

Measuring brain structure: Voxel Based Morphometry (VBM)



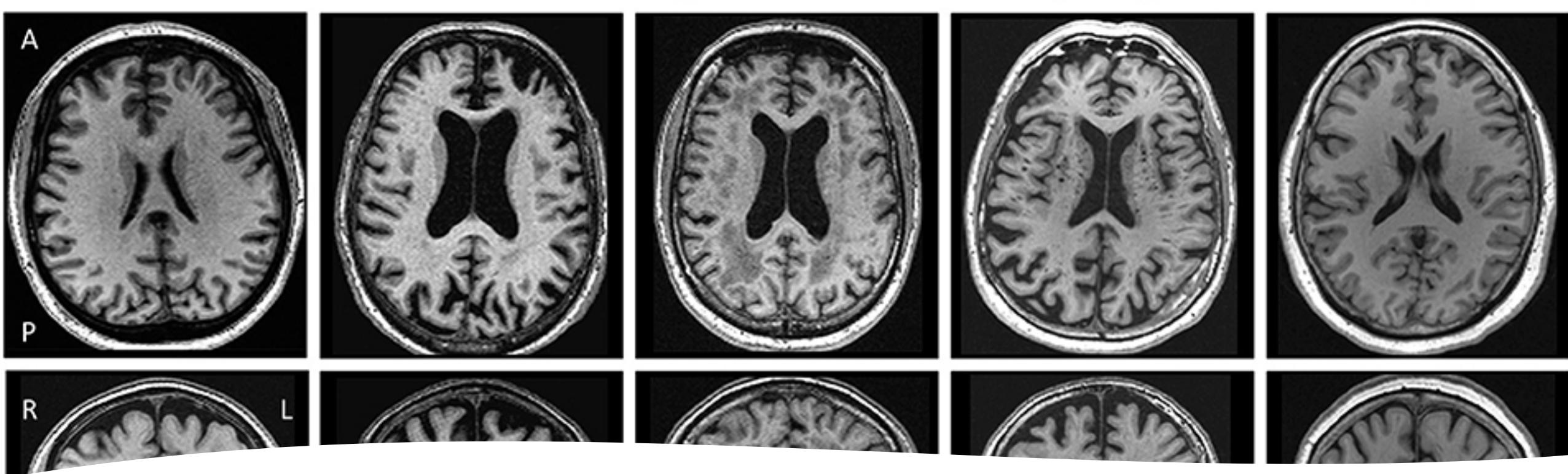
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@valegiunca



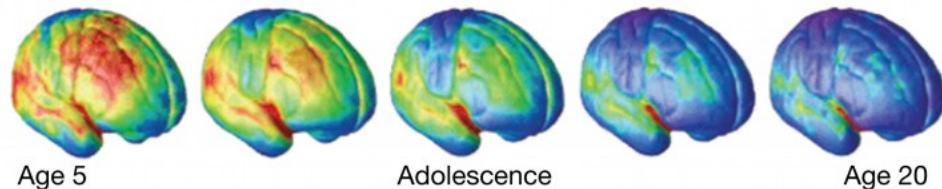
By the end of
this lecture,
you will know

- What we can gain from studying brain structure
- What we want from our MRI image of the brain
- What voxel based morphometry (VBM) is
- How we conduct a VBM study

What can we learn from studying brain structure?

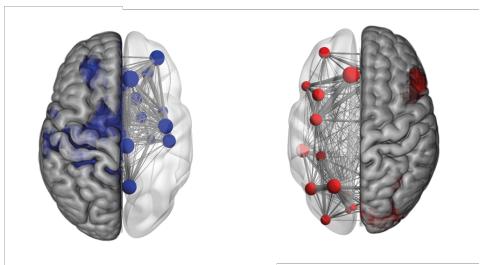
Gotya et al 2014

Dynamic mapping of human cortical development



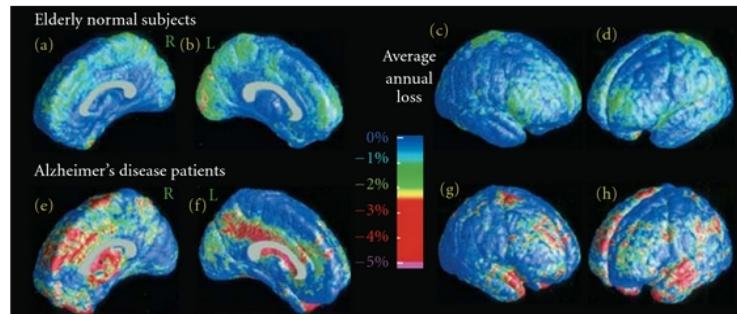
Source: "Dynamic mapping of human cortical development during childhood through early adulthood," Nitin Gogtay et al., Proceedings of the National Academy of Sciences, May 25, 2004; California Institute of Technology.

Developmental changes (typical and non-neurotypical)



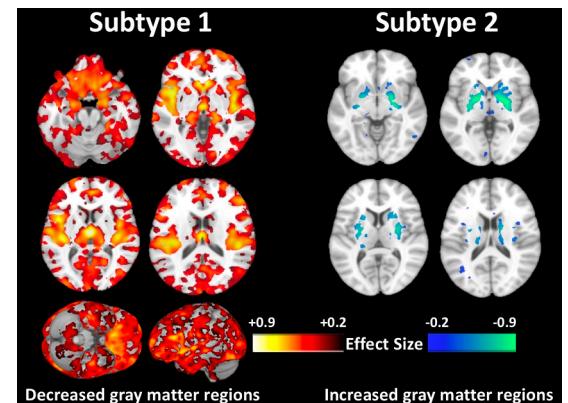
Structure-function relationships

Healthy ageing



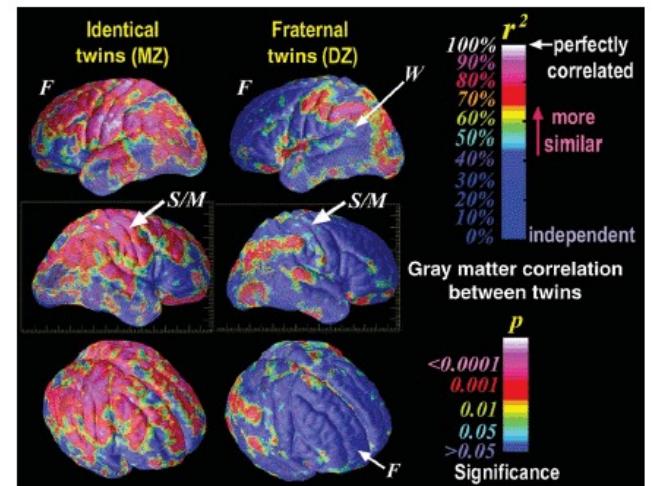
Matsuda 2013

and et al 2020

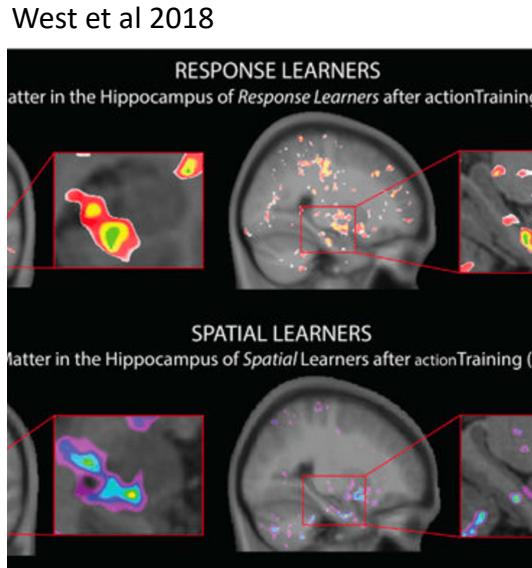


Disease detection

Thompson et al 2001



Cognitive training



What do we want from structural MRI?

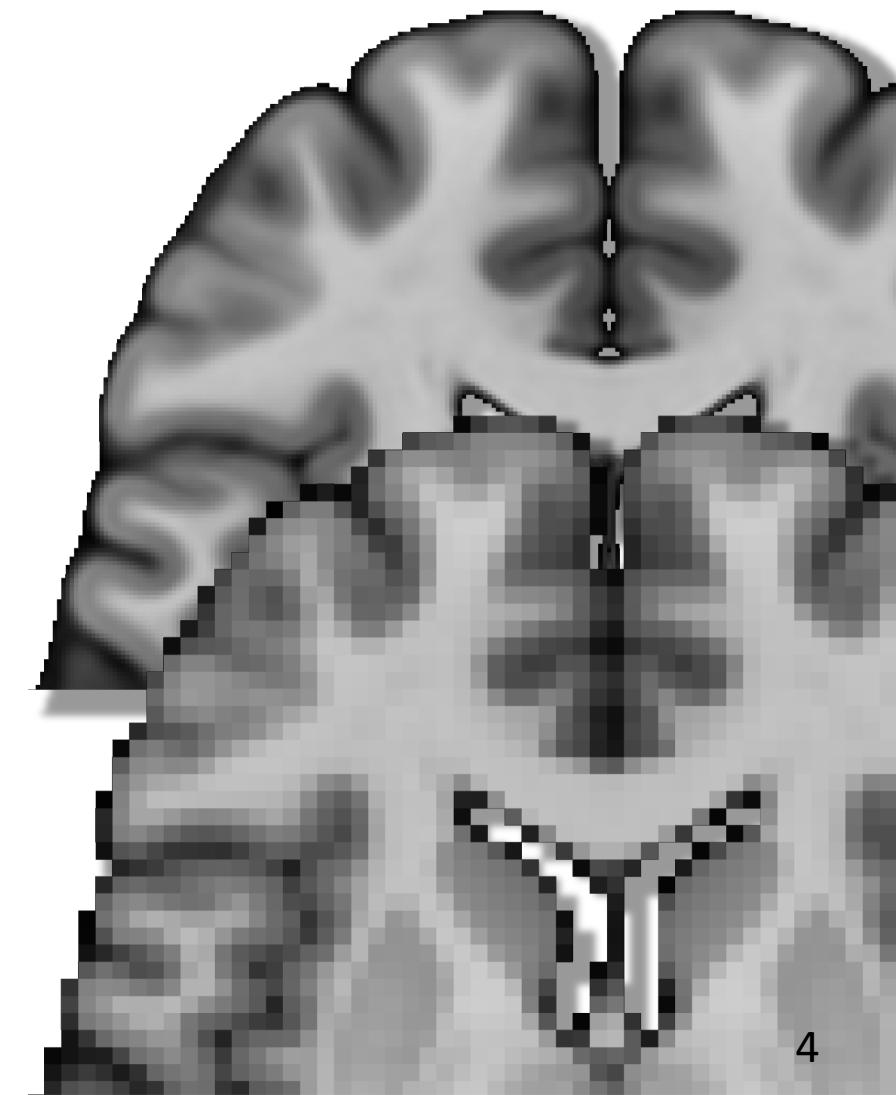
Anatomical detail

- Small voxels minimize partial volume

High tissue contrast

- Easily distinguish tissues

High signal to noise ratio



T1-Weighted imaging

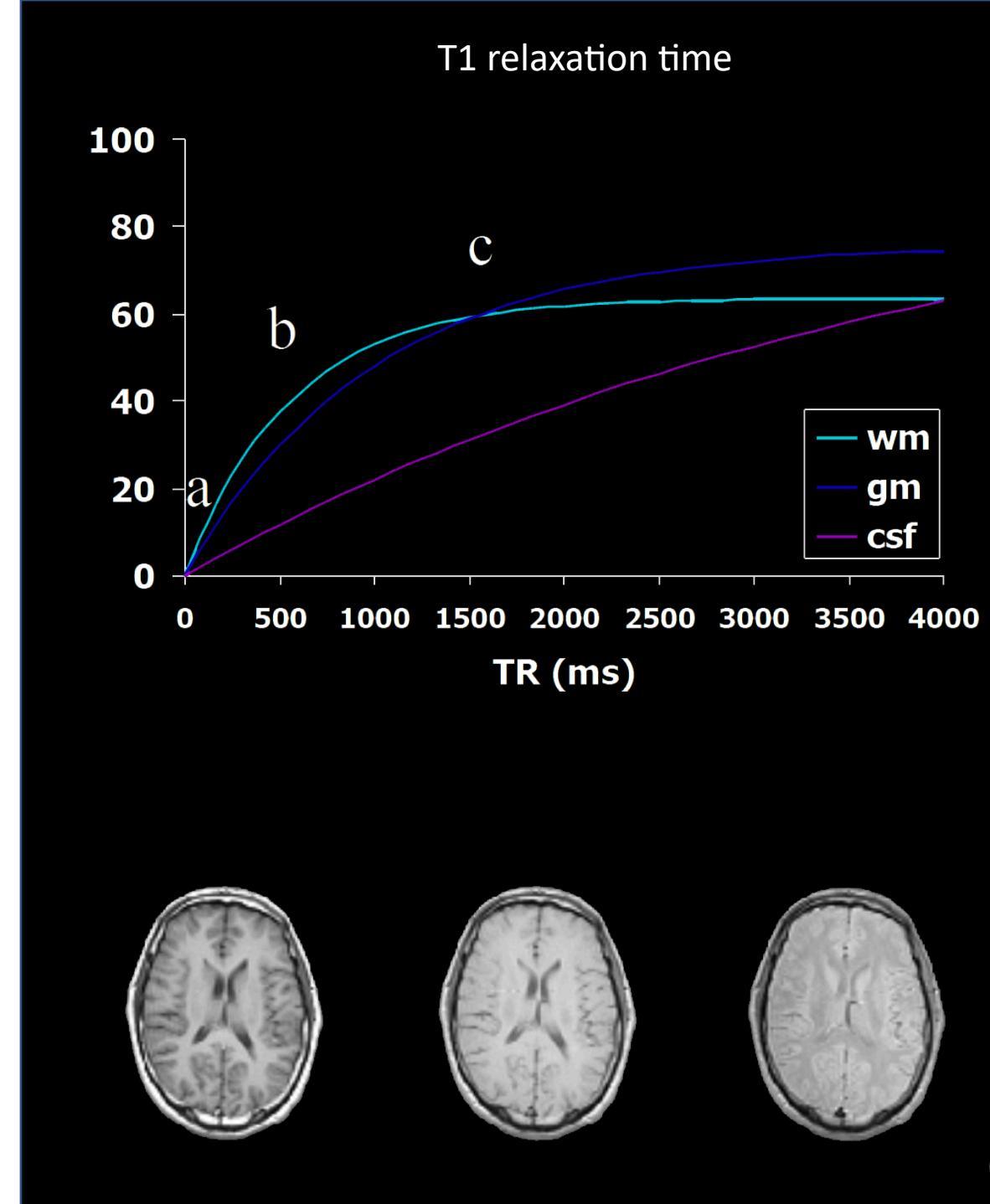
T1-weighted imaging

→ This imaging produces contrast between fatty tissue (grey and white matter) and CSF (CSF = dark)



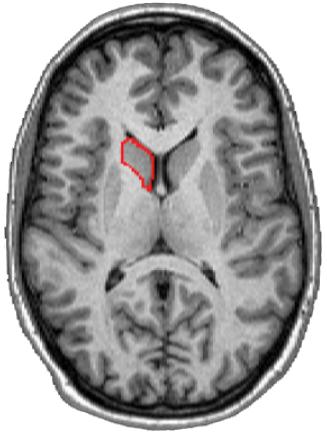
T1-Weighted imaging

- Relaxation time is responsible for most contrast in MR images.
 - Tissues vary in their relaxation time
 - T1 or “longitudinal” relaxation time.
 - i.e., how much time before protons in the tissue realign with the static magnetic field.



Using images to measure brain structure

MANUAL



Trace regions & calculate volume

- ✗ Time consuming
- ✗ Investigators' variations
- ✗ Anatomical definitions vary
- ✗ May miss subtle differences

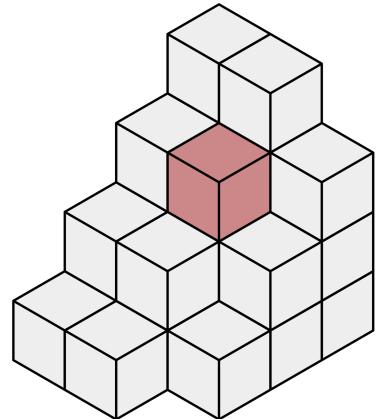
AUTOMATED



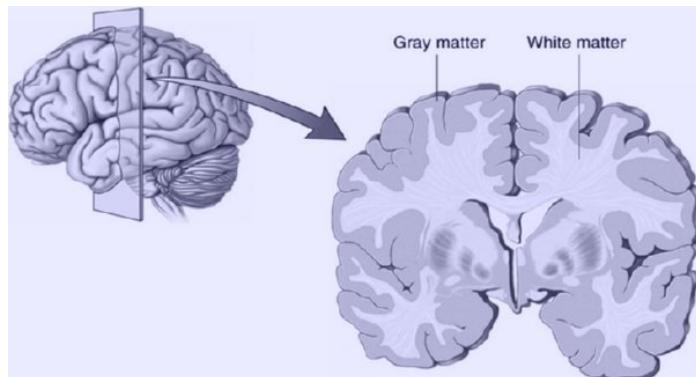
Voxel Based Morphometry

- ✓ Fast
- ✓ Unbiased
- ✓ Regional changes in volume
- ✓ Whole brain

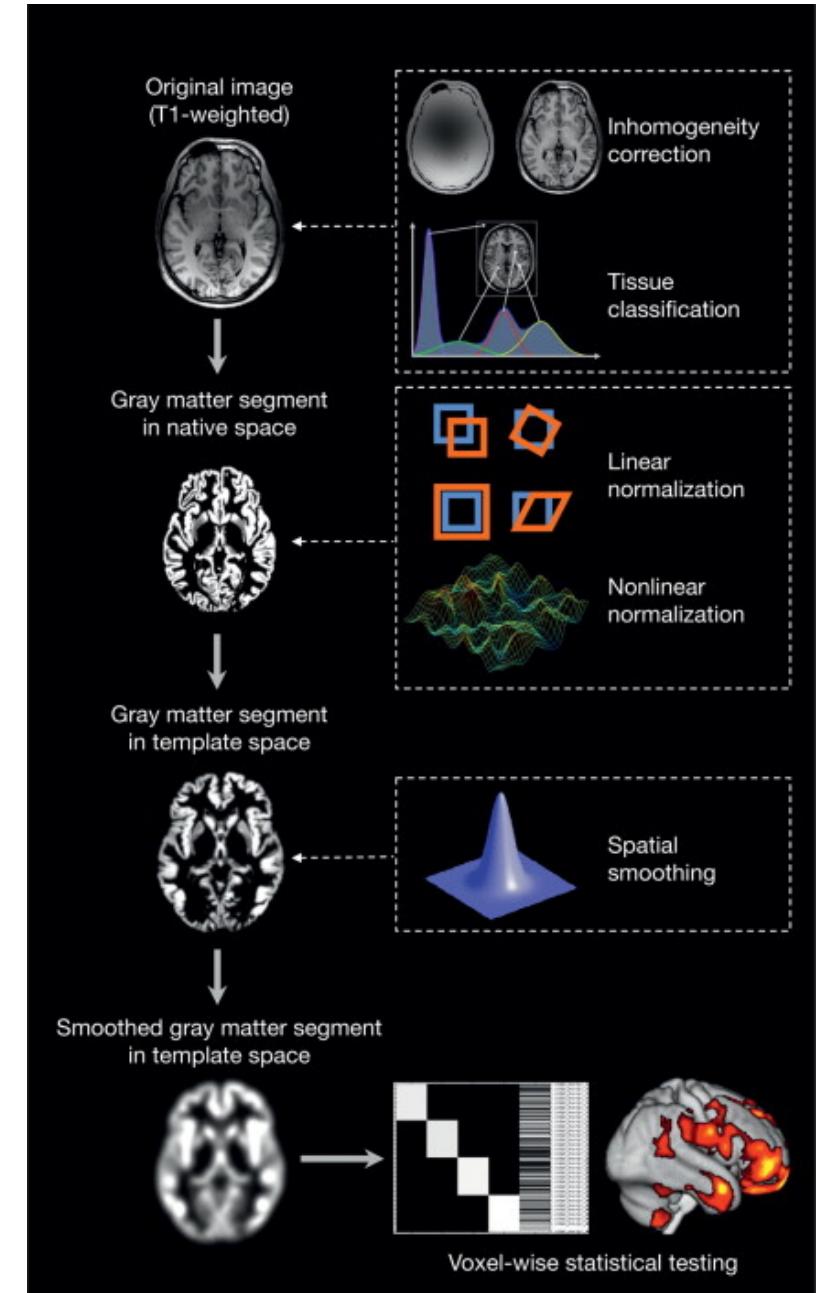
Voxel Based Morphometry



This analysis method uses individual voxel elements (e.g. 1mm³ cube/1mm³ isotropic)



Measurement of forms
(e.g. brain structure)



How do we perform VBM analysis?

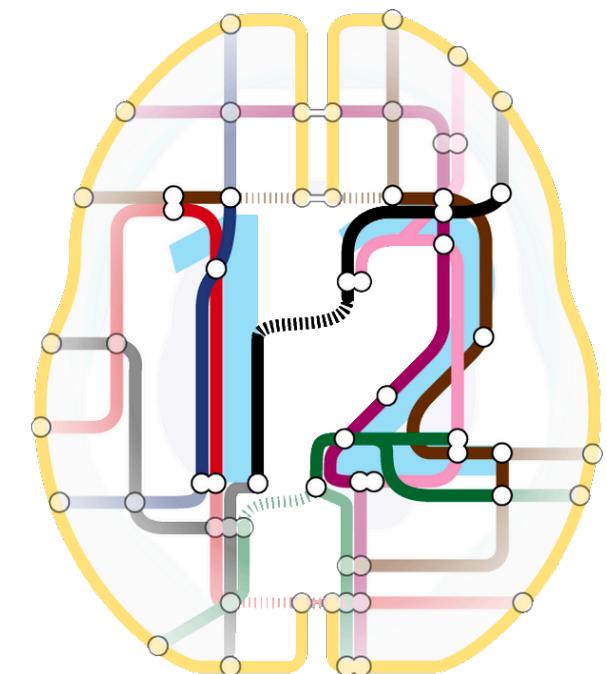
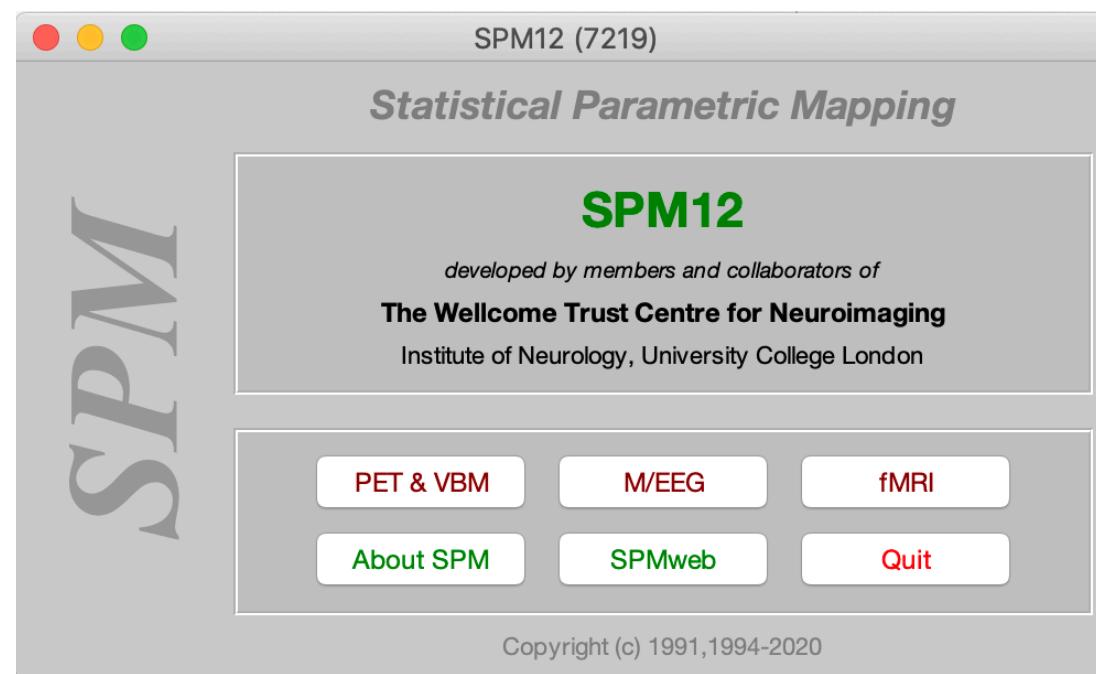
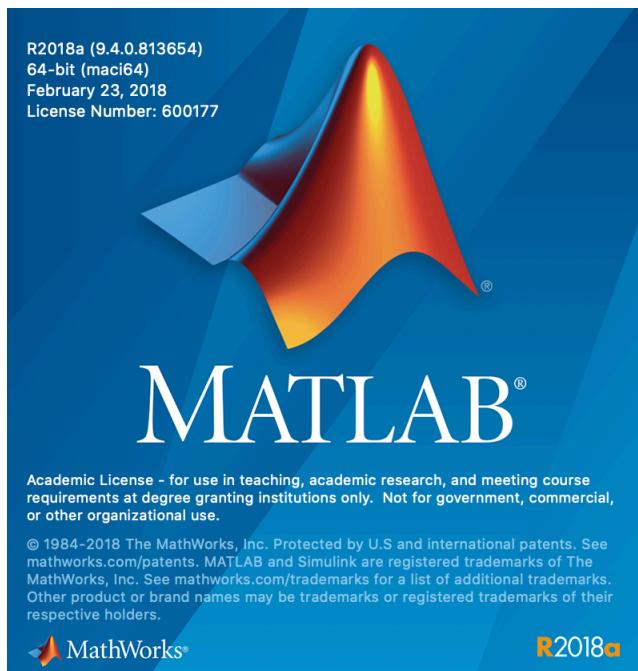
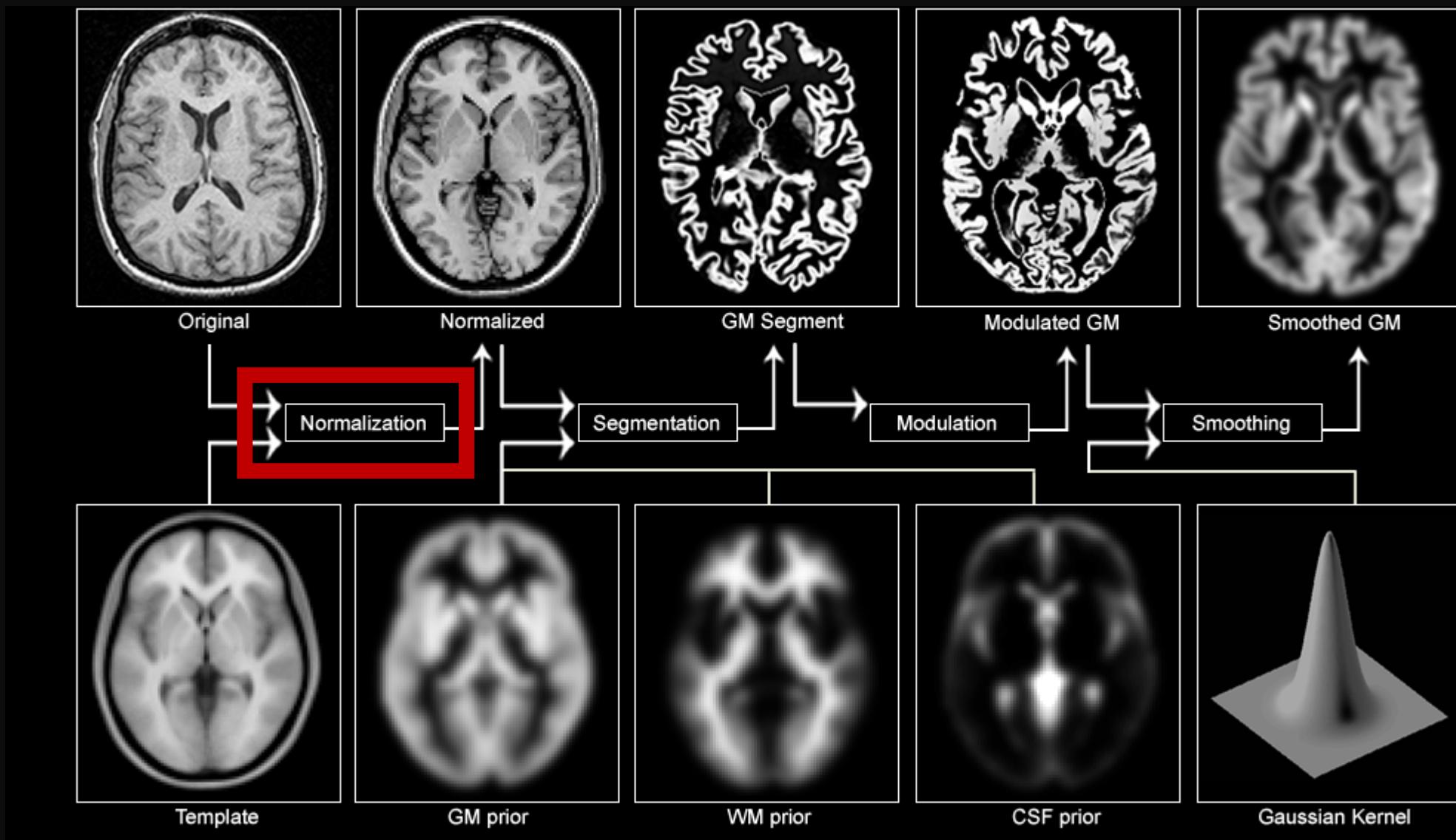


Image preprocessing for VBM



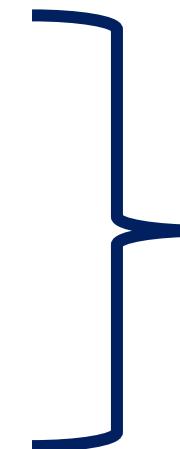
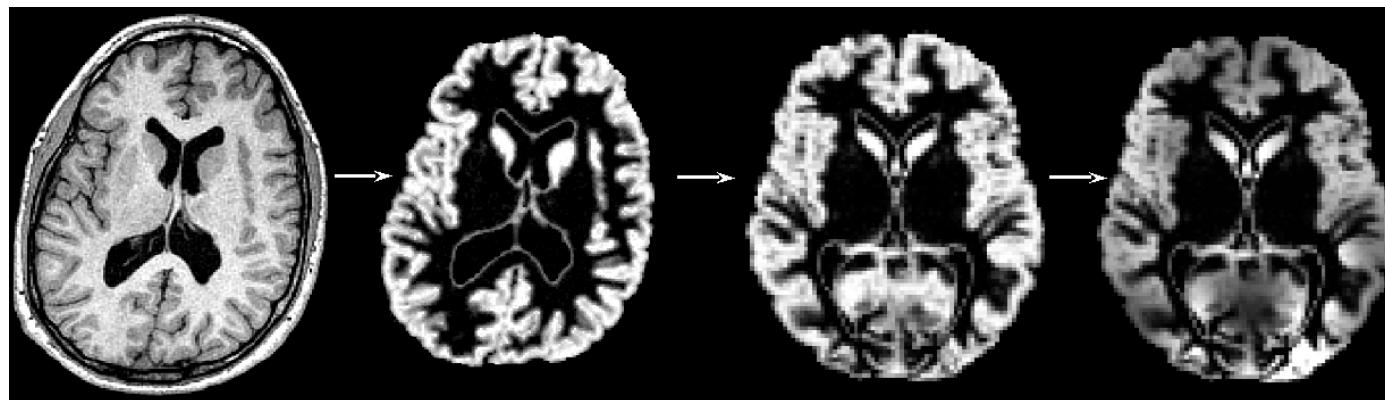
Spatial normalisation

Different brain shapes and sizes



Group analysis requires all brains into the same stereotactic grid/space.

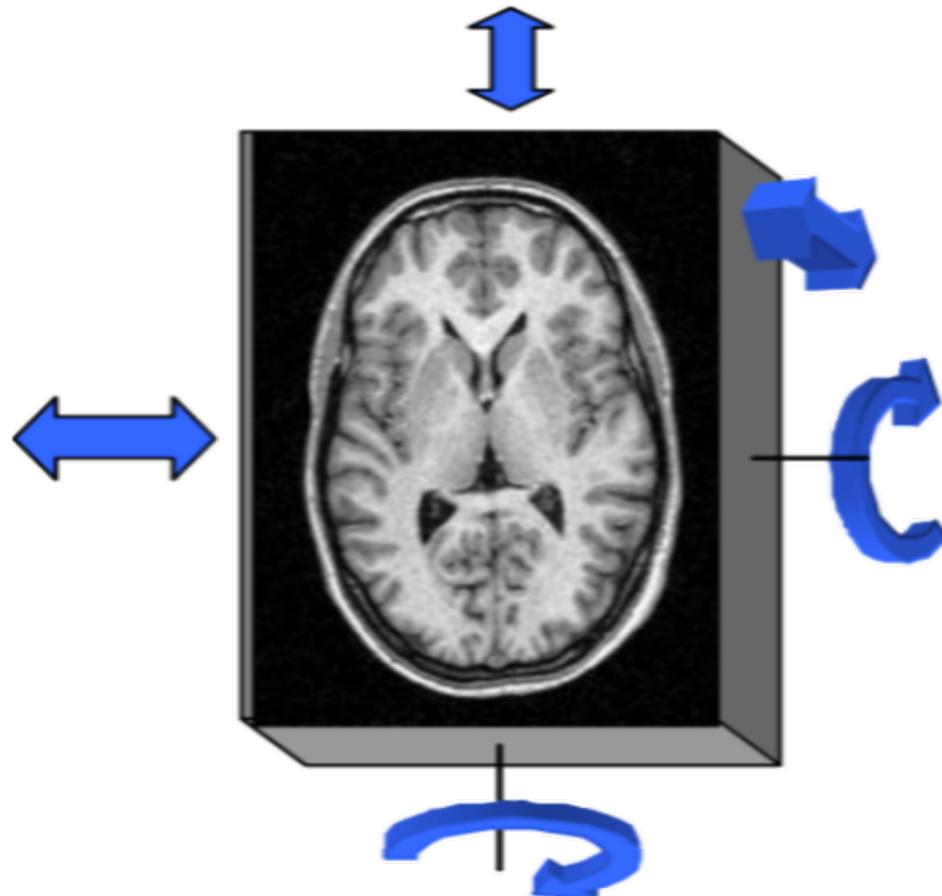
Affine transformations
+
Non-linear transformations



Standard space

1

Affine transformations



Normalization to template

→ Matching of overall position & size

12 parameters

→ Translation, rotation,
scaling and shearing

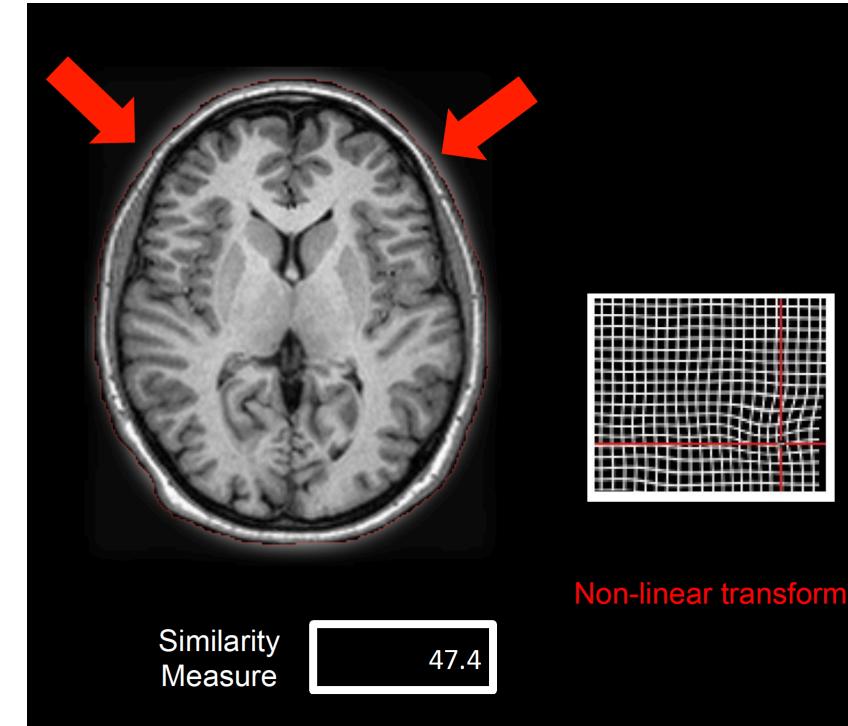
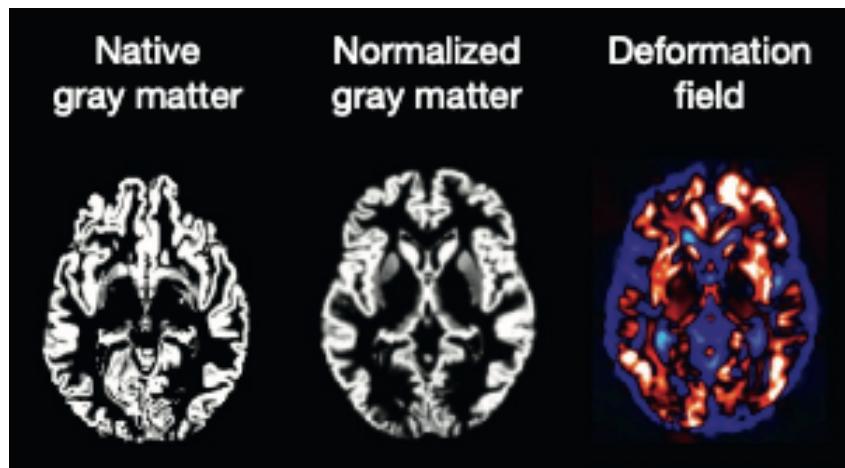
LOCAL DIFFERENCES?

Non-linear transformations

Credit: Matthew Kempton

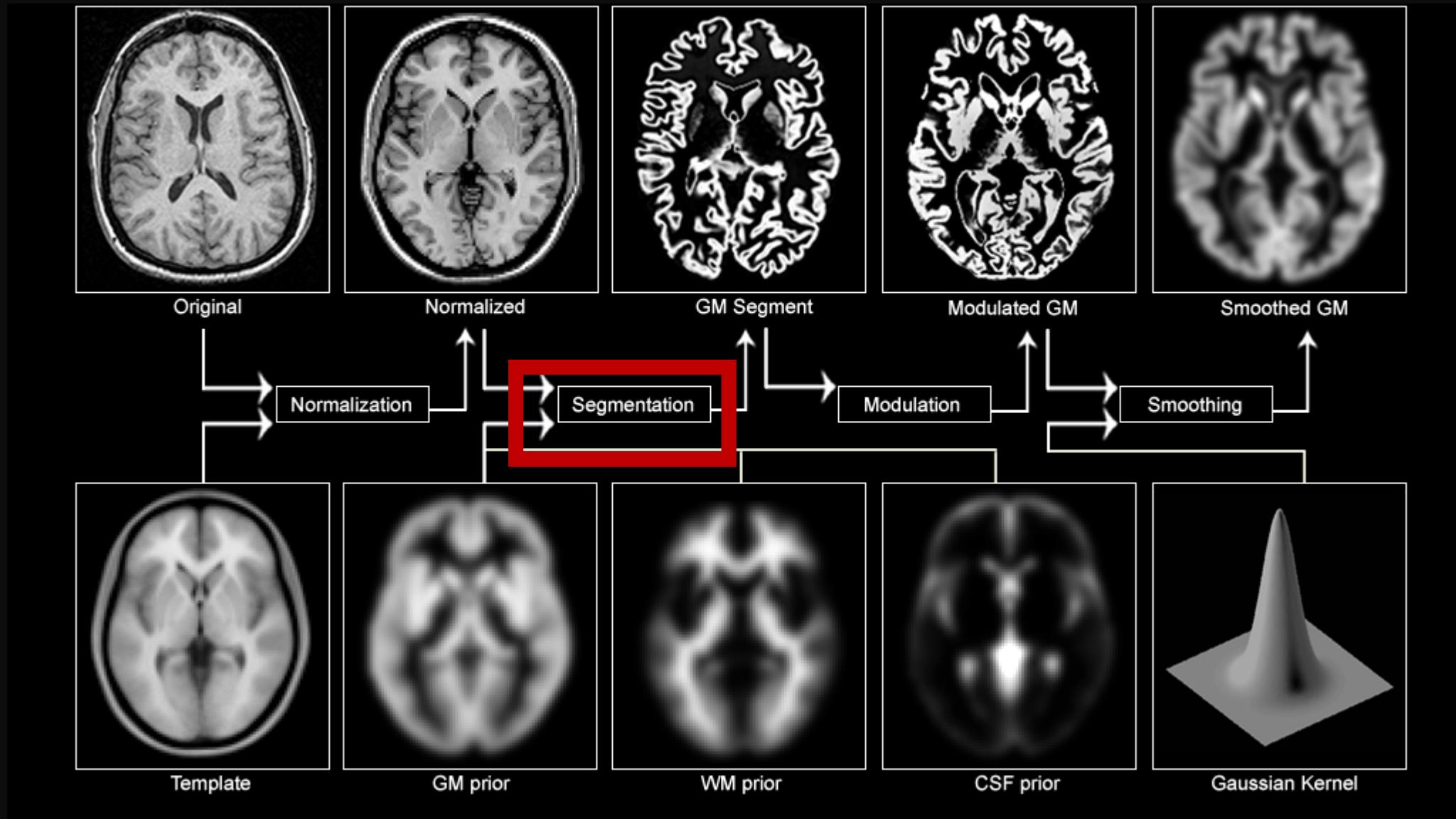
Image is spatially warped to fit it onto the desired template.

- Aligns common structures (e.g. ventricles & sulci) to a common space.
- Accounts for global non-linear shape differences.

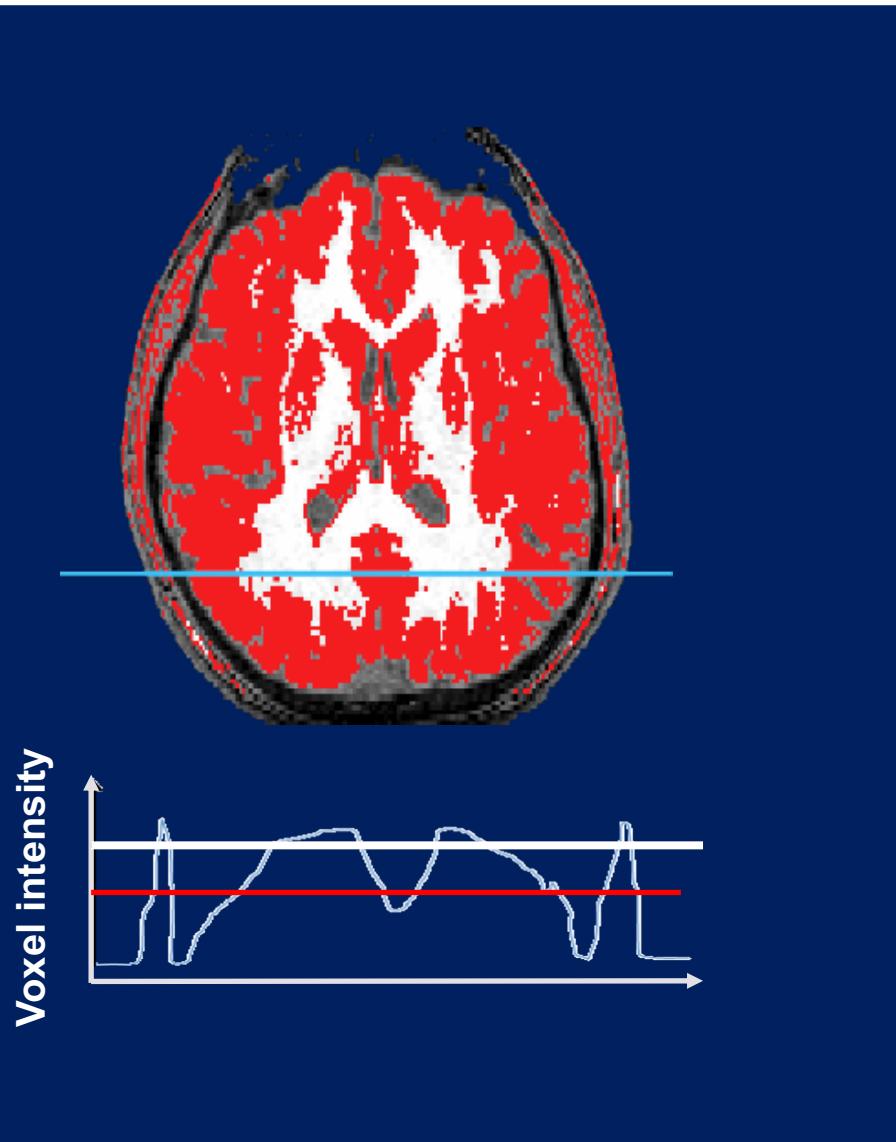


Deformation (warping) fields = how much warping has occurred for each T1 to fit to template.

Image preprocessing for VBM



Can we classify tissues just using Intensity thresholding?



NOT REALLY

Limitations:

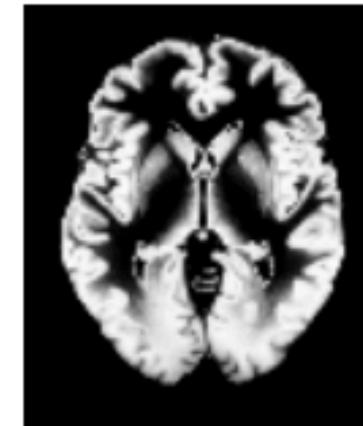
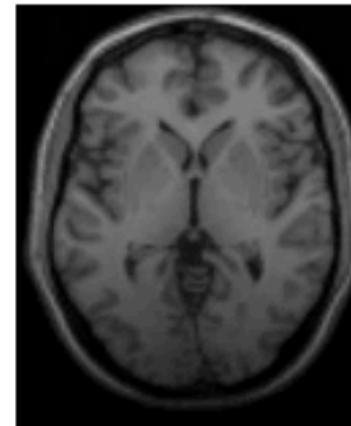
- Arbitrary thresholds.
- Spatial biases in MR Artifacts
- Image noise, e.g., random white matter voxels with low intensity incorrectly classified as gray matter.

1

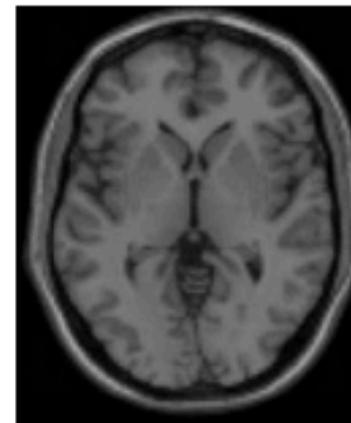
Inhomogeneity correction



NO
CORRECTION



Correction

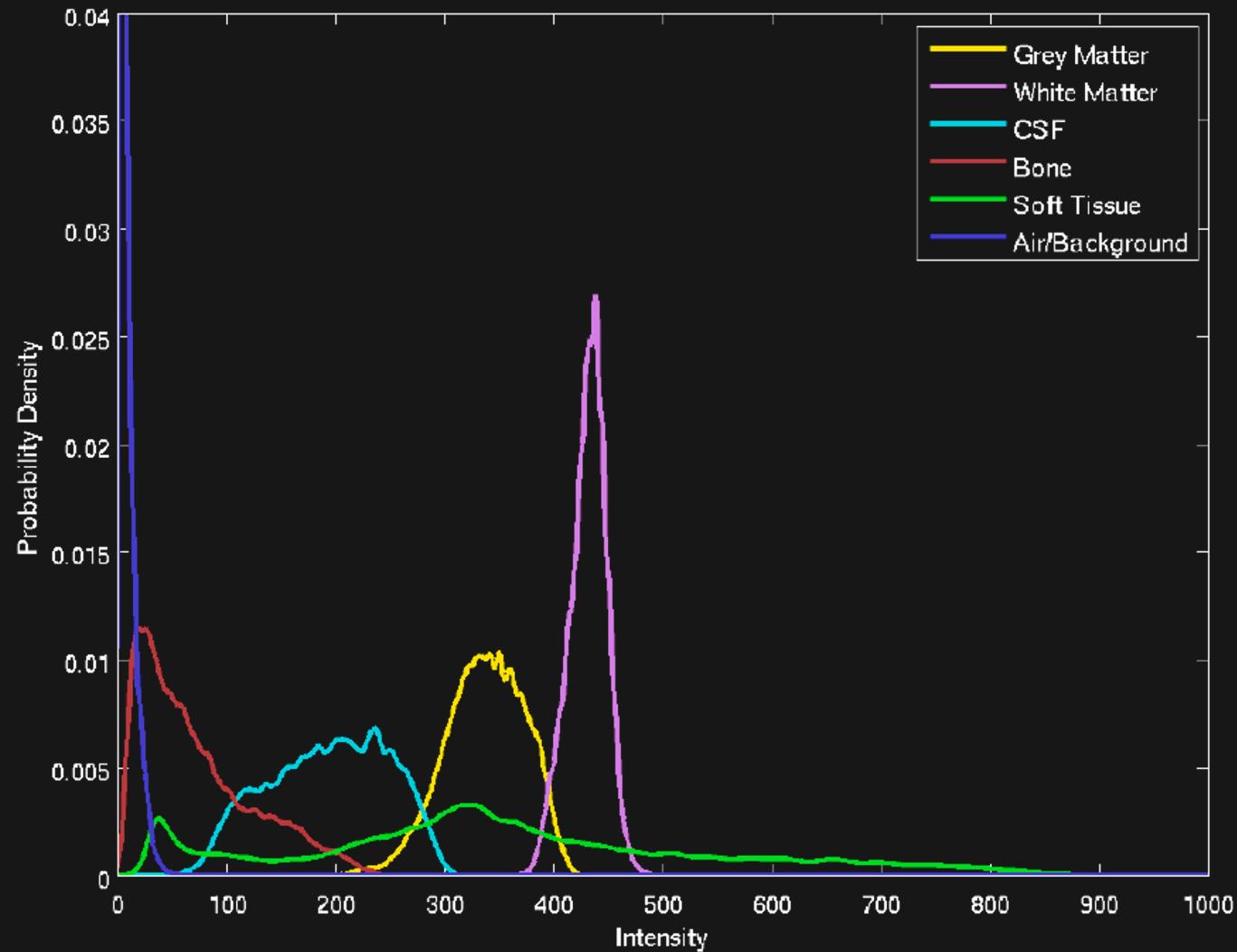


T1



GM

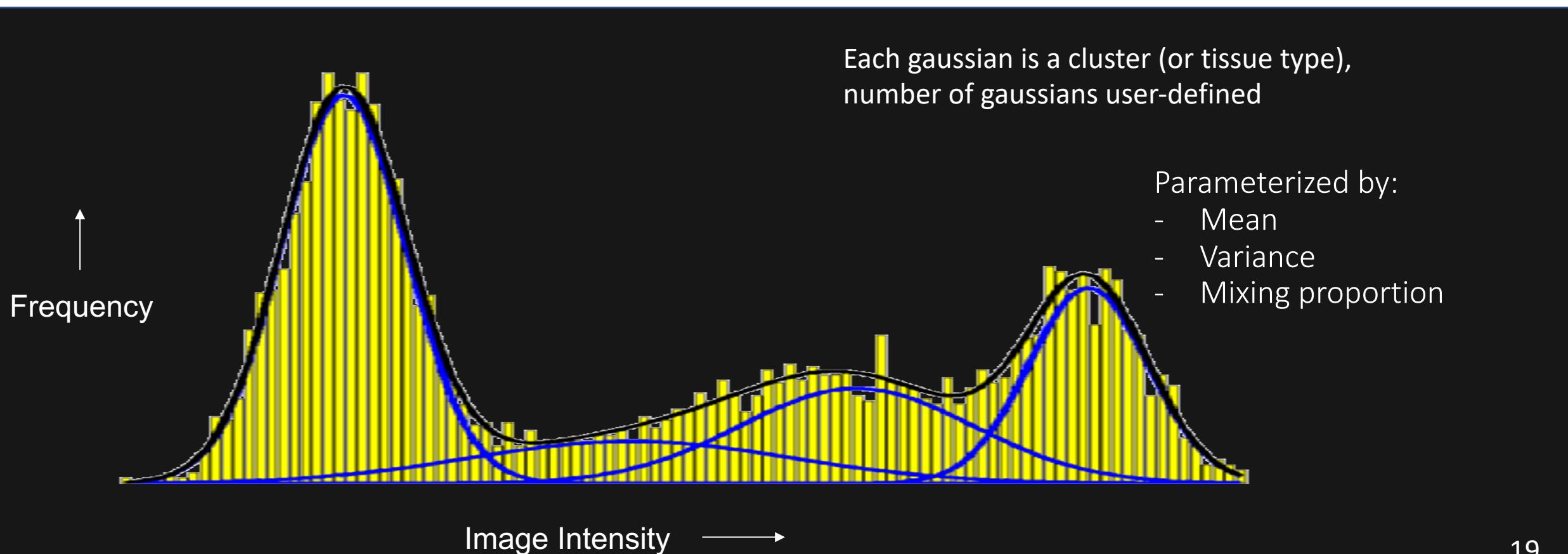
Mixtures of Gaussians (MOG)



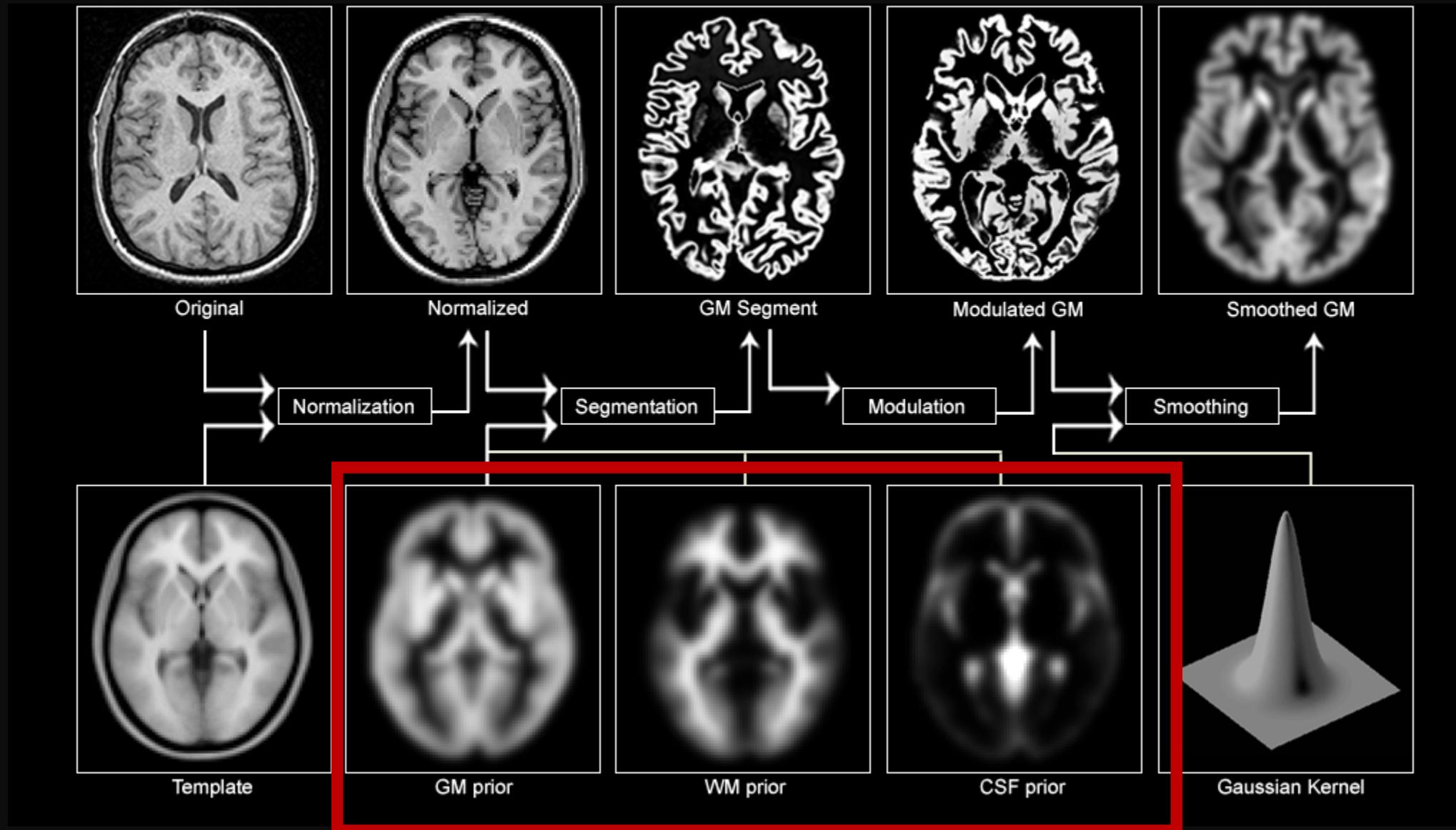
Mixtures of Gaussians (MOG)

Classification based on Mixture of Gaussians model (MOG)

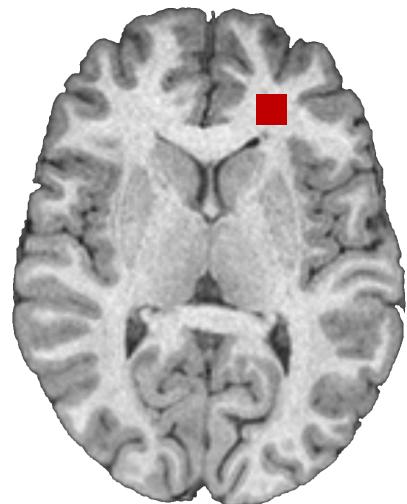
→ Representation of the intensity probability density by a number of Gaussian distributions.



Segmentation using prior spatial information



Segmentation using prior spatial knowledge



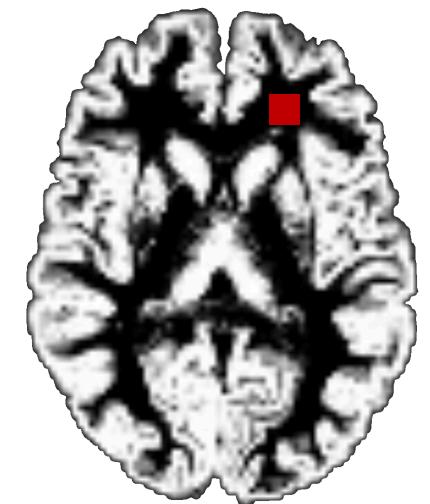
T1 normalized

Voxel value = 159



Standard space
Tissue probability map

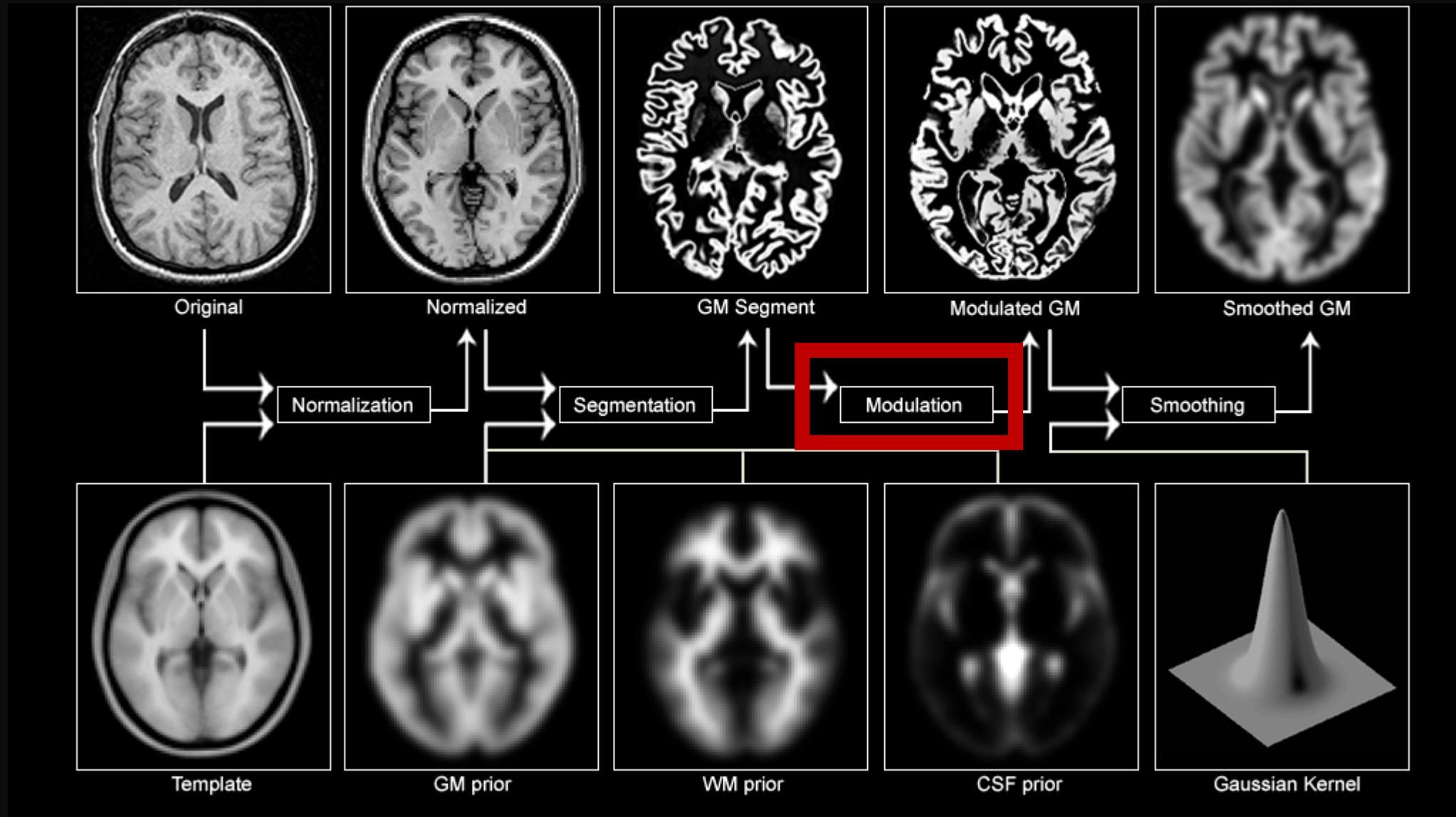
Voxel value = 0



Individual GM

Voxel value = 0

Image preprocessing for VBM

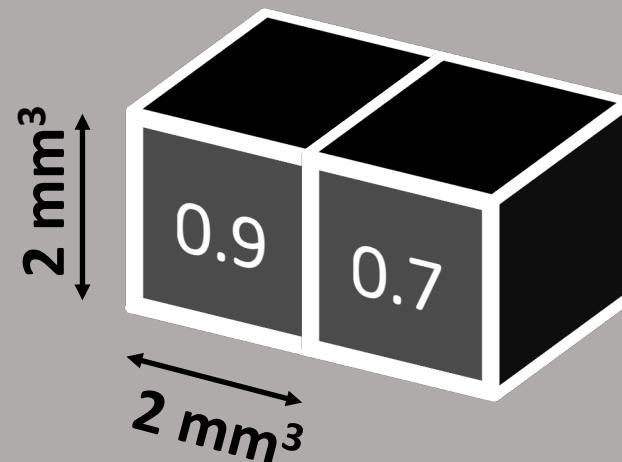


Modulation

Is the sum of all GM voxels a good estimate of tissue volume?

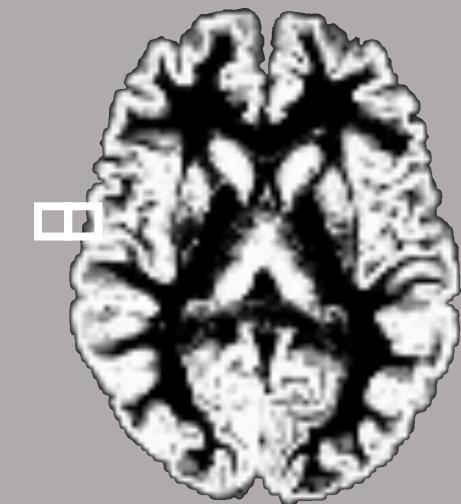
NO!

Volume change due to spatial normalization!



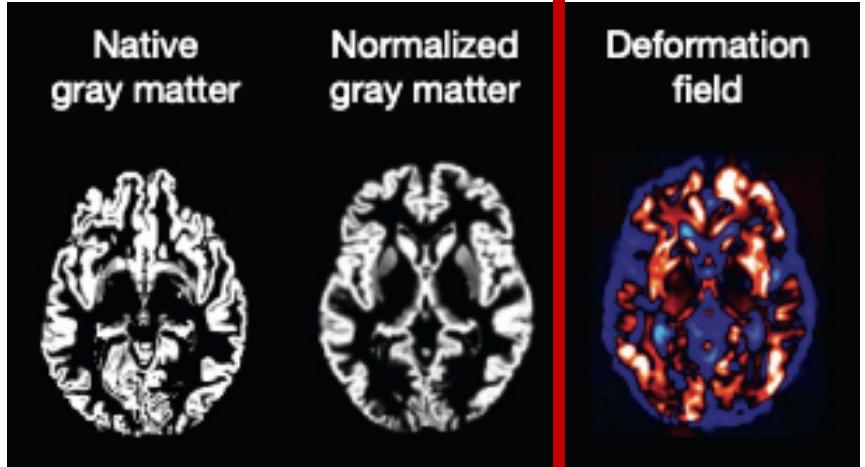
$$\begin{aligned} &= 0.9 \times (2 \times 2 \times 2) \\ &= 7.2 \text{ mm}^3 \text{ tissue} \end{aligned}$$

$$\begin{aligned} &= 0.7 \times (2 \times 2 \times 2) \\ &= 5.6 \text{ mm}^3 \text{ tissue} \end{aligned}$$



Individual GM

Modulation



Kurth et al. 2015

Encoding of
relative volume

Deformation field contains information
on how much each voxel was deformed.



Scaling based on the amount of
deformation during normalization

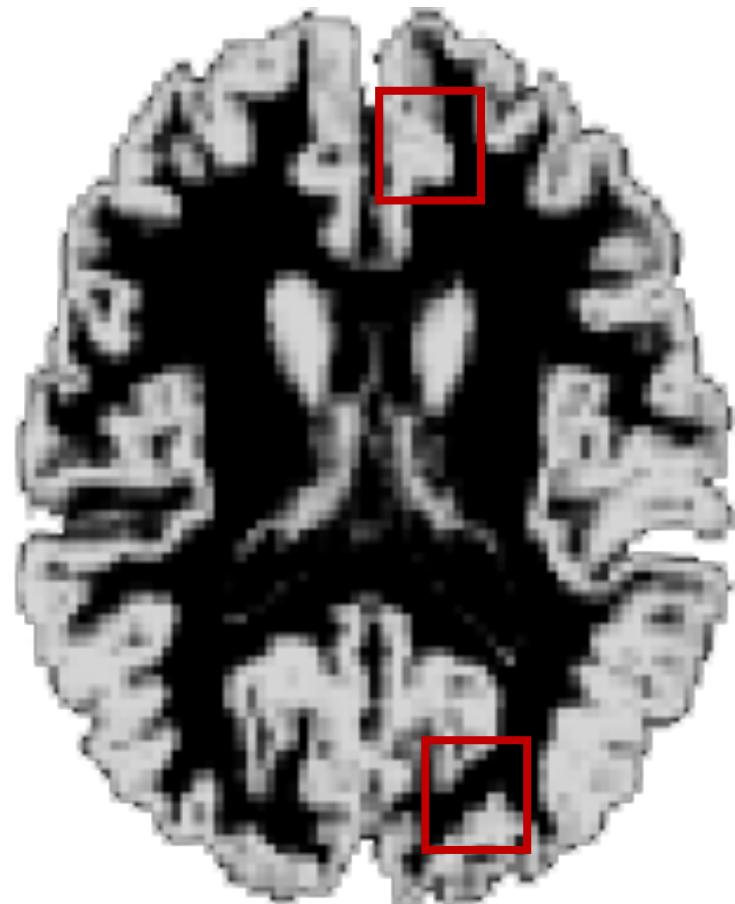
Can we correct for volume changes by multiplying the image with a constant?

NO!



Deformation is not equivalent in all voxels

Modulation



Non-modulated



Modulated

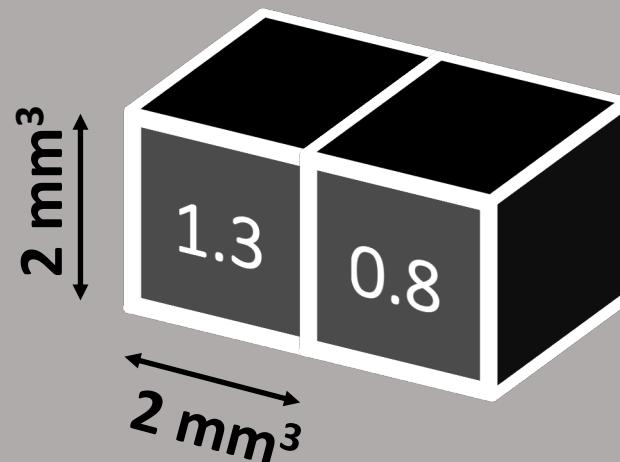
More
squashing

More
stretching

Modulation

Is the sum of all MODULATED GM voxels a good estimate of tissue volume?

YES!



$$= 1.3 \times (2 \times 2 \times 2)$$

$$= 10.4 \text{ mm}^3 \text{ tissue}$$

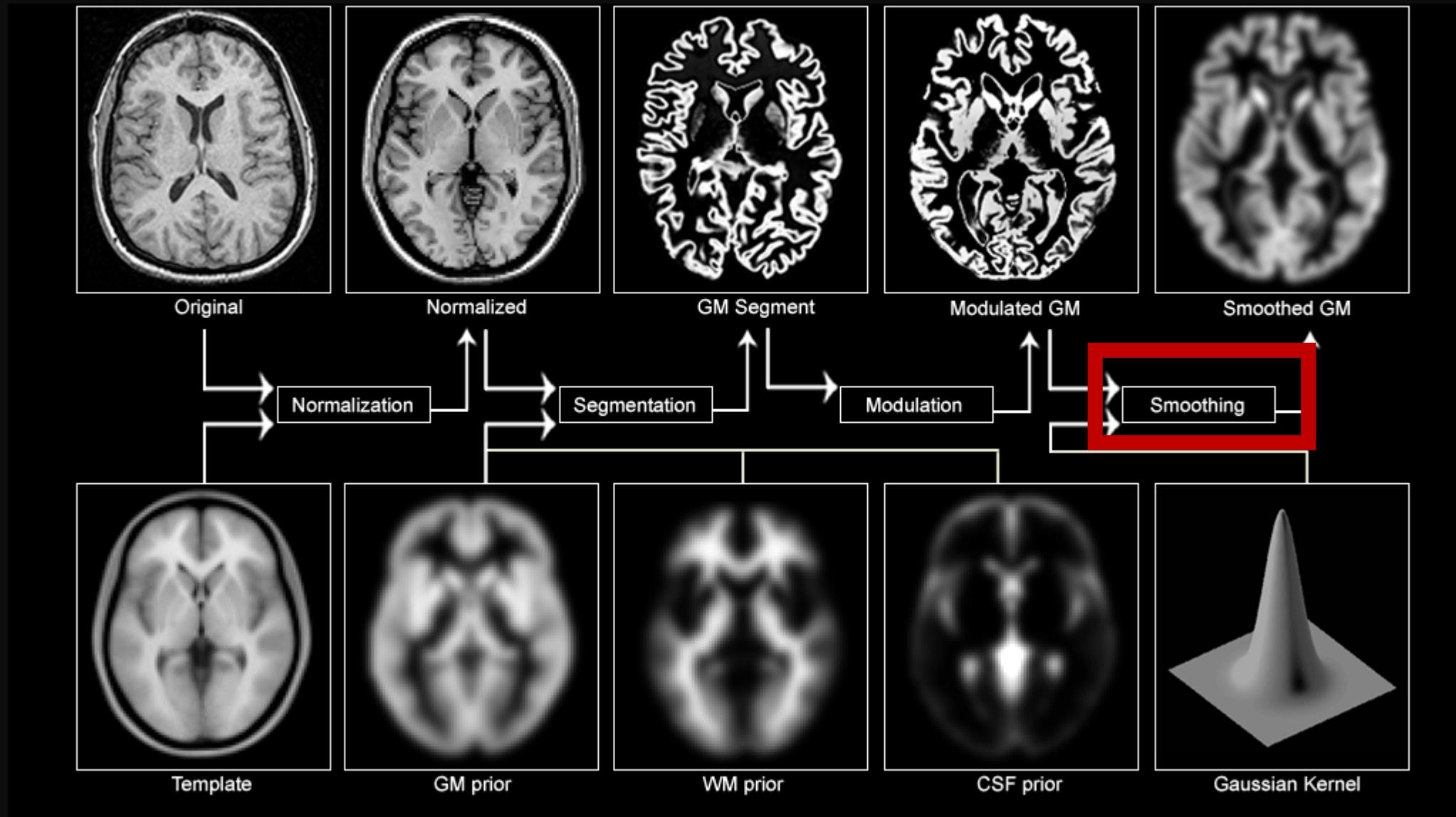
$$= 0.8 \times (2 \times 2 \times 2)$$

$$= 6.4 \text{ mm}^3 \text{ tissue}$$



Individual's
modulated GM

Image preprocessing for VBM

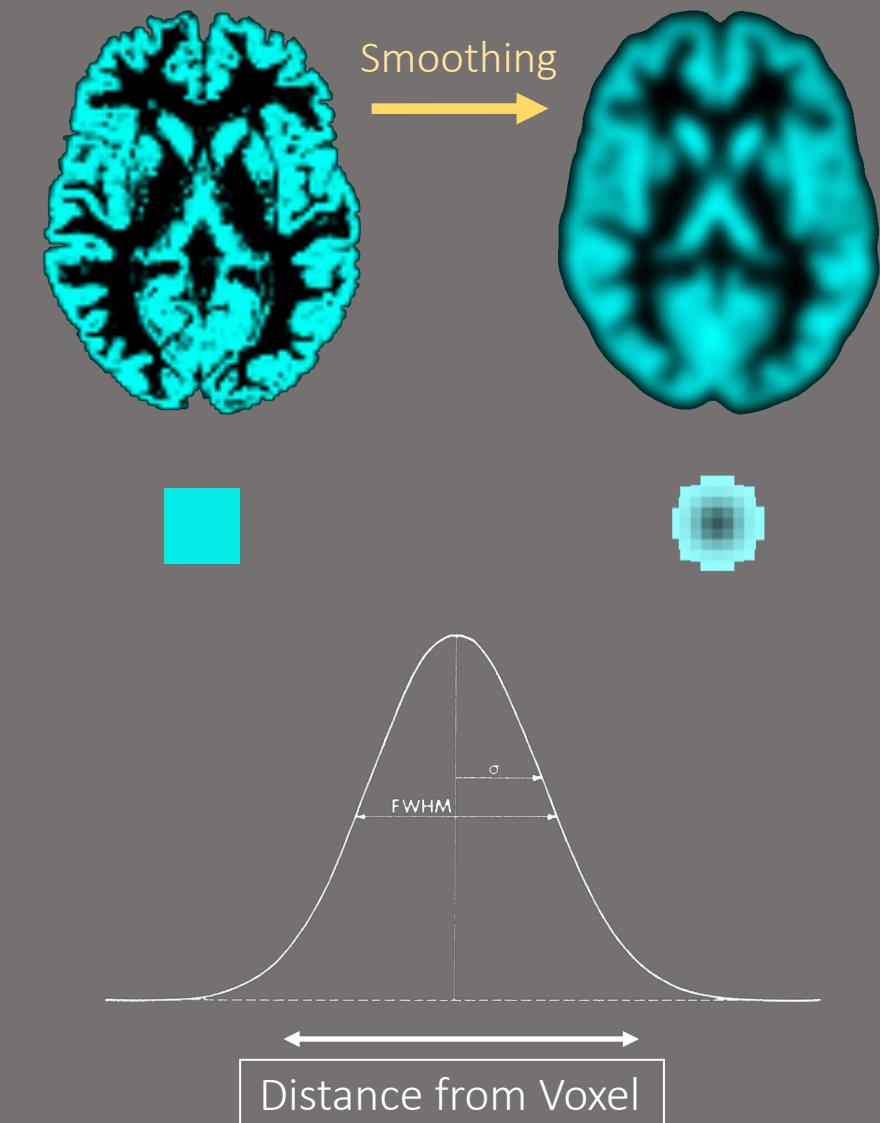


Smoothing

Each data point becomes the weighted average of the neighbours

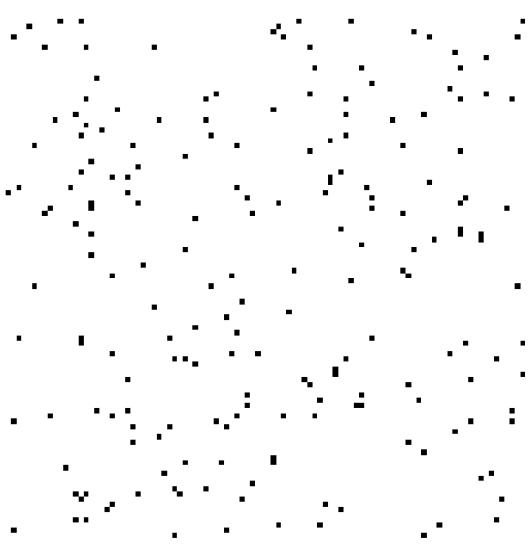
- 1 Improves spatial overlap by blurring over minor anatomical differences and registration errors.
- 2 Increase SNR
- 3 Makes data more normally distributed (central limit theorem).

Convolution with a 3D Gaussian kernel, of specified full-width at half-maximum (FWHM) in, e.g. 8mm.

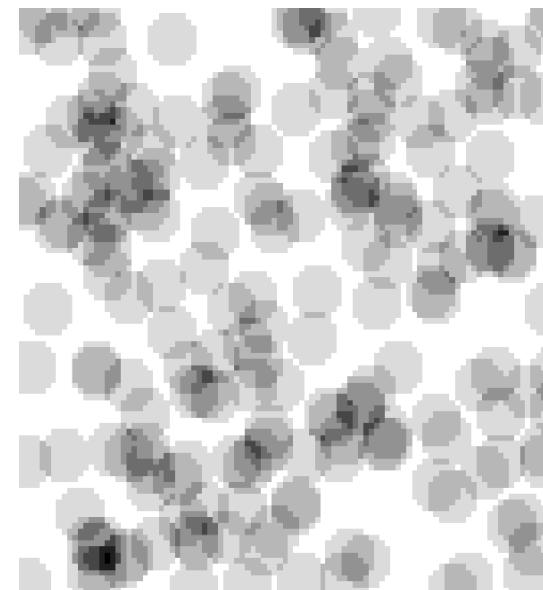


What is a convolution?

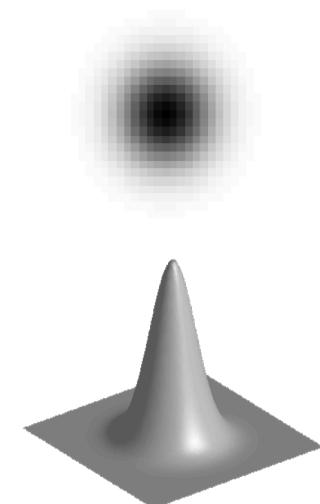
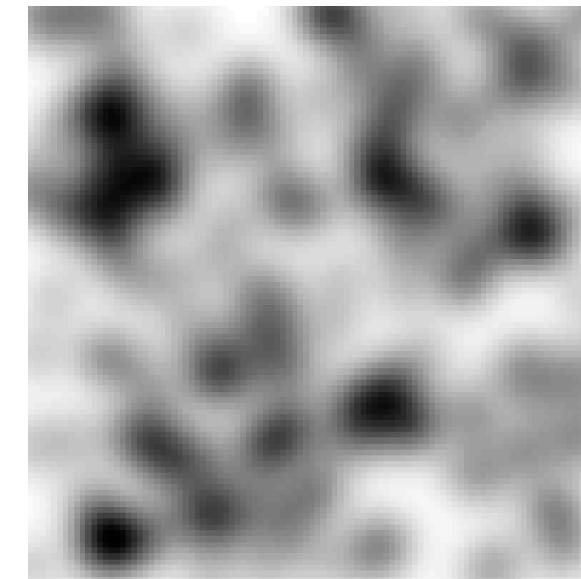
Before convolution



Convolved with a circle

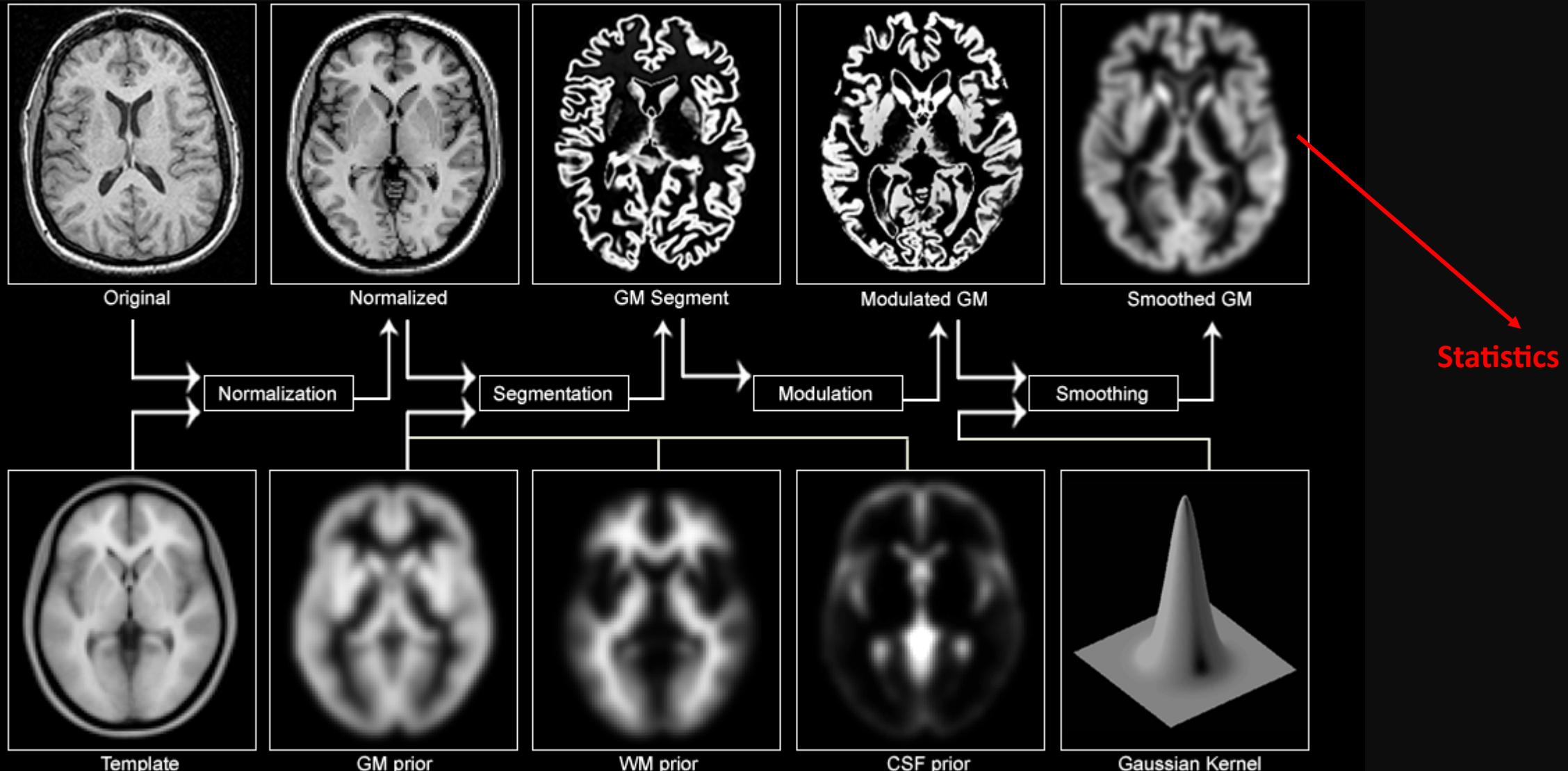


Convolved with a Gaussian



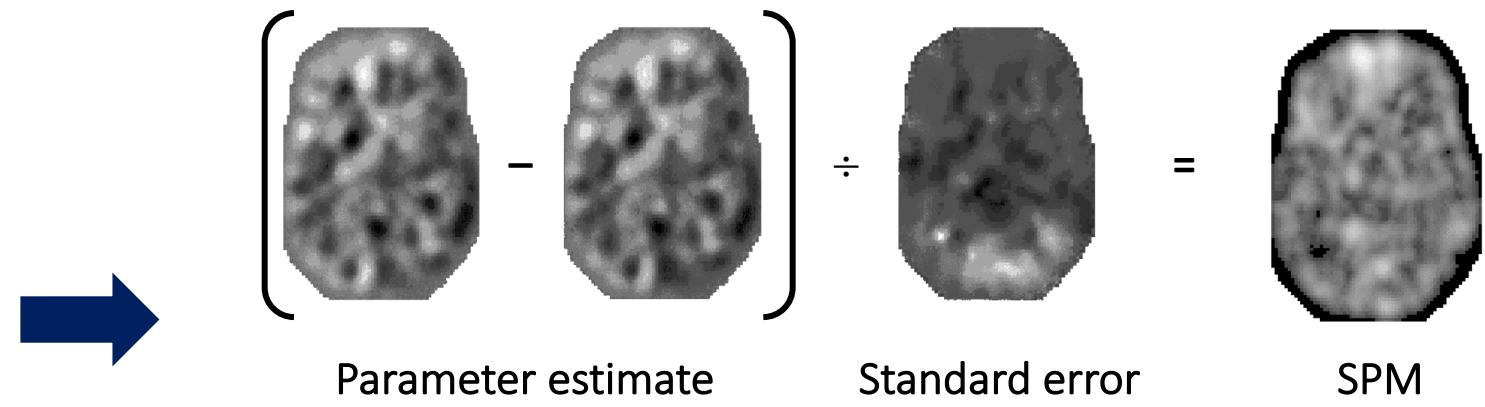
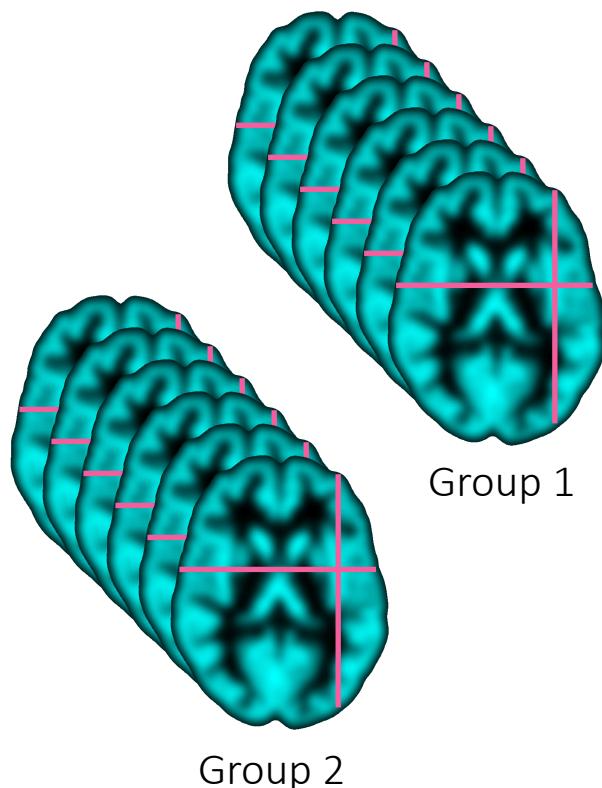
Each point/voxel after smoothing effectively becomes the result of applying a weighted region of interest (ROI).

Image preprocessing for VBM



Statistical parametric mapping (SPM)

GROUP COMPARISON

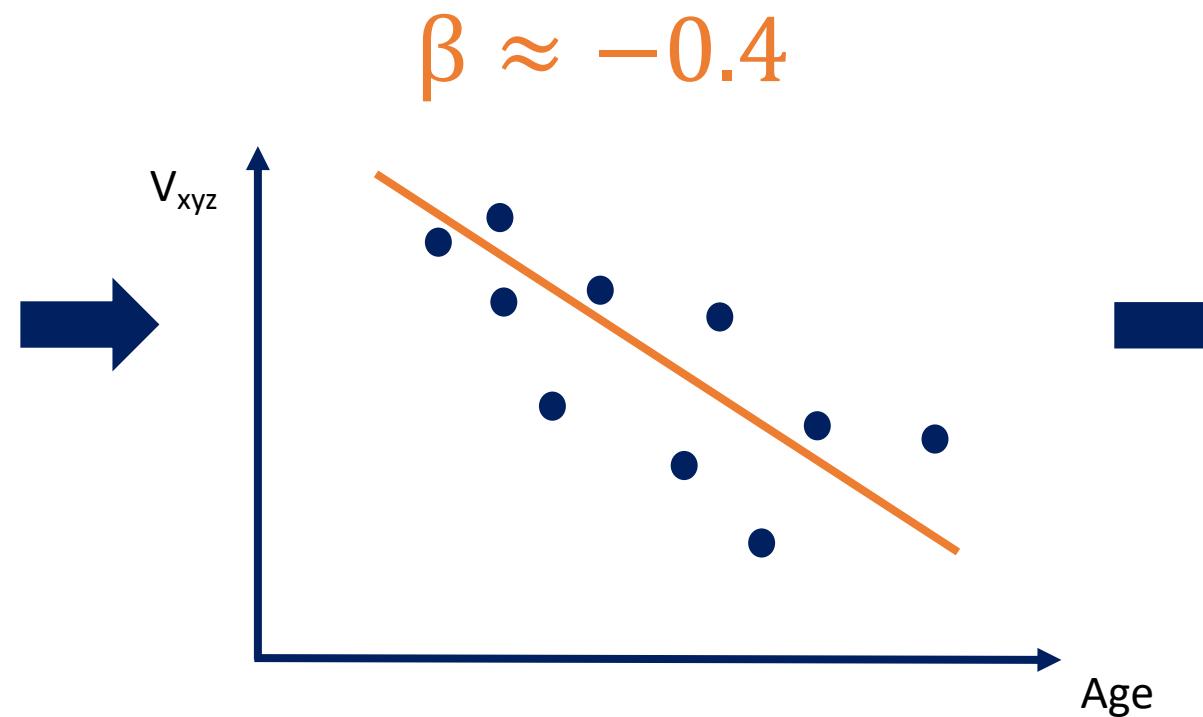
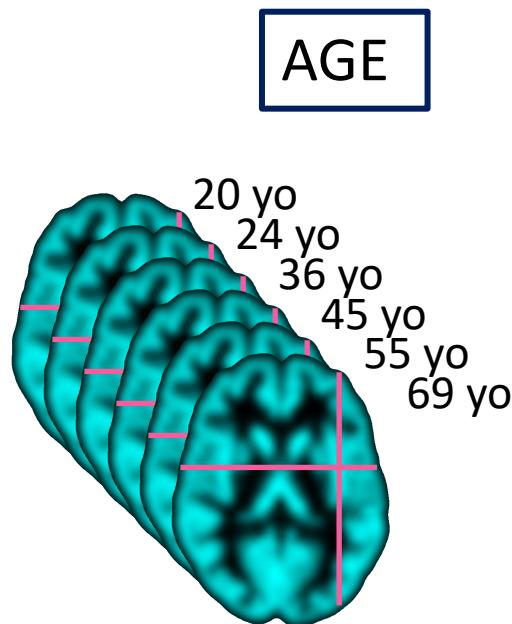


$$t = \frac{\bar{x}_a - \bar{x}_b}{\sqrt{\frac{S_a^2}{n_a} + \frac{S_b^2}{n_b}}}$$

Analysis for each individual voxel

Statistical parametric mapping (SPM)

CORRELATION WITH VARIABLE

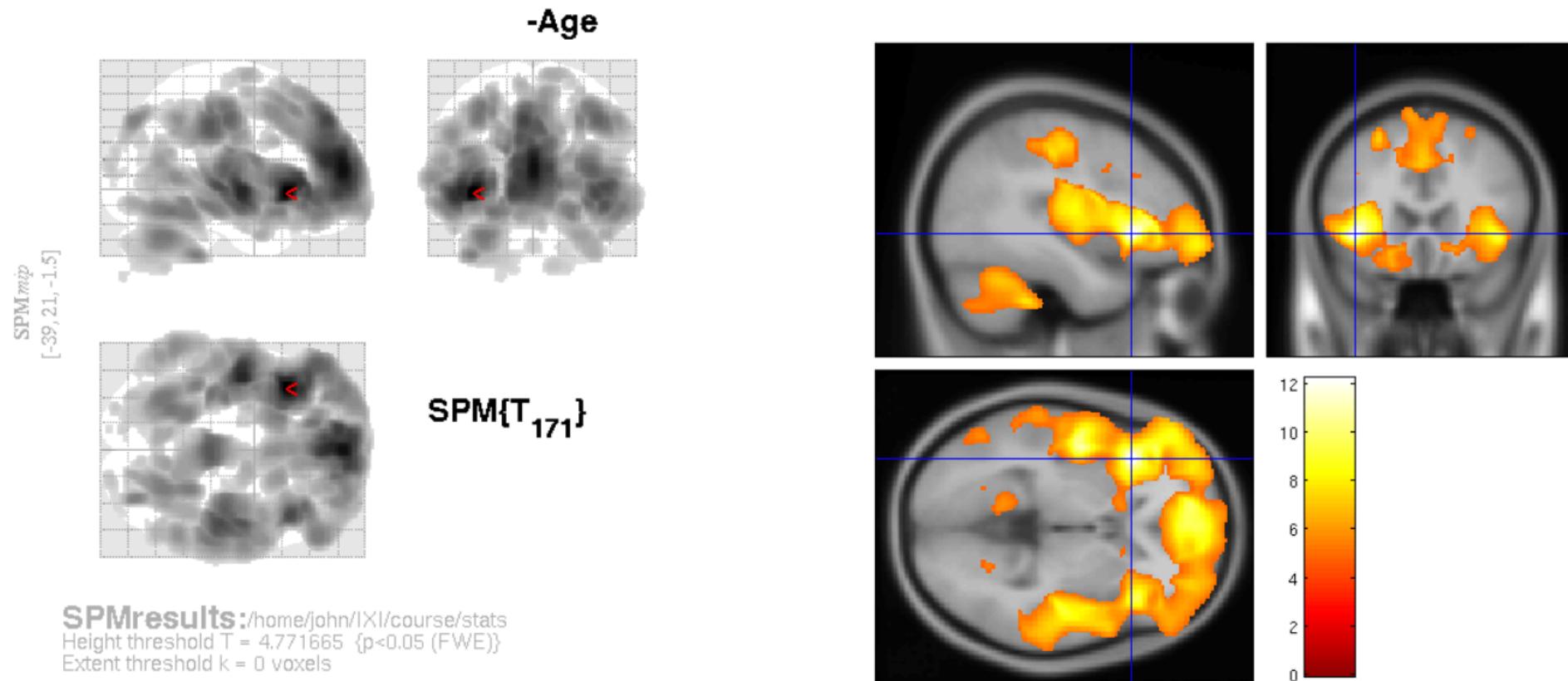


Anaysis for each individual voxel

Results

Highlighting of significant voxels

- Due to group differences
- Due to correlation to a variable (e.g. Age, disease duration)



Multiple comparison correction

Mass-univariate statistical tests for each voxel:
~ 200,000 statistical tests could be conducted

Given a probability of falsely rejecting the null at 5% ($p<0.05$), we expect **10,000 voxels to show significant differences by chance.**

VOXEL BASED CORRECTION

- Lower the alpha, e.g., $p<0.001$. 200 voxels.
- Bonferroni correction

$$\alpha_{new} = \frac{\alpha}{n} = \frac{0.05}{200\ 000} = 0.00000025$$

Very conservative + ignores spatial determinants

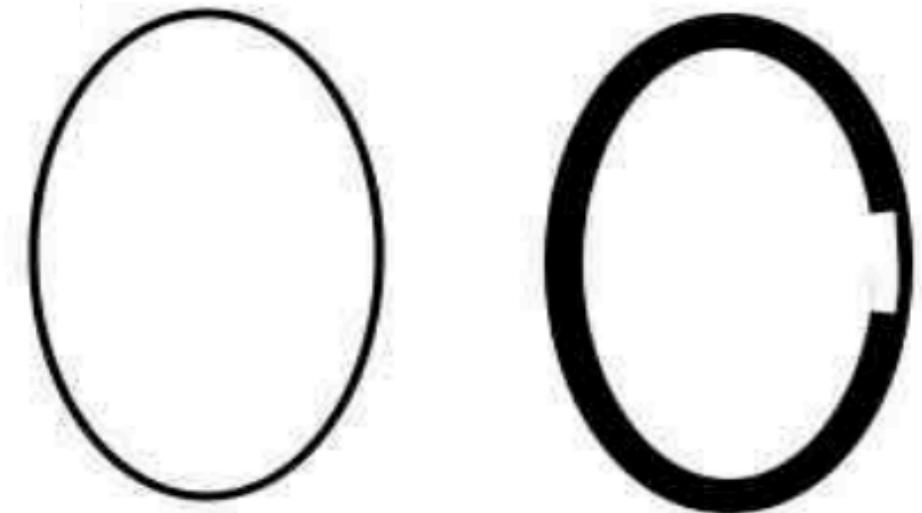
CLUSTER LEVEL CORRECTION

- Threshold at the cluster level
- Larger clusters less likely to occur by chance
- Could lose information on real smaller clusters

Cofounding and global variable

The VBM analysis should factor in potentially confounding variables, such as sex, age or **total volume**.

GLOBAL OR LOCAL DIFFERENCES?



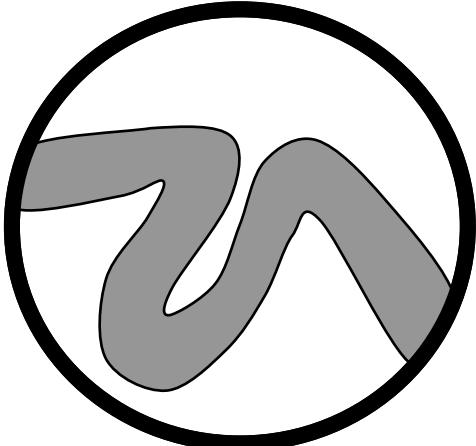
RIGHT -> Globally thicker BUT locally thinner

→ Results depend on whether we control for global differences

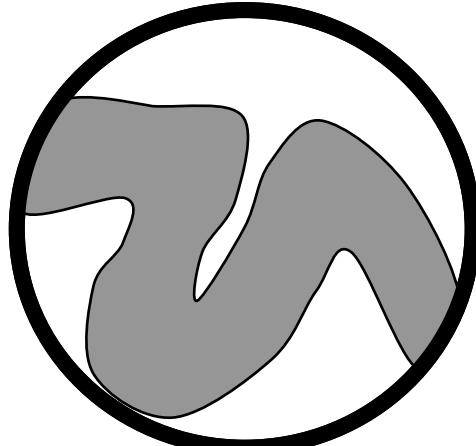
We can use ANCOVA-type models to remove variance explained by total/global volume

Interpretation of differences

Folding



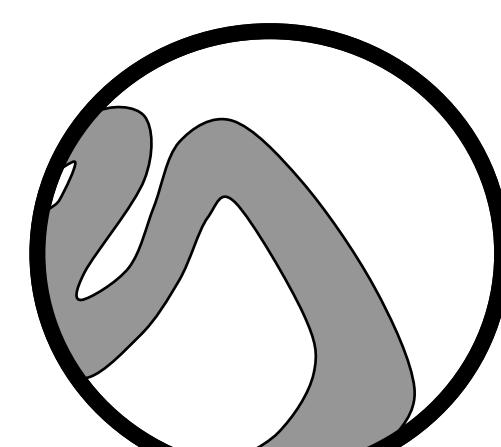
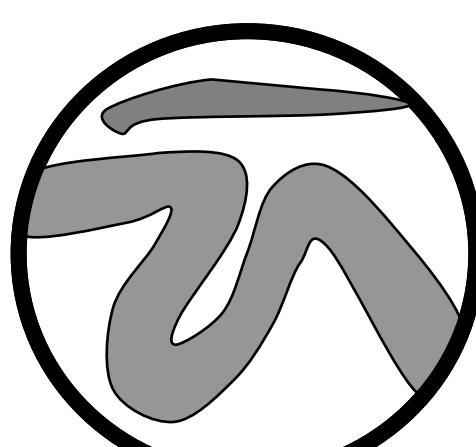
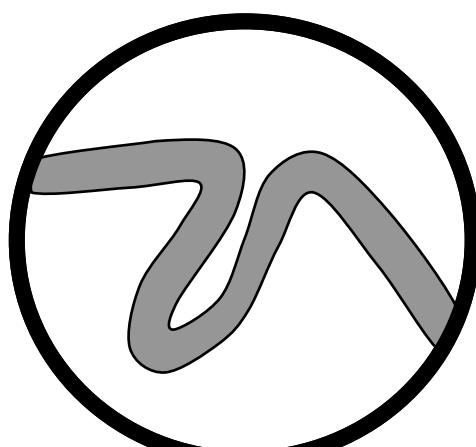
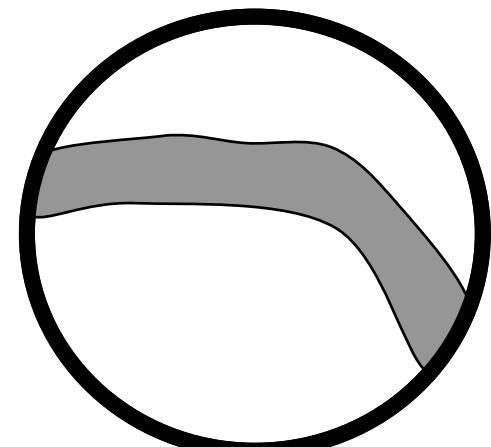
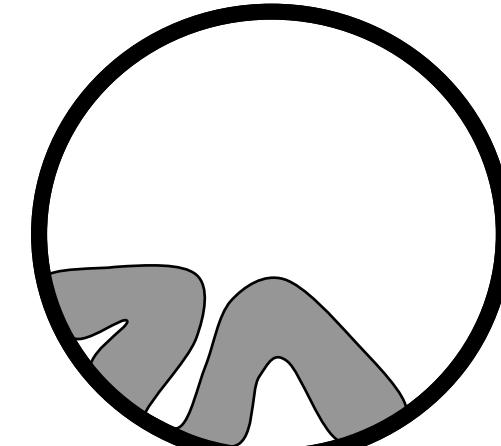
Thickness



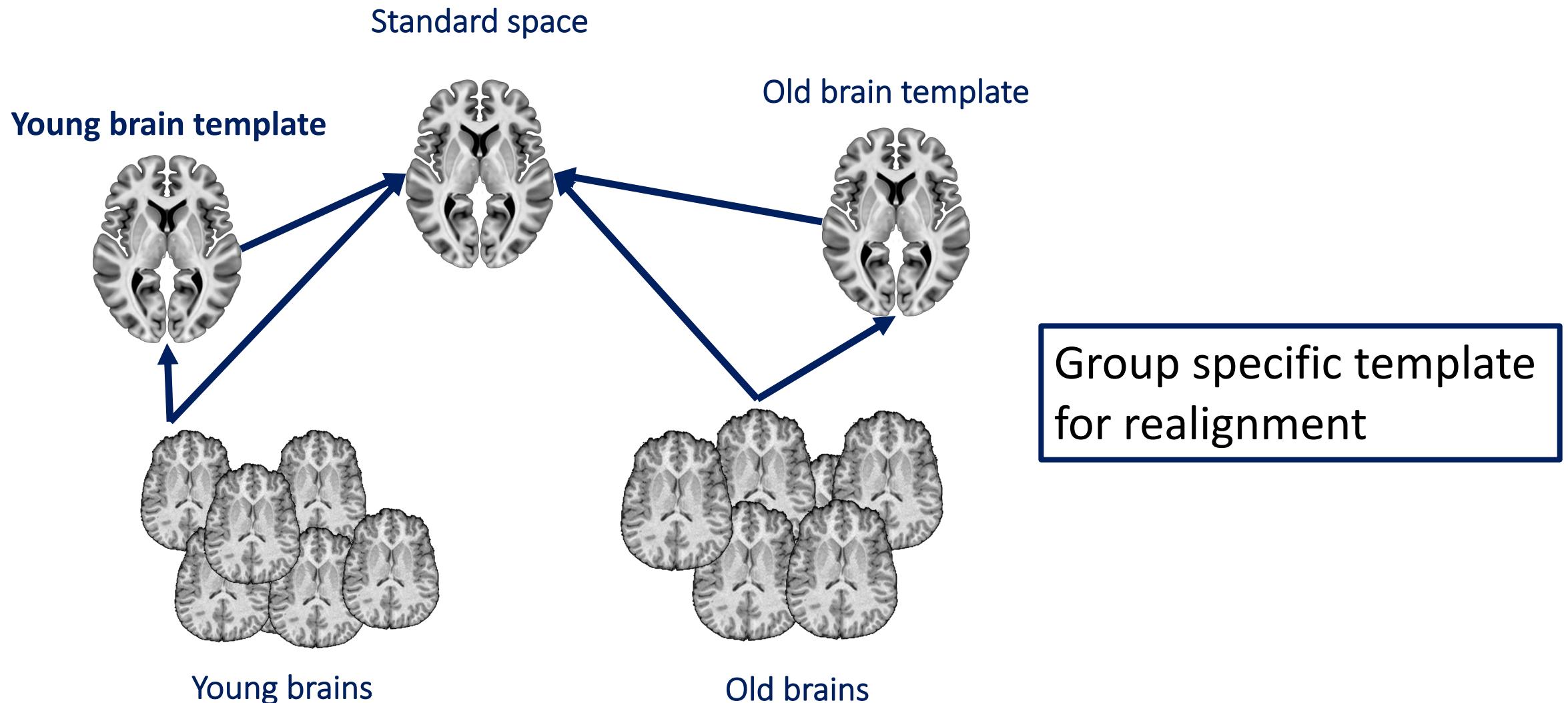
Mis-classify



Mis-register



DARTEL: Can help improve some issues caused by registration



Questions?

Thanks to Amy Jolly for the help with the slides