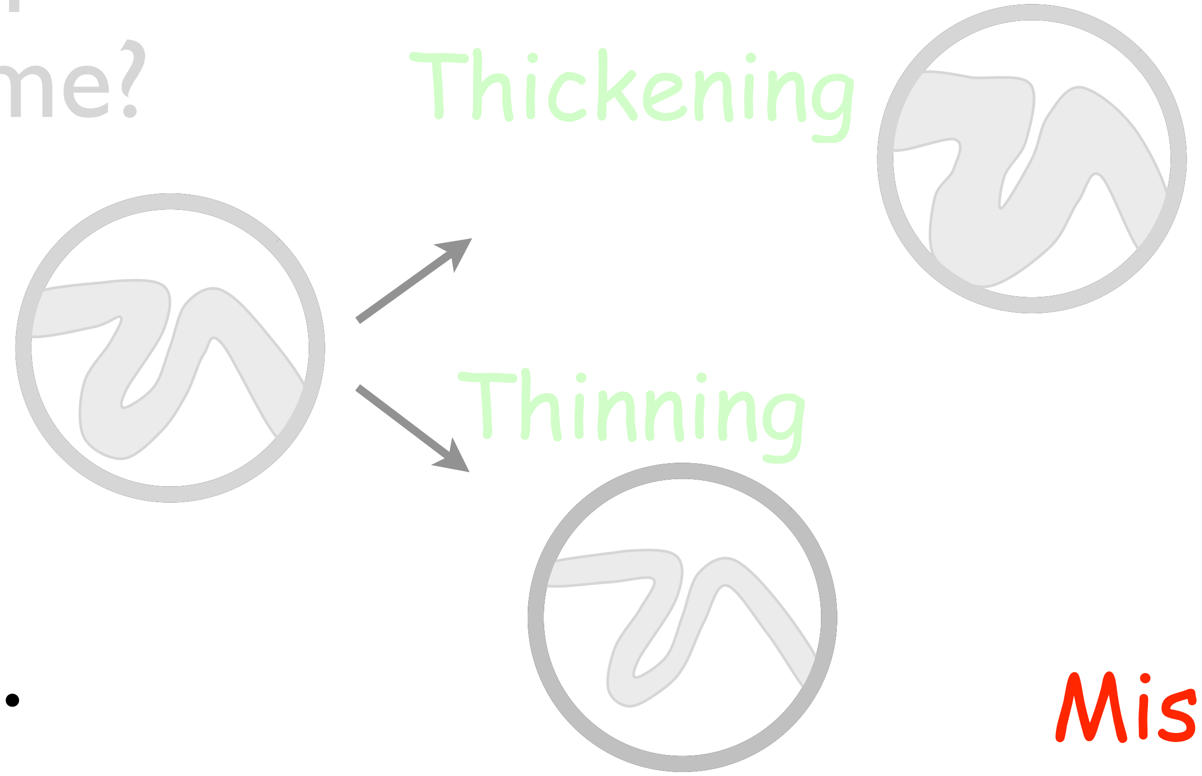


Illustrations courtesy of John Ashburner

Voxel-based analysis of GM volume

- Controversial approach - back to the issues:

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



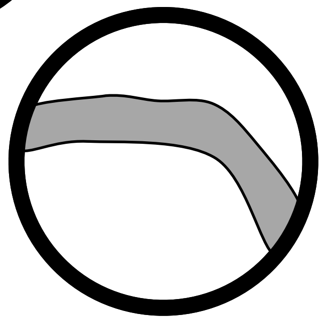
Thickening

Thinning

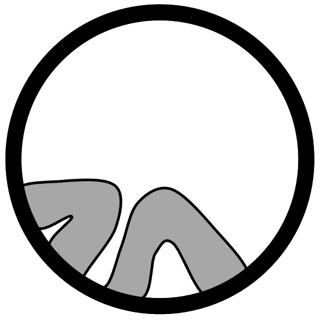
Or ...

- Difference in the contrast?
- Difference in gyrification pattern?
- Problem with registration?

Mis-classify



Folding



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?

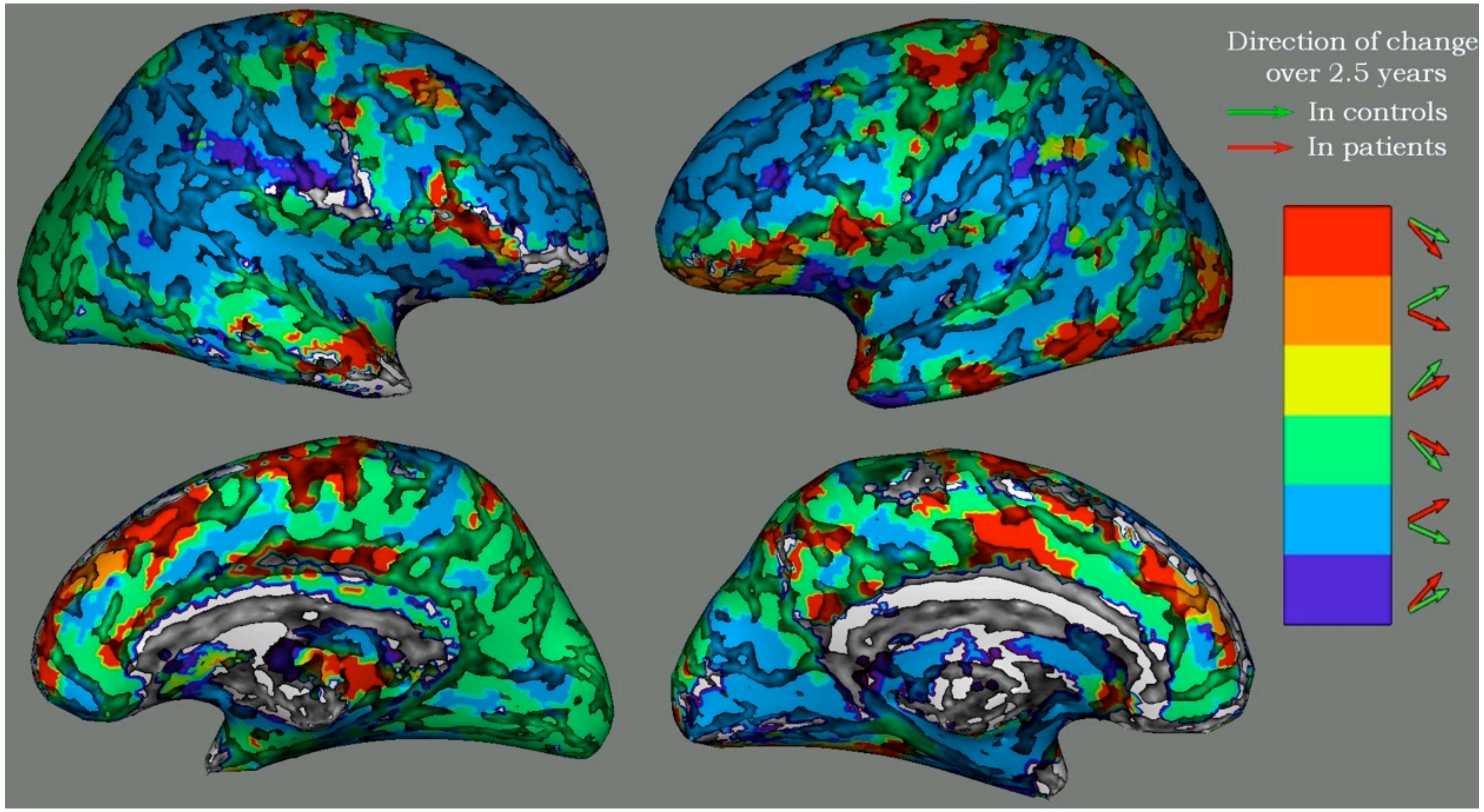
⟶ See Ridgway et al., NeuroImage 2008 for best practice

Multiple- and single-timepoint analysis of brain change

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

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

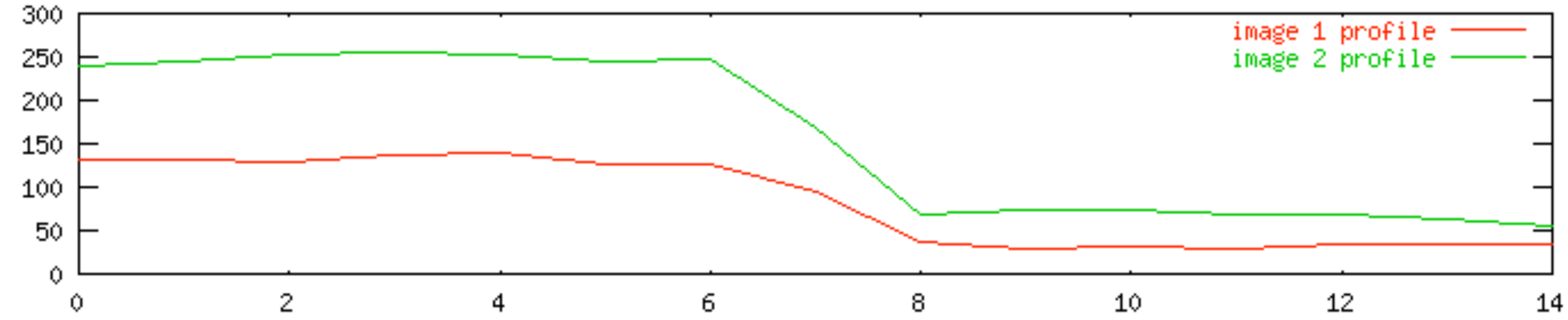
SIENA

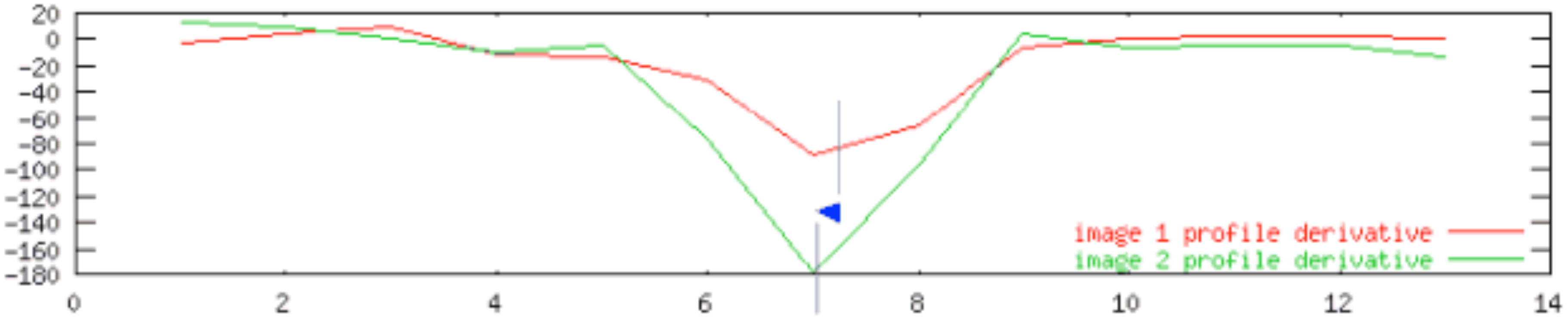
Structural Image Evaluation (with Normalisation) of Atrophy

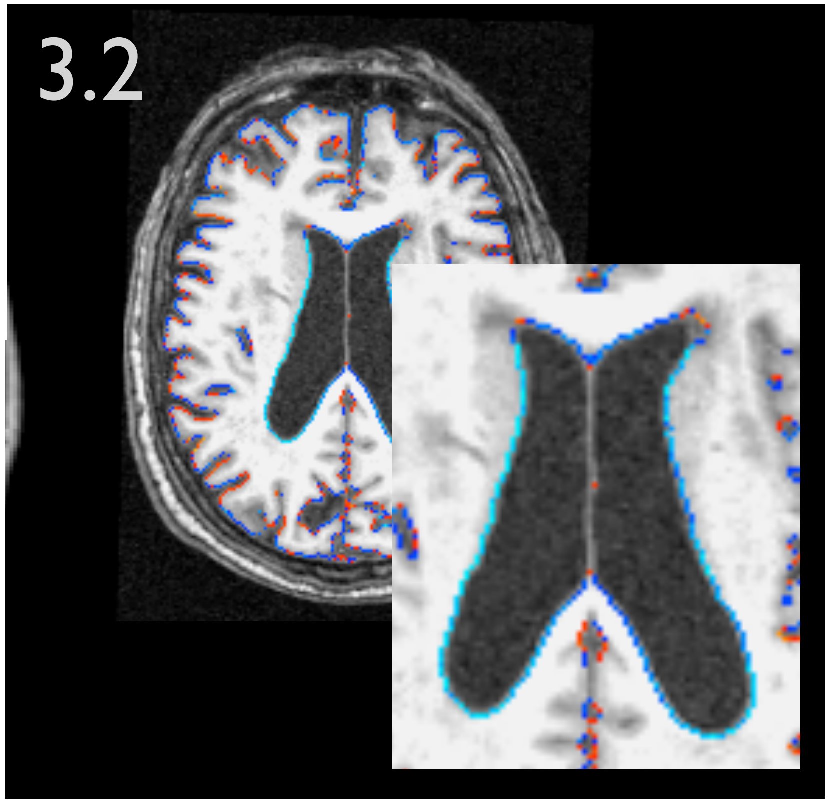
	voxelwise local-only estimation (*map*)	global-only estimation (*number*)
single timepoint (atrophy *state*)	FSL-VBM	SIENAX
two timepoints (atrophy *rate*)	Longitudinal FSL-VBM	SIENA

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)







Multiple- and single-timepoint analysis of brain change

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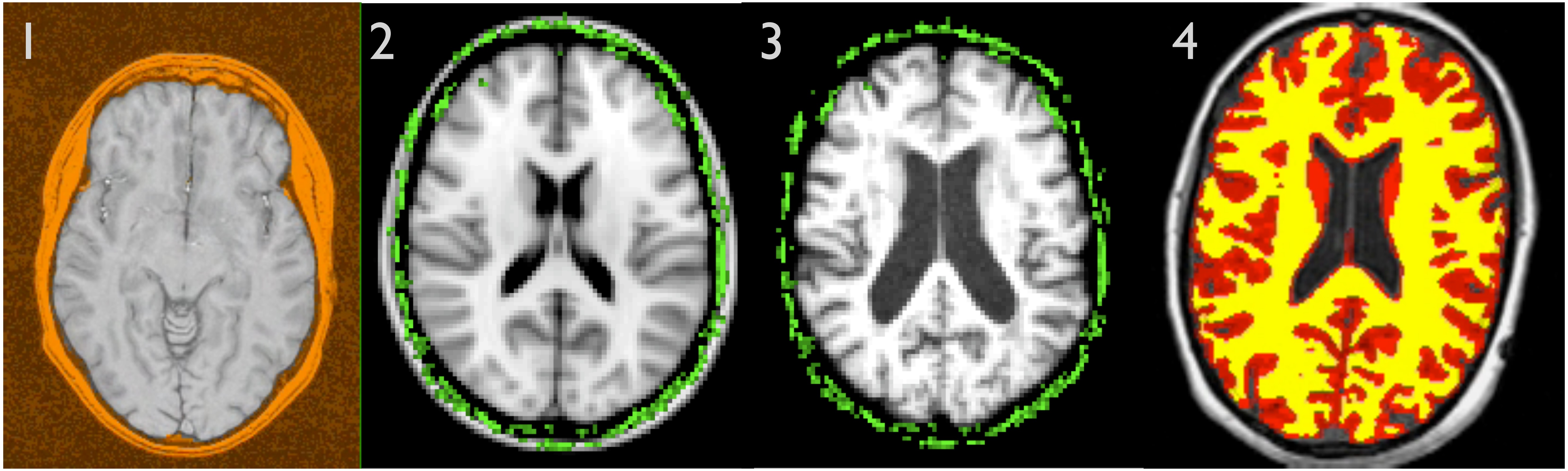
SIENAX Cross-sectional atrophy estimation

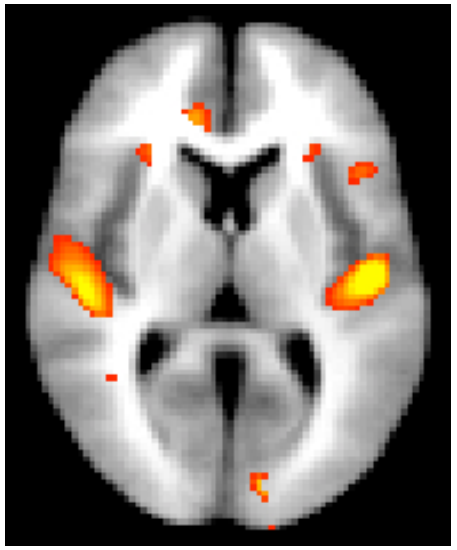
1. BET : find brain and skull
2. FLIRT : register to standard space using skull for scaling
3. Use standard-space masking to remove residual eyes/optic nerve
4. FAST : partial volume segmentation of tissues
5. Output : normalised brain volume (NBV)

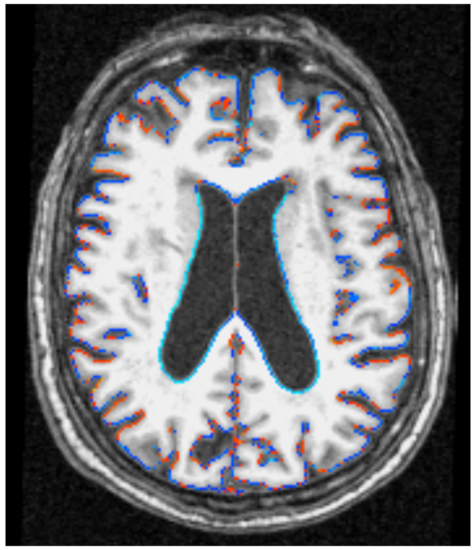
Note: NBV is useful for including as a *head/brain-size covariate* in other structural analyses (e.g. FIRST, VBM, etc.)



Structural Segmentation

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

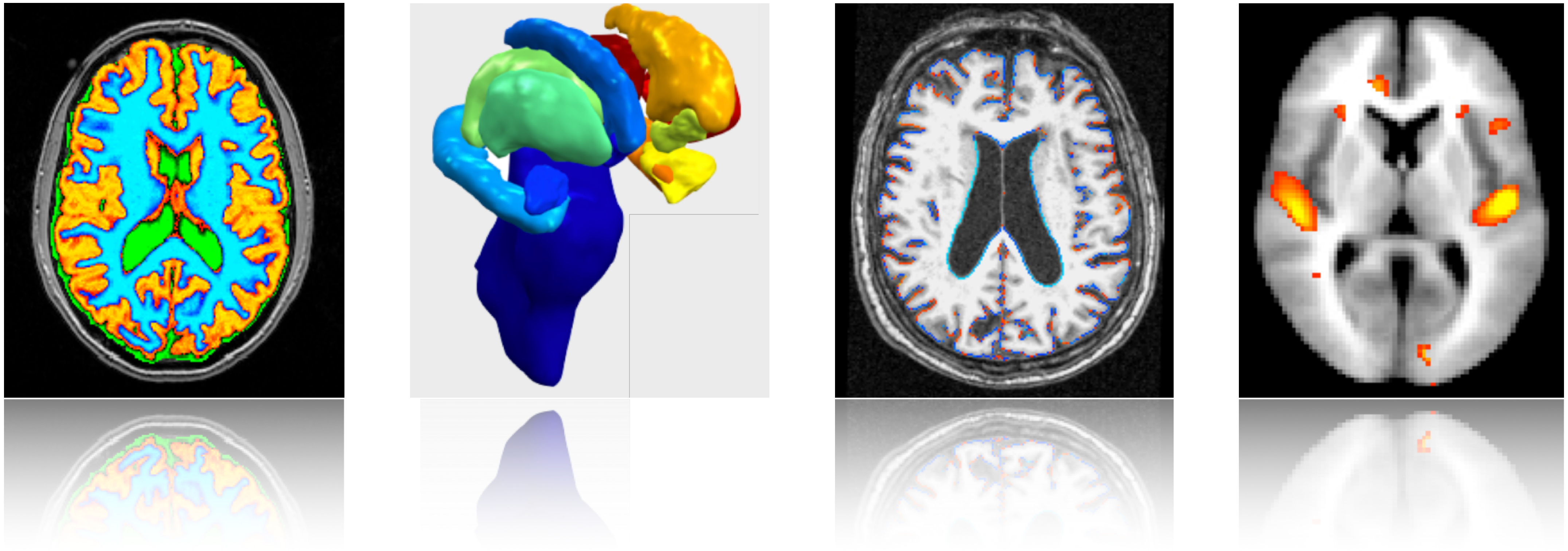




Summary

- 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

The End



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