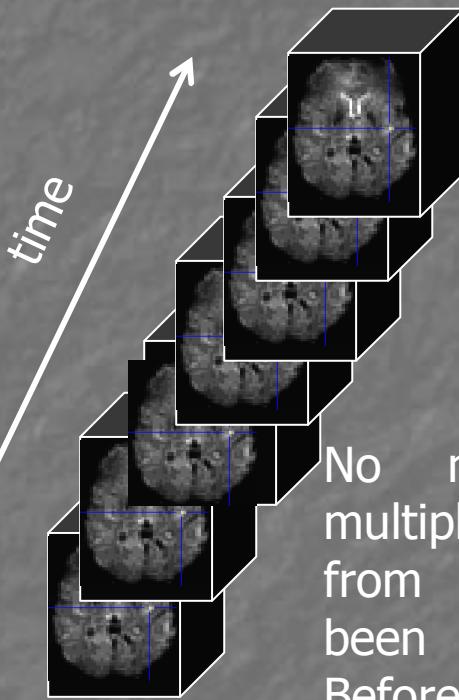


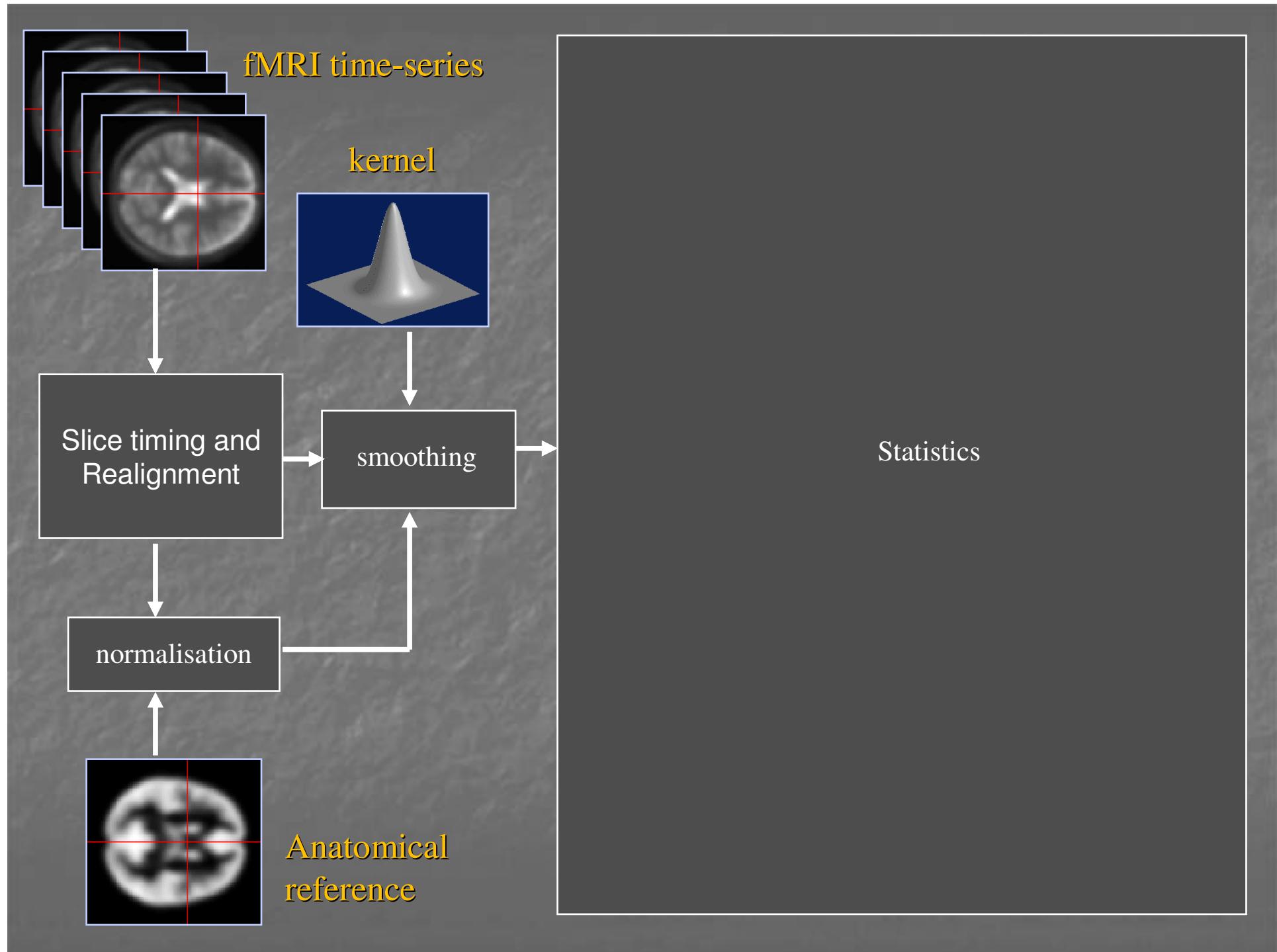
Functional MRI data preprocessing

Cyril Pernet, PhD

Data have been acquired, what's next?



No matter the design, multiple volumes (made from multiple slices) have been acquired in time. Before getting data out, we need to make sure the signal from each voxel contains the right temporal and spatial information.

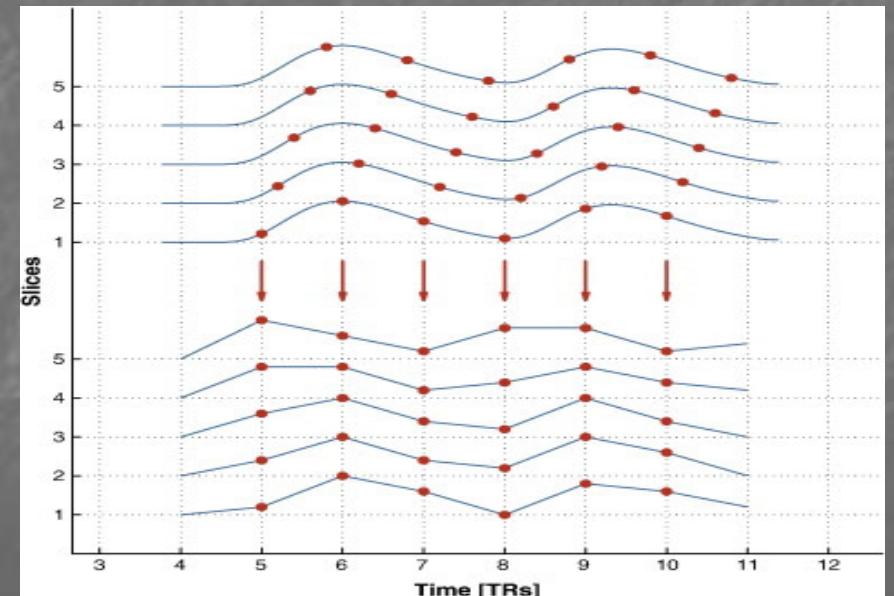


Slice Timing Correction

R. Henson, C. Buechel, O. Josephs, K. Friston
The slice-timing problem in event-related fMRI
NeuroImage, 9 (1999), p. 125-125

Slice Timing Correction

- Most of the time, fMRI data are acquired using sequential 2D imaging like single shot EPI. Since fMRI statistics are about analyzing the time course of the BOLD signal, exact timing with regard to the stimulus presentation is crucial.
- For instance, if you set a TR of 2 sec and acquire 30 slices, the acquisition time of 1 slice is ~ 66.66 ms ($2000/30$) and STC compensates for these sampling differences .

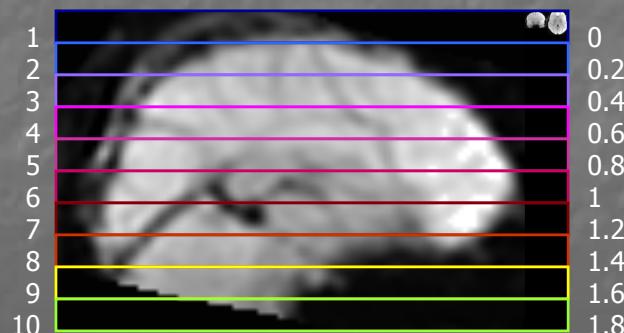


Slice Timing Correction

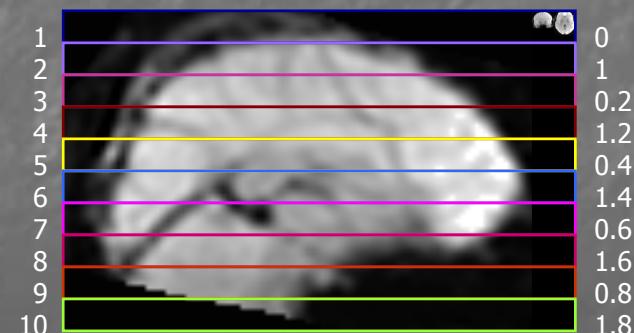
- STC consists in shifting the signal phase by a given amount to temporally align data. It is therefore mandatory to select a reference slice. The reference slice is usually the slice acquired in the middle of the sequence (maximum interpolation of TR/2) but any slice can be used.



Data are acquired either in sequential or interleaved mode and the middle of the sequence **is not** the middle of the brain!



Sequential acquisition
Ref slice 6



Interleaved acquisition
Ref slice 2

Slice Timing Correction

- TR of e.g. 2 sec with the middle temporal slice as reference is comparable to a dataset with a TR of 1 sec when the first (or last) slice acquired are used as a reference slice. This can be a reasonable practice, if the region of interest and putative activations are located near the first (or last) slice because it suppresses temporal interpolation effects in these areas.



Note that all regressors in the GLM also need to be adjusted for this shift in time according to the reference slice (e.g. TR / 2).

Slice Timing Correction

- Possible introduction of aliasing effects for signals at frequencies above the Nyquist sampling limit. Given a typical TR of 2 s ($f = 0.25 \text{ Hz}$) a minimal inter-stimulus interval (ISI) of more than 4 s is recommended. When using the slice acquired in the middle of the acquisition period (TR) as a reference slice, the signal needs to be shifted by TR / 2, therefore reducing the suggested minimal ISI to 2 s.
- It is sometimes advocated to not do the STC especially for TR<2 sec. However, Sladky et al. showed that is always beneficial. When not performed, the reduction of parameter estimates (effects) were more pronounced for long TRs, event-related designs and designs with shorter SOA (up to 63% !).

motion correction (realignment)

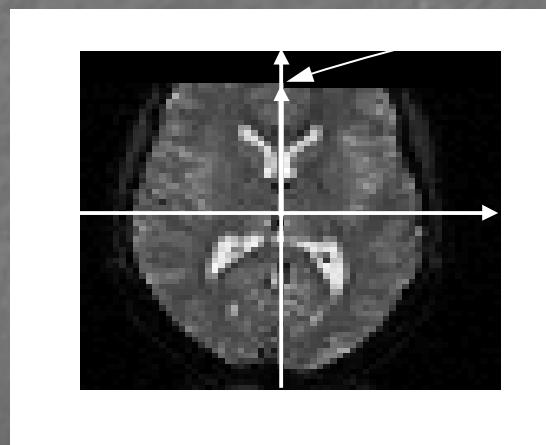
JV. Hajnal, R. Myers, A. Oatridge, JE. Schwieso, IR. Young, GM. Bydder
Artifacts due to stimulus-correlated motion in functional imaging of the brain.
Magn Reson Med, 3 (1994), p283–291.

Motion artefacts

- Subjects will always move in the scanner: swallowing for instance lead to motion along the x axis or some movements may be related to the tasks performed.
- Motion will results in a mismatch of the location of subsequent images in the time-series. Since the sensitivity of the statistical analysis is determined by the amount of residual noise in the image series, mismatch of the location will add to this noise and reduce the sensitivity.
- This type of motion problem corresponds to wholesale movements (*bulk-motion*) and is well corrected by realignment algorithms.

Motion correction: How?

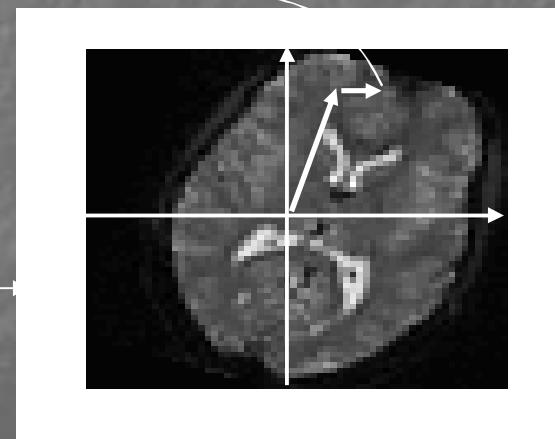
- Determine the rigid body transformation that minimises some cost function (a way to define the difference between 2 images as e.g. least square (SPM) or normalized correlation ratio (FSL)).
- Rigid body transformation is defined by: 3 translations in X, Y & Z directions and 3 rotations around the X, Y & Z axes.



Transform
co-ordinate



$$\begin{aligned}\Delta x &= 10\text{mm} \\ \Delta y &= 0 \\ \Delta \theta &= 10^\circ\end{aligned}$$



Motion correction: Quality check

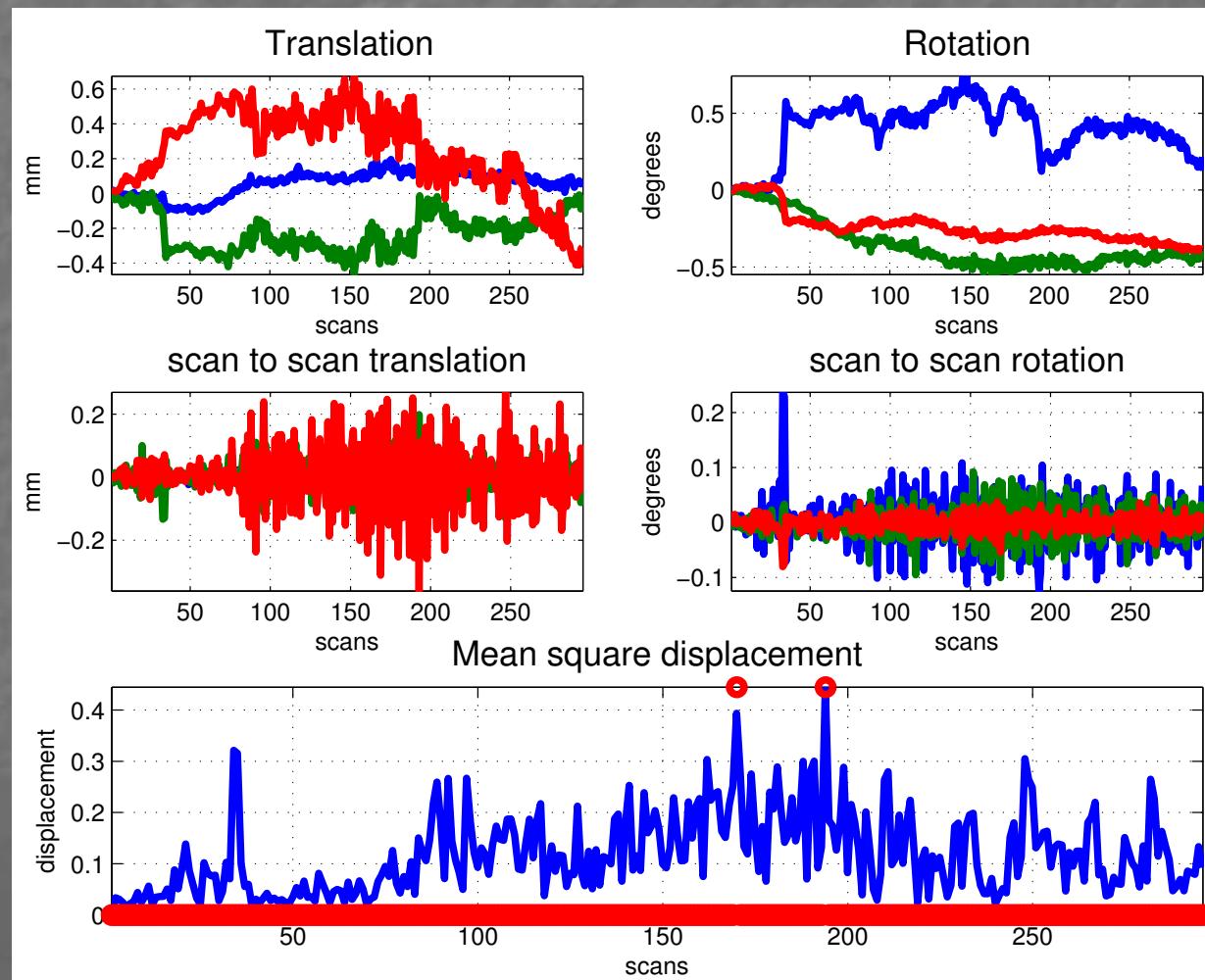
- Plots the estimates from the head motion algorithm
(might be useful to change angles into degrees and also plot the 1st derivative – outlier detection can then be run to identify ‘bad’ scans)
- Compute whole head distance between volumes and to the mean (mean square difference)
- Inspect the realigned data as a movie



Lots of tools available on websites
For SPM users, I wrote a script to do this automatically
see <https://sourceforge.net/projects/spm-qa-tools>

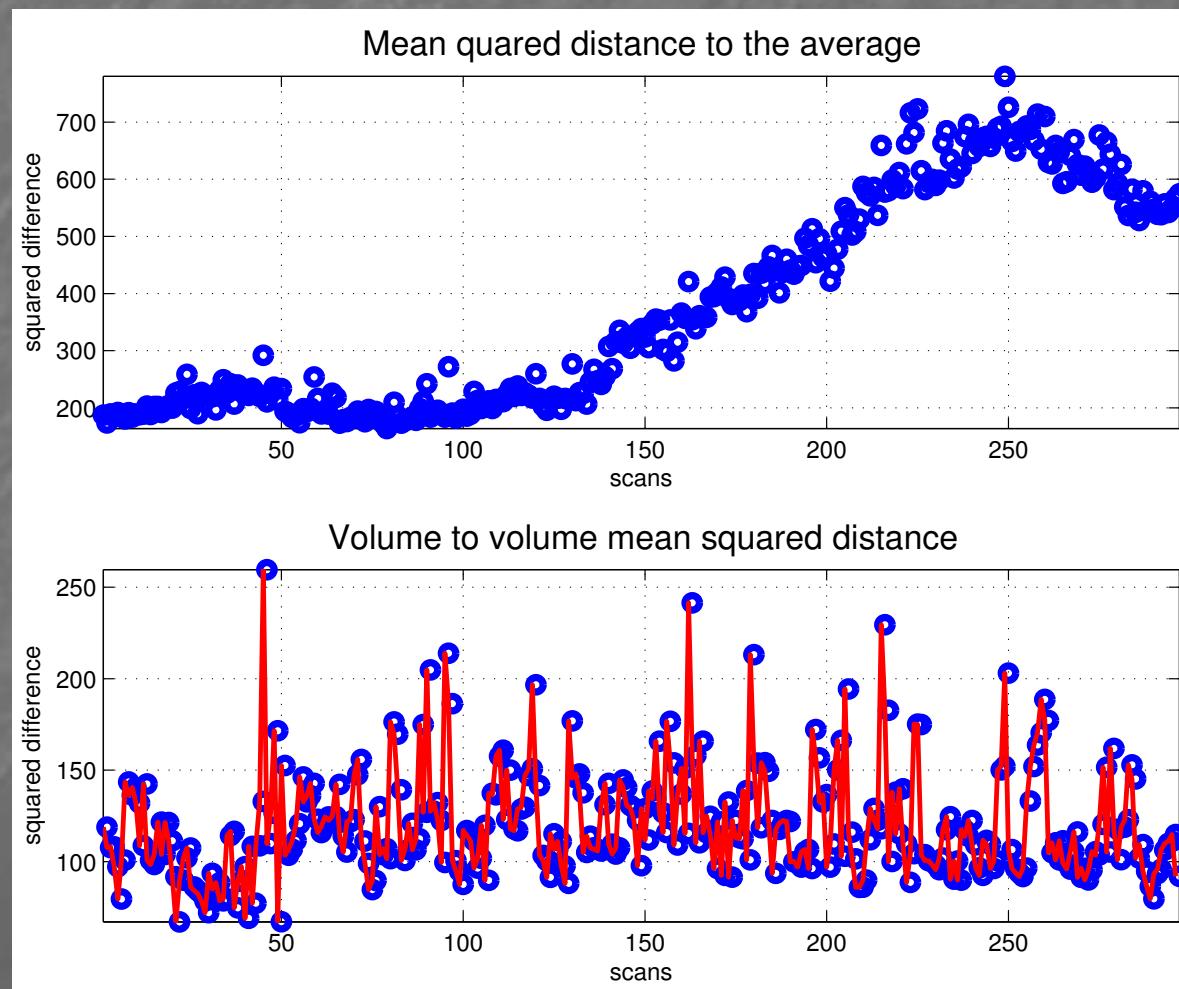
Motion correction: Quality check

Plots of head motion



Motion correction: Quality check

Whole head distances



Motion correction: Quality check

Movies

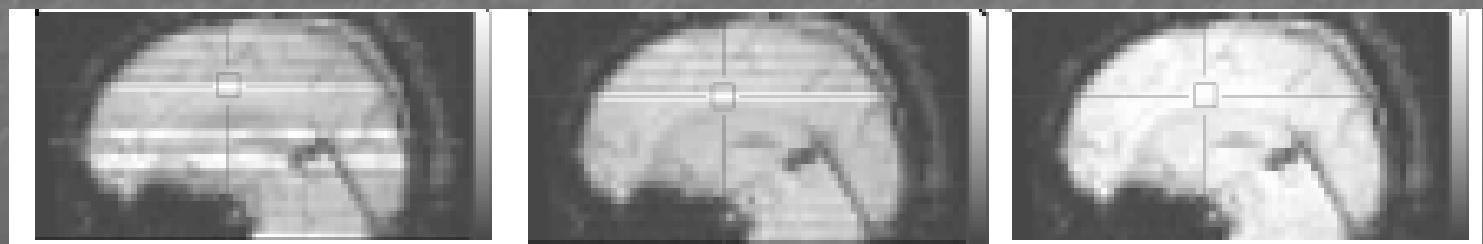


Even more motion artefacts

- Motion can also alter the MR signal because protons that moves into a voxel from a neighbouring slice have an excitation different from that expected by the scanner and the signal will not reflect well the tissue in that voxel. This *spin history effect* is not corrected using motion correction algorithms and Independent Component Analysis (ICA) or dedicated methods must be used.



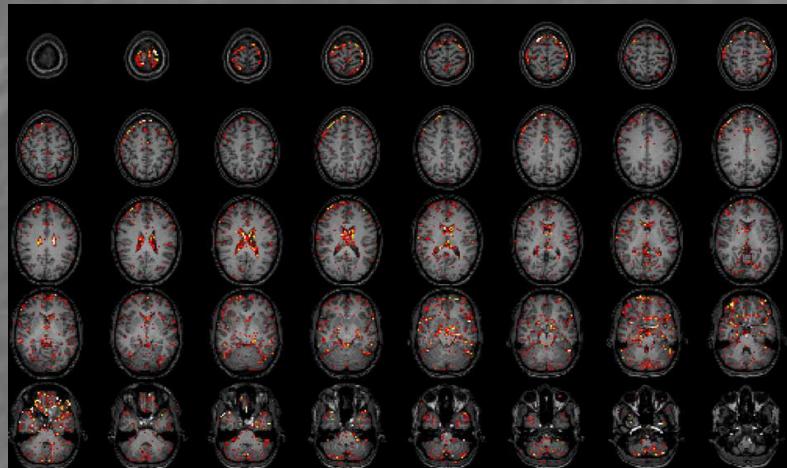
The *spin history effect* is seen as alternating bright and dark stripes with interleaved acquisitions. One can mitigate this by modelling bad images as dummy regressors and include movement parameter estimates into the analysis.



Picture credit: http://wagerlab.colorado.edu/wiki/doku.php/help/fmri_quality_control_overview

Even more motion artefacts

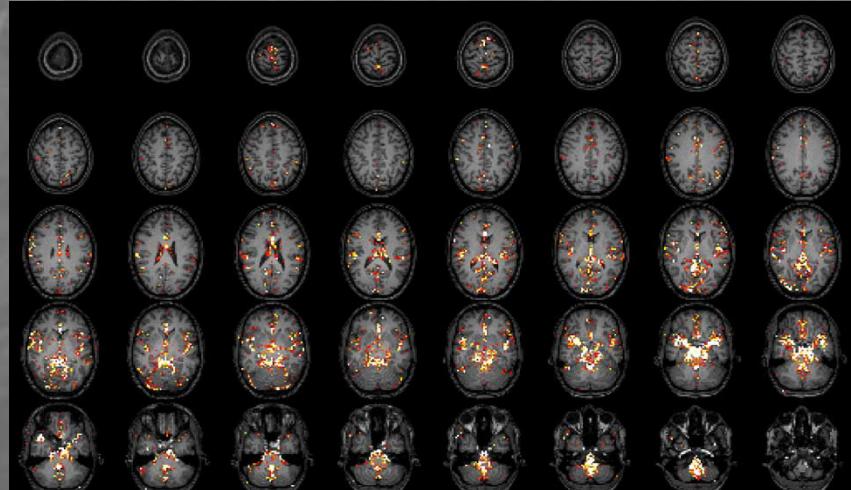
■ Physiological artefacts



cardiac-induced noise is dominant near larger vessels (e.g. medial cerebral artery and Circle of Willis)

- Physio monitoring
- Don't trust those regions

respiratory-induced noise is dominant near the edges of the brain as well as near in the larger veins and in the ventricles.



Spatial Normalization

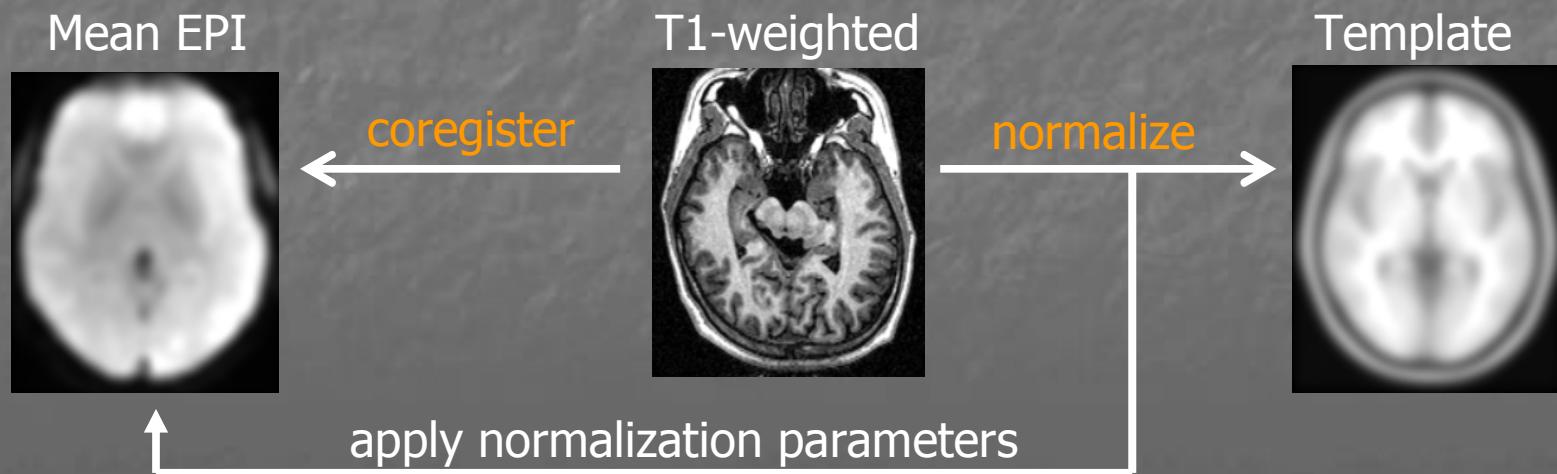
M, Holden
A review of geometric transformations for nonrigid body registration.
IEEE Trans Med Imaging, 27 (2008) , p 111-128

Normalization: Why?

- Inter-subject averaging
 - extrapolate findings to the population as a whole
 - increase activation signal above that obtained from single subject
 - increase number of possible degrees of freedom allowed in statistical model
- Enable reporting of activations as co-ordinates within a known standard space
 - e.g. the space described by **Talairach & Tournoux**, or the **MNI space** (SPM, FSL)

Normalization: How?

- Current methods works mainly on T1 weighted images (i.e. anatomical), so in practice one uses a 3 steps approach in which one i) coregister T1 and T2* (fMRI) data so that they are aligned and in the same space and ii) normalize the anatomical image (i.e. transform it to match the template) and iii) apply the parameters obtained to the fMRI images



T1 image preprocessing

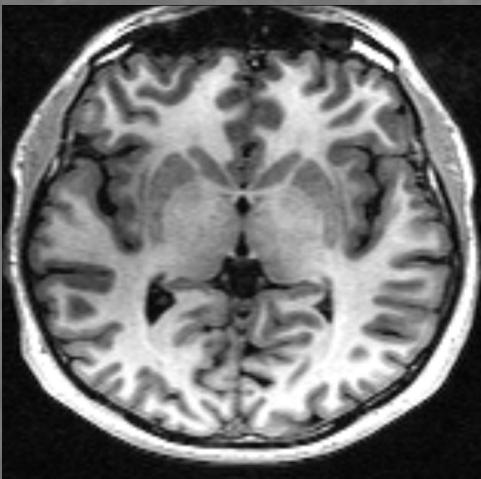
- The anatomical image is 1st preprocessed, depending on the method this includes: i) **Noise reduction**: improves local features using local smoothing (SUSAN algorithm in FSL), ii) **Bias correction**: from 3 Teslas, there is often broad intensity variations in space that need to be corrected, iii) **Brain extraction**: remove non brain tissue, iv) **Segmentation**: separate grey matter, white matter and CSF



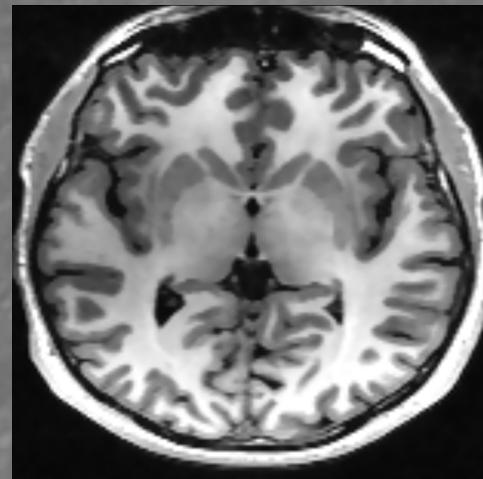
In SPM, the unified segmentation approach (Ashburner and Friston (2005) NeuroImage, 26, 839-851) combines/optimizes bias correction, segmentation, and normalization all in one, such as the prior probability of a voxel to belong to a tissue class is determined using a probabilistic atlas. In this framework 2 voxels with the same values can be classified differently using anatomical knowledge.

T1 image preprocessing

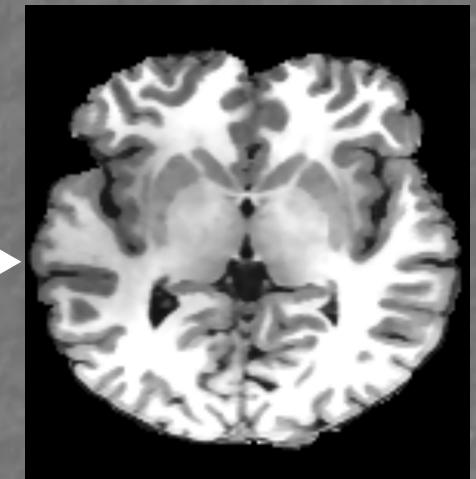
Original T1-weighted



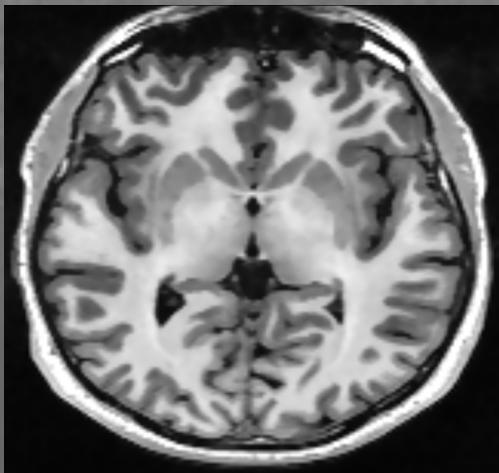
Noise reduction



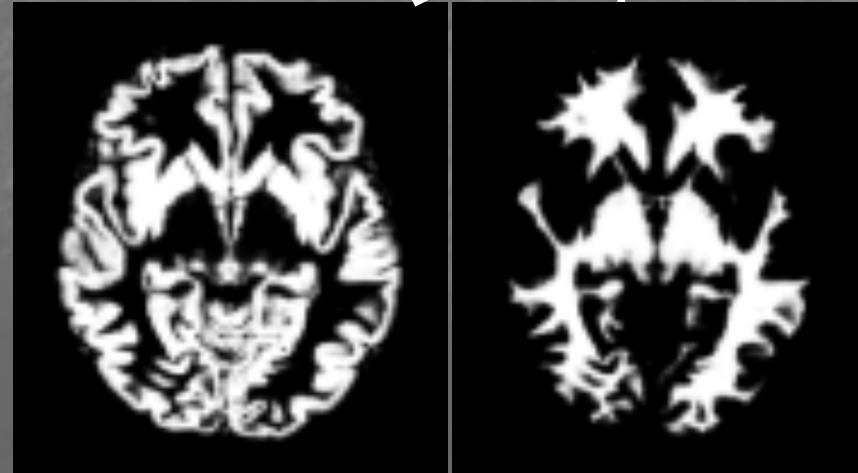
Brain extraction



Bias correction



Segmentation

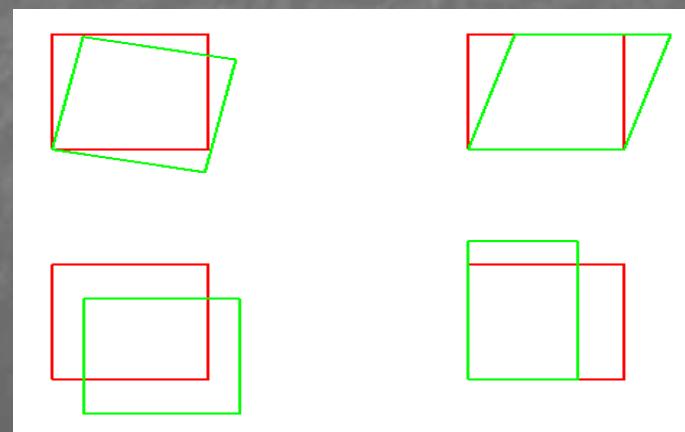


Volume-based normalization

- The first part of spatial normalisation is a 12 parameter **affine transformation**:

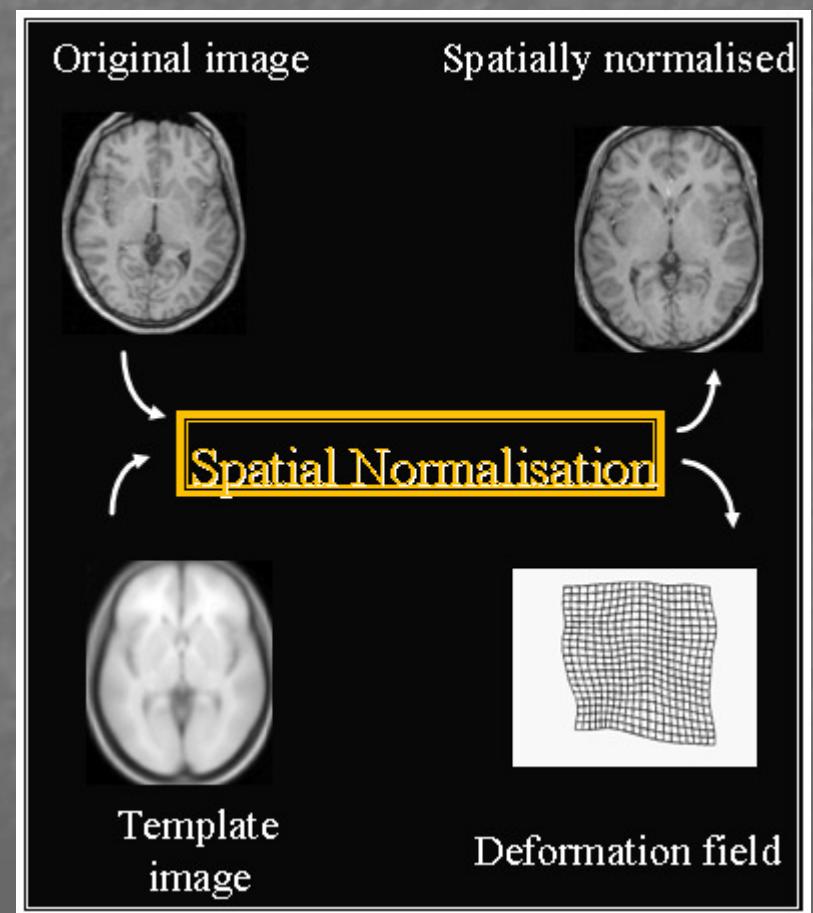
- 3 translations } **Rigid body transformation** (realignment)
→ does not change the size or shape of images
 - 3 rotations }
 - 3 scaling }
 - 3 shears }
- Allow change in overall size and shape

Affine transformation: any set of points that fell on a line prior transformation will continue to fall on a line after the transformation



Volume-based normalization

- The second part of the normalization uses non-linear deformations.
- DARTEL toolbox in SPM or FNIRT in FSL rely on diffeomorphism, that is the transformation from one image to the other can be represented as a vector field, describing the movements to apply at each voxel.



Surface-based Normalization

- Often more accurate to register cortical features than 'old' volume based methods. Often limited to cortical surface.
- A combined method (surface based for cortical and volume based for deep brain structures) is available in Freesurfer.

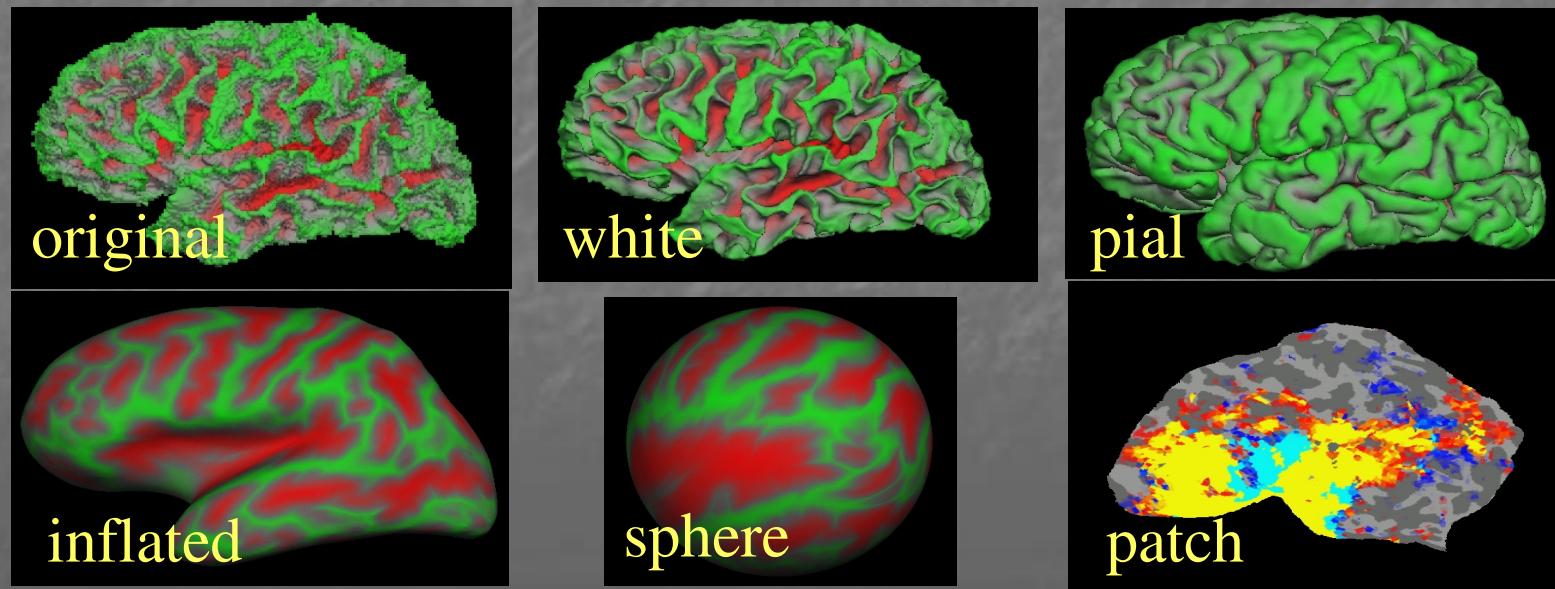
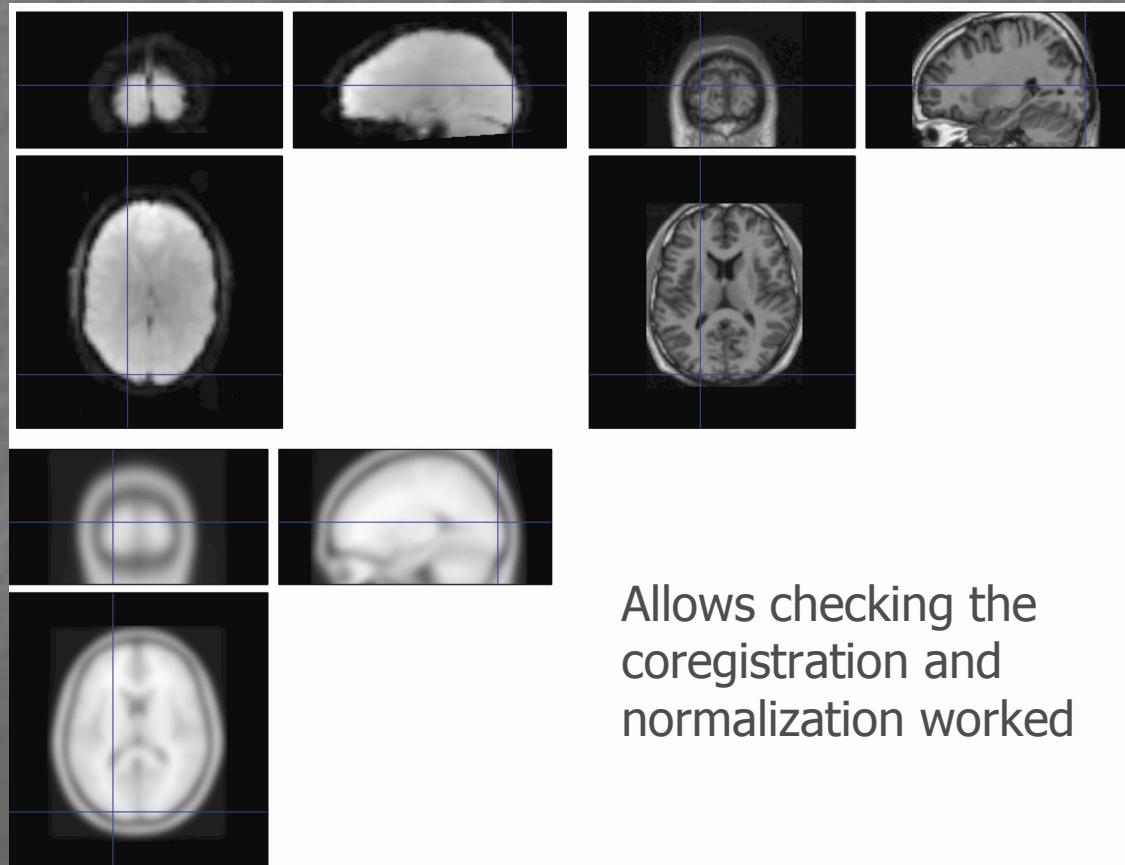


Image credit: Sarah Whittle &
Dominic Dwyer free-surface talk

Normalization: quality check

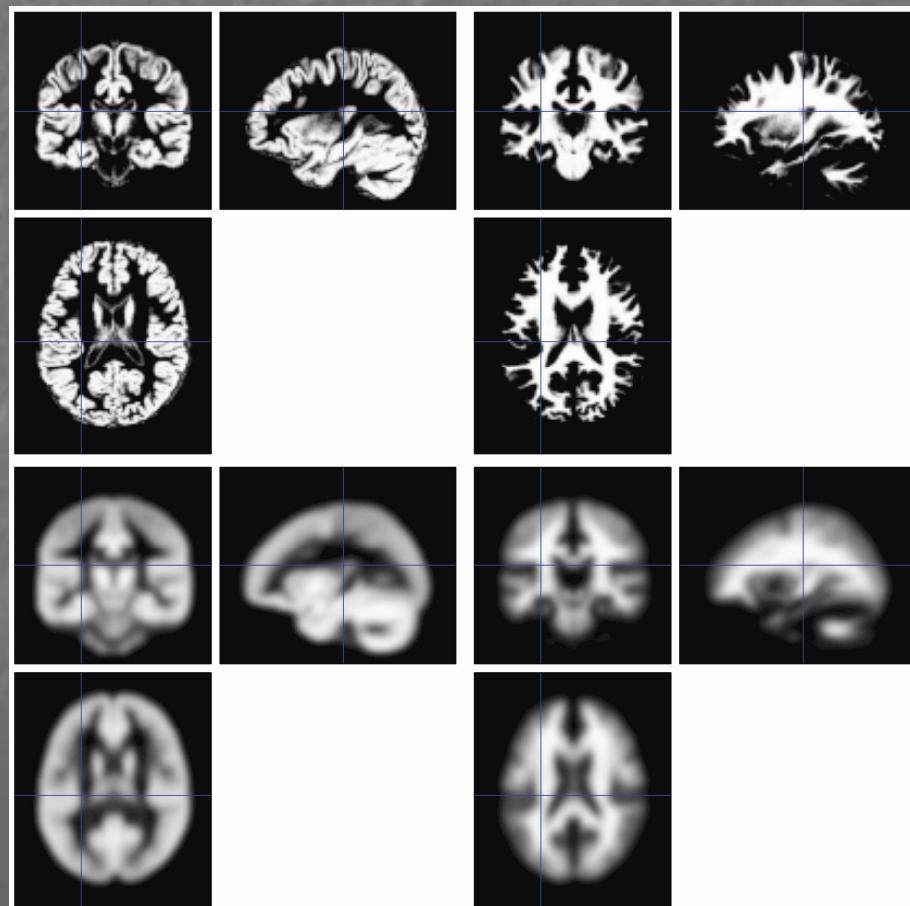
- Visual inspection using e.g. CheckReg in SPM
 - Mean T2*, T1, Template



Allows checking the coregistration and normalization worked

Normalization: quality check

- Segmented (normalized) gray matter and white matter vs. priors (i.e. the gray and white matter images used with the template)



Sometimes the overall shape looks ok but the segmentation was not too good – best to check this as well



Normalization: quality check

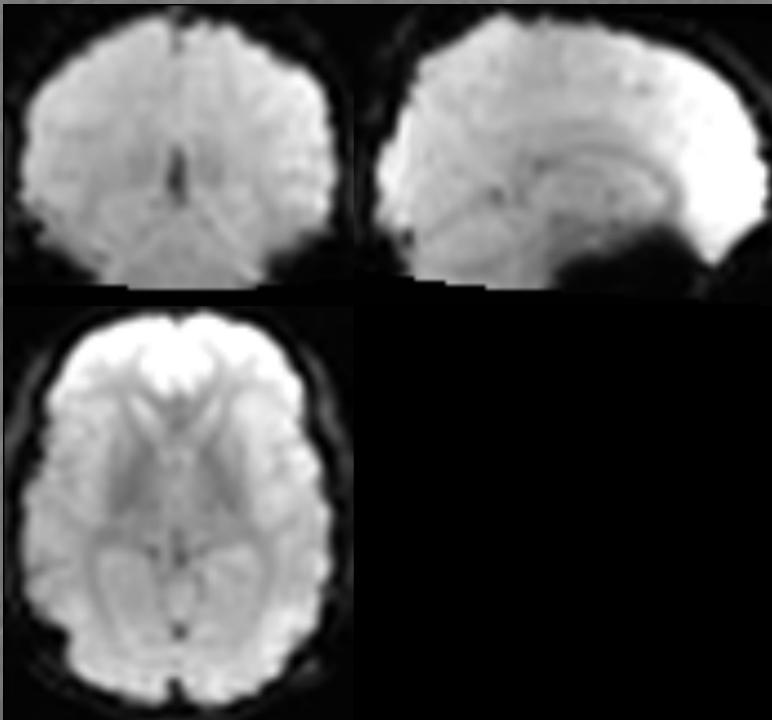
- Outlines of template vs. normalized T1
- Average normalized images
- Distance of normalized data to the template
- Movie



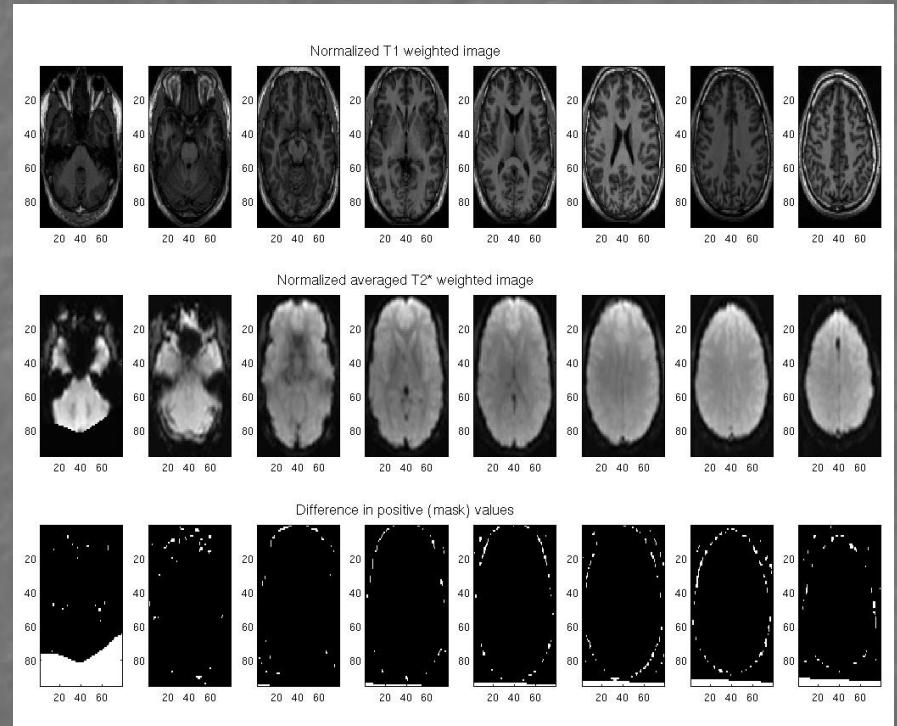
Lots of tools available on websites
For SPM users, I wrote a script to do this automatically
see <https://sourceforge.net/projects/spm-qa-tools>

Normalization: quality check

Average of Normalized T2* Image



Outlines Average/T1



Interpolation methods

P. Thevenaz, T. Blu & M Unser
Interpolation revised
IEEE Trans Med Imaging, 19 (2000), p 739-758

Write down the new images

- Each transformation (realignment, segment, normalize) comes with different methods of interpolation
- Each time an image is transformed, voxels don't align with the original ones and new voxels have to be created – their value is inferred from neighbours.

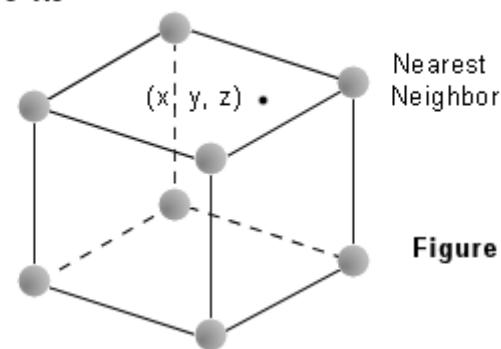


There is no need to apply each transformation. Parameters are stored in the header and for a new transform, previous parameters are applied and the new transform computed. Only when all is computed, one has to write images. At this stage all parameters are applied. This allows to interpolate voxel values only once.

Write down the new images

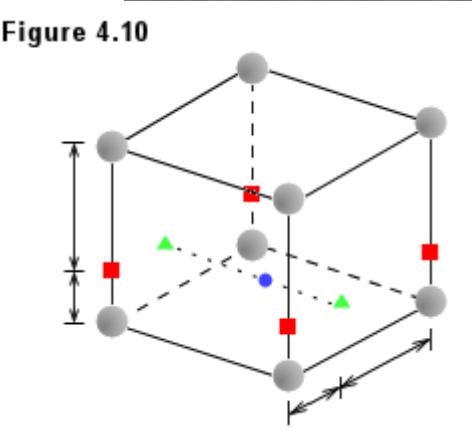
Interpolation methods include i) nearest neighbour ii) linear interpolation iii) higher-order interpolation like sinc interpolation or spline.

Figure 4.9

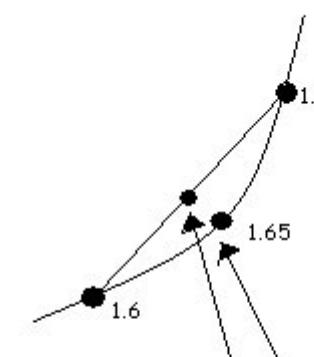


Loss of resolution

Figure 4.10



Tends to blur images

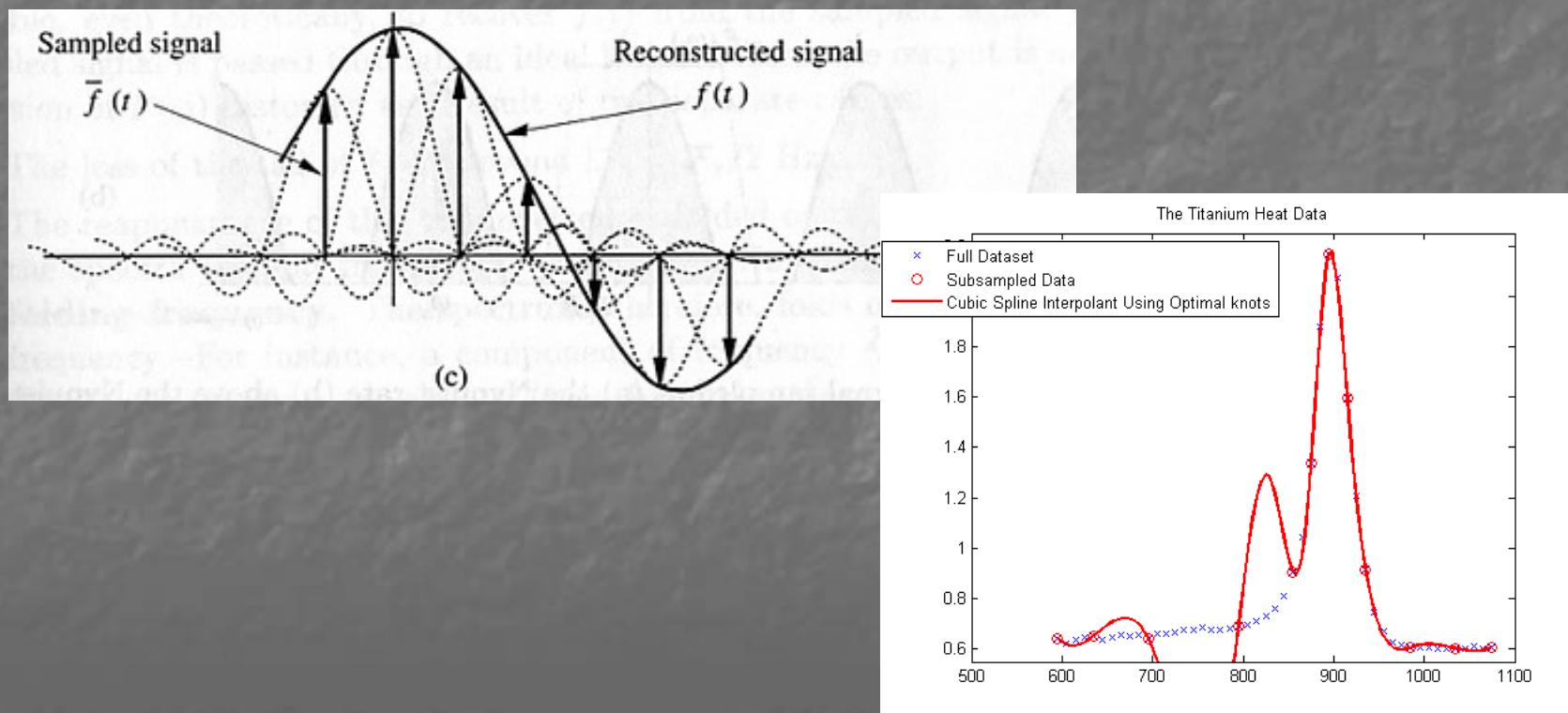


we want to know
what's going on at
this point (1.65)

<http://imp4-2008.blogspot.co.uk/>

Write down the new images

Interpolation methods include i) nearest neighbour ii) linear interpolation iii) higher-order interpolation like sinc interpolation or spline.

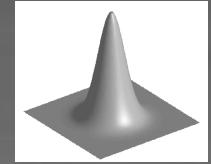


Smoothing

Smoothing: Why?

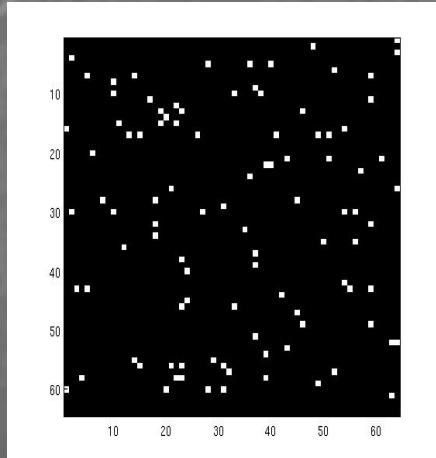
- Increase signal to noise by removing high-frequency information (small-scale changes in the image)
- Inter-subject averaging as spatial normalization cannot perfectly align all structures
- Increase validity of statistics when using random field theory.

Smoothing: How?

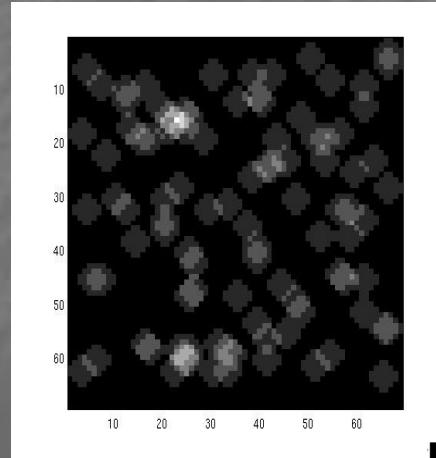


Each voxel, after smoothing, effectively becomes the result of applying a weighted region of interest. In SPM, smoothing is a convolution with a 3D Gaussian kernel, and the kernel is defined in terms of FWHM (full width at half maximum)

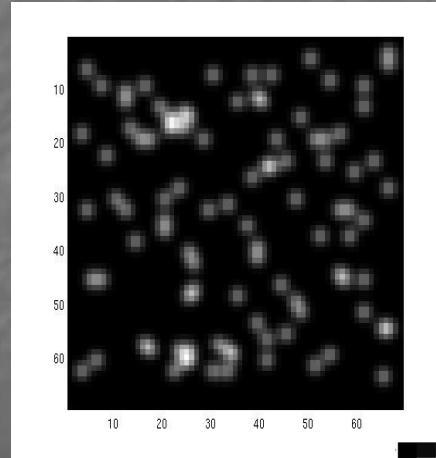
Before convolution



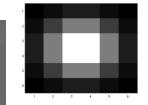
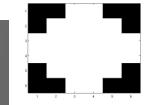
Convolved with a circle



Convolved with a Gaussian

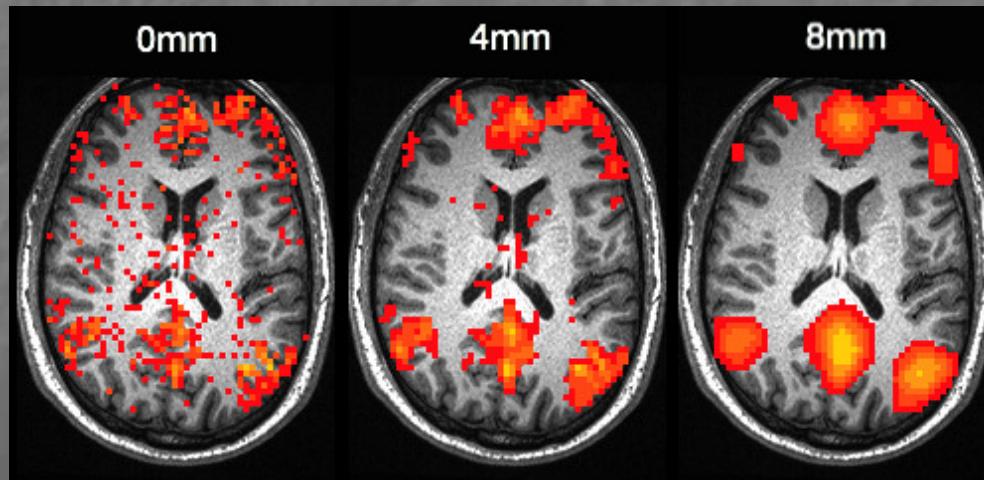


2D illustration using the conv2 function in Matlab



Smoothing: How much?

- Depends on effects to be detected → Matched filter theorem: smoothing kernel = expected signal.
- Practically FWHM 2 times the voxel size is appropriate for random fields theory, whilst improving SNR.
- May consider varying kernel size if interested in different brain regions (e.g. hippocampus -vs- parietal cortex))



Picture credit: <http://fcp-indi.github.com/docs/user/smoothing.html>