fMRI 1: preprocessing and diagnostics

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Outline

- How to pre-process fMRI data

- How to assess data quality (and adequacy of preprocessing corrections)

- A brief intro to the automatic analysis (AA) batch processing package for Matlab
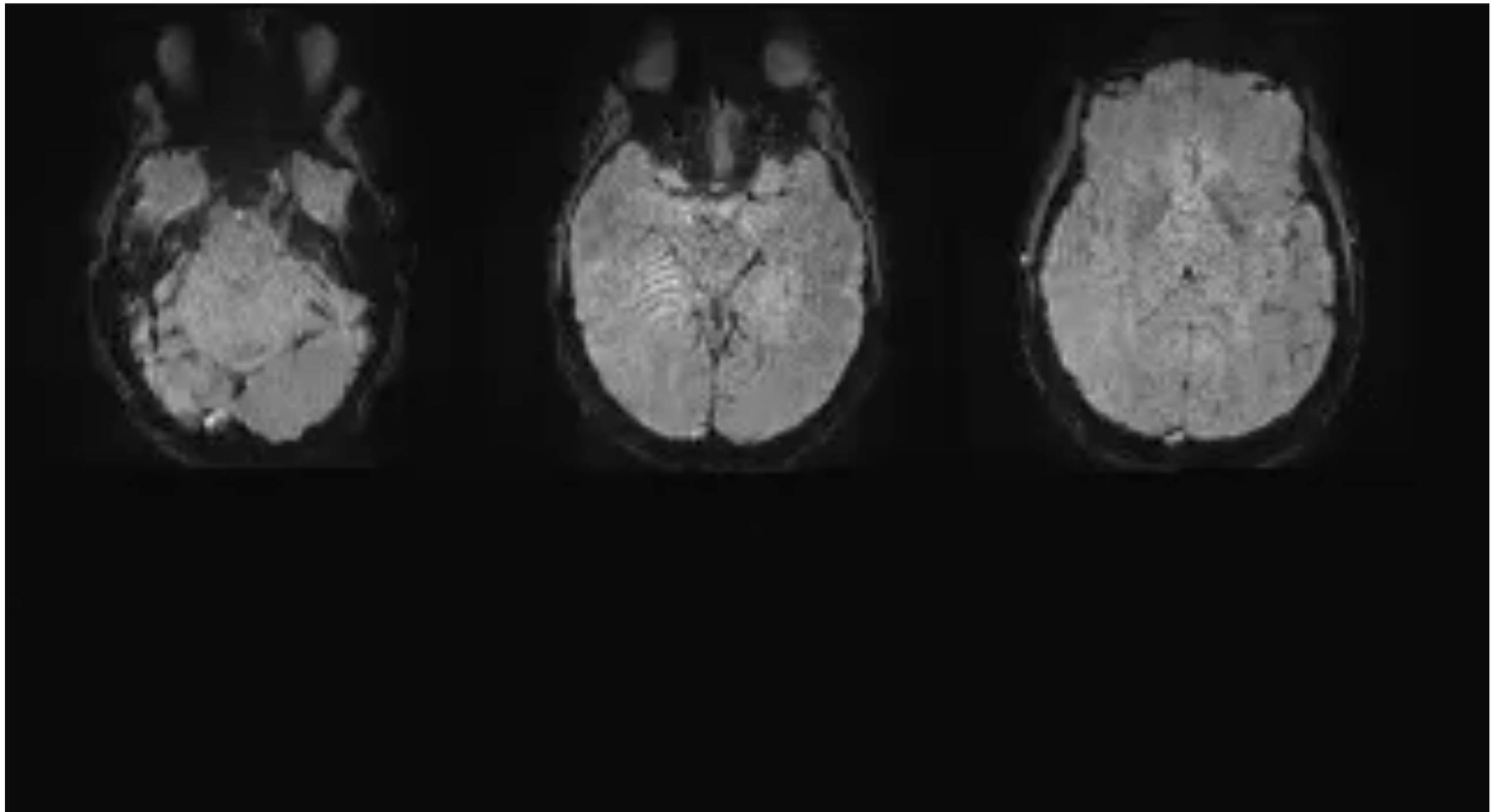
A typical fMRI dataset

- Anatomical data: T1-weighted, 3D, 1 per subject or session
  - (ME)MPRAGE sequence, minimally distorted
  - High spatial resolution (~1 mm isotropic)
  - Optimised for structural contrast (grey vs white matter)
  - Acquisition time ~5 minutes

- Functional data: T2*-weighted, 4D, 1 per scan
  - EPI sequence, distorted
  - Lower spatial resolution (2-3 mm, perhaps non-isotropic)
  - Optimised for functional contrast (oxy- vs de-oxy haemoglobin)
  - Acquisition time ~2 seconds per image (20-30 slices)

- Fieldmaps: 2×3D, 1 per session
  - Dual-echo GE sequence, undistorted
  - Lower spatial resolution (similar to fMRI)
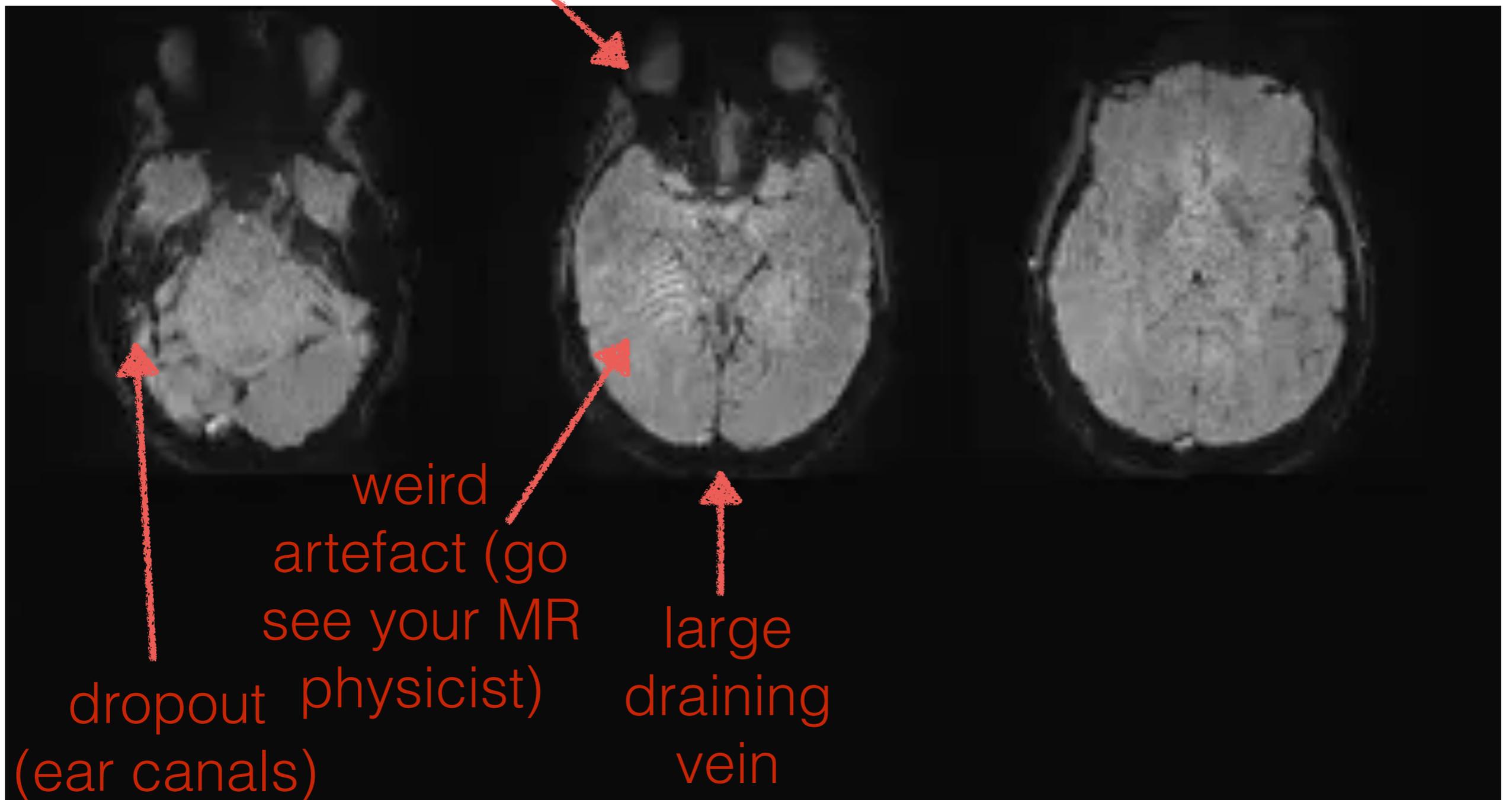 - Map of magnetic field inhomogeneities
  - Acquisition time ~1-2 minutes.
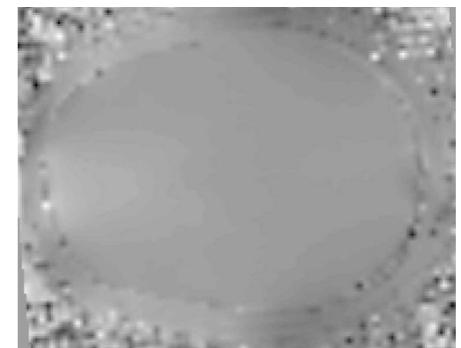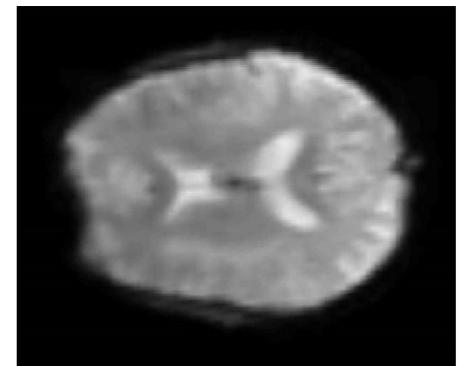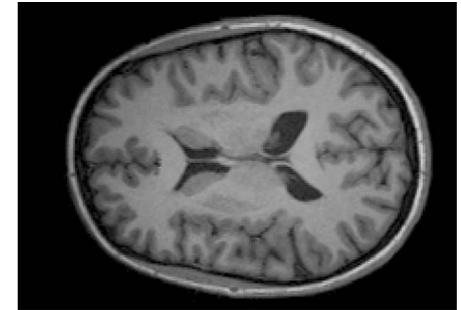
What does fMRI data look like?

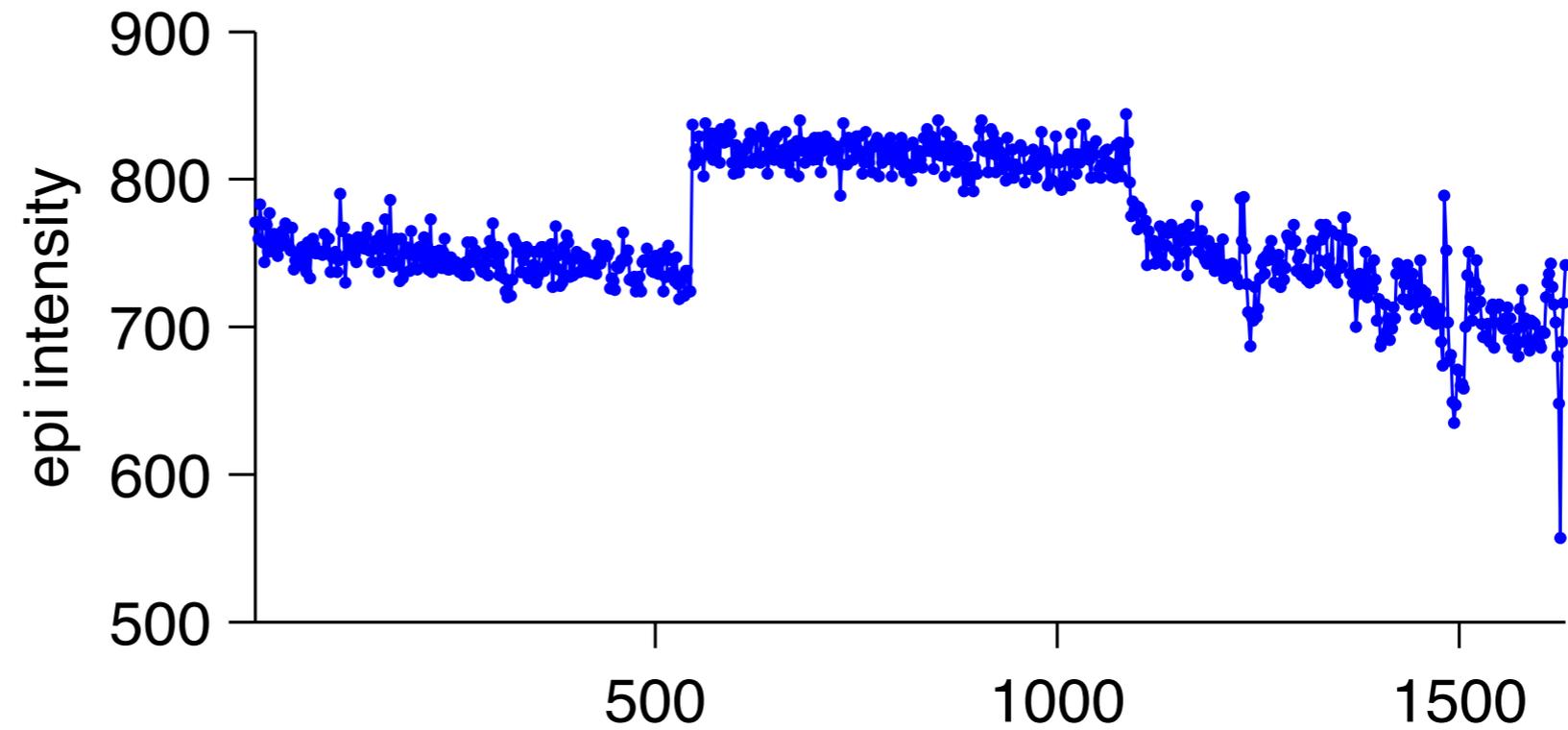3D EPI, GRAPPA R=2, 2mm iso voxels, TR=1.06s
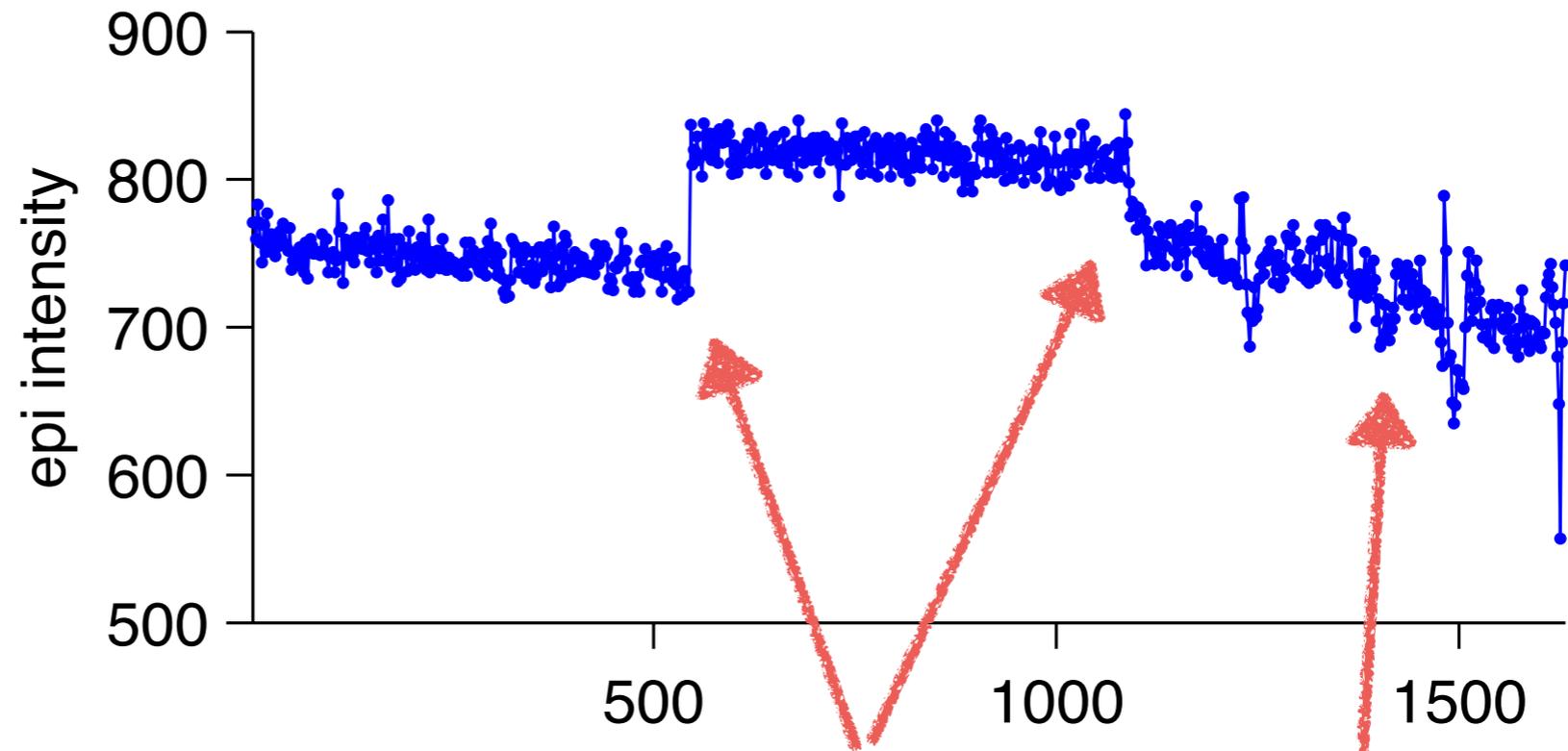
What does fMRI data look like?

eye blink / movement effect
(not just in eye balls!)

dropout
(ear canals)

weird
artefact (go
see your MR
physicist)

large
draining
vein

Example voxel - raw data
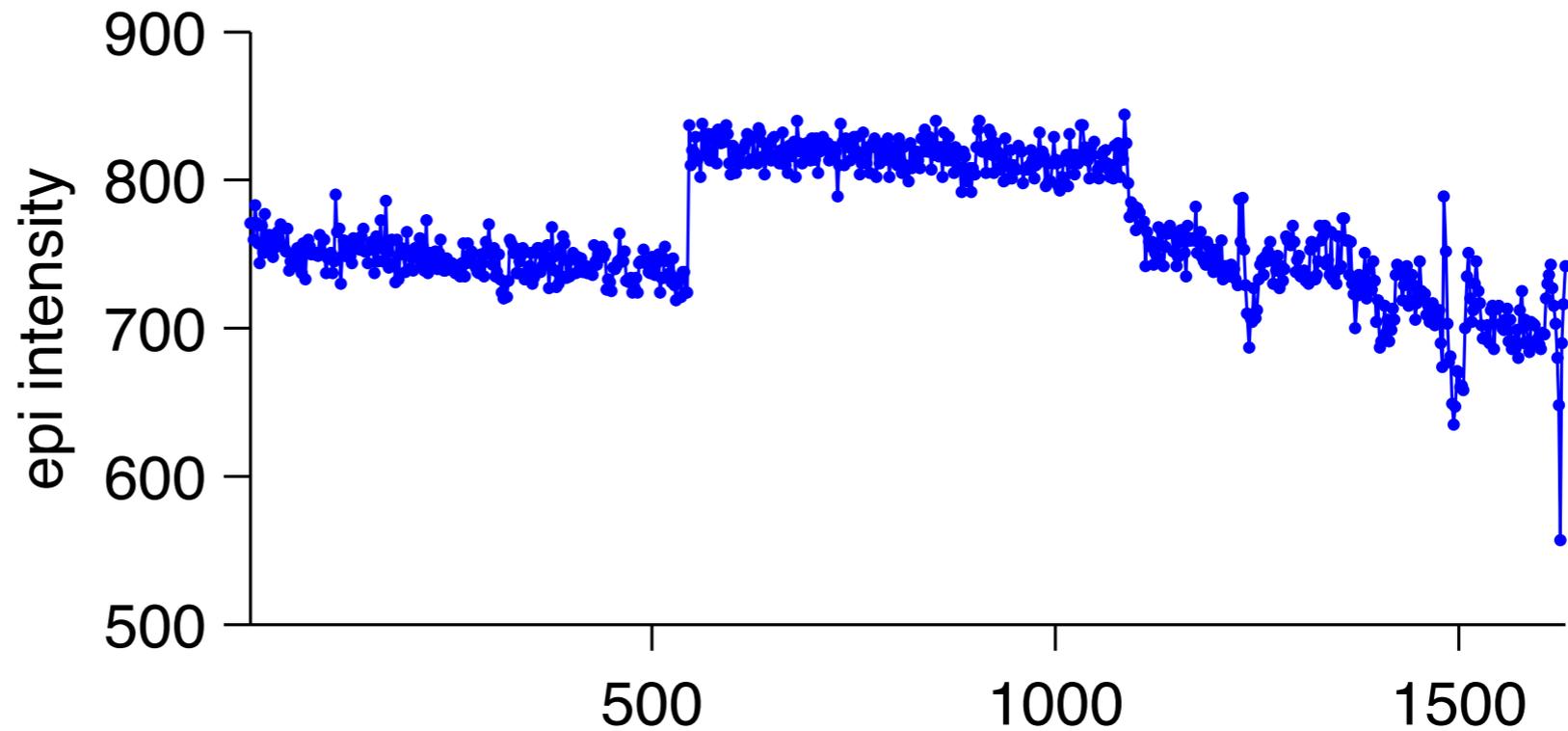
Example voxel - raw data

run transitions
(head movement
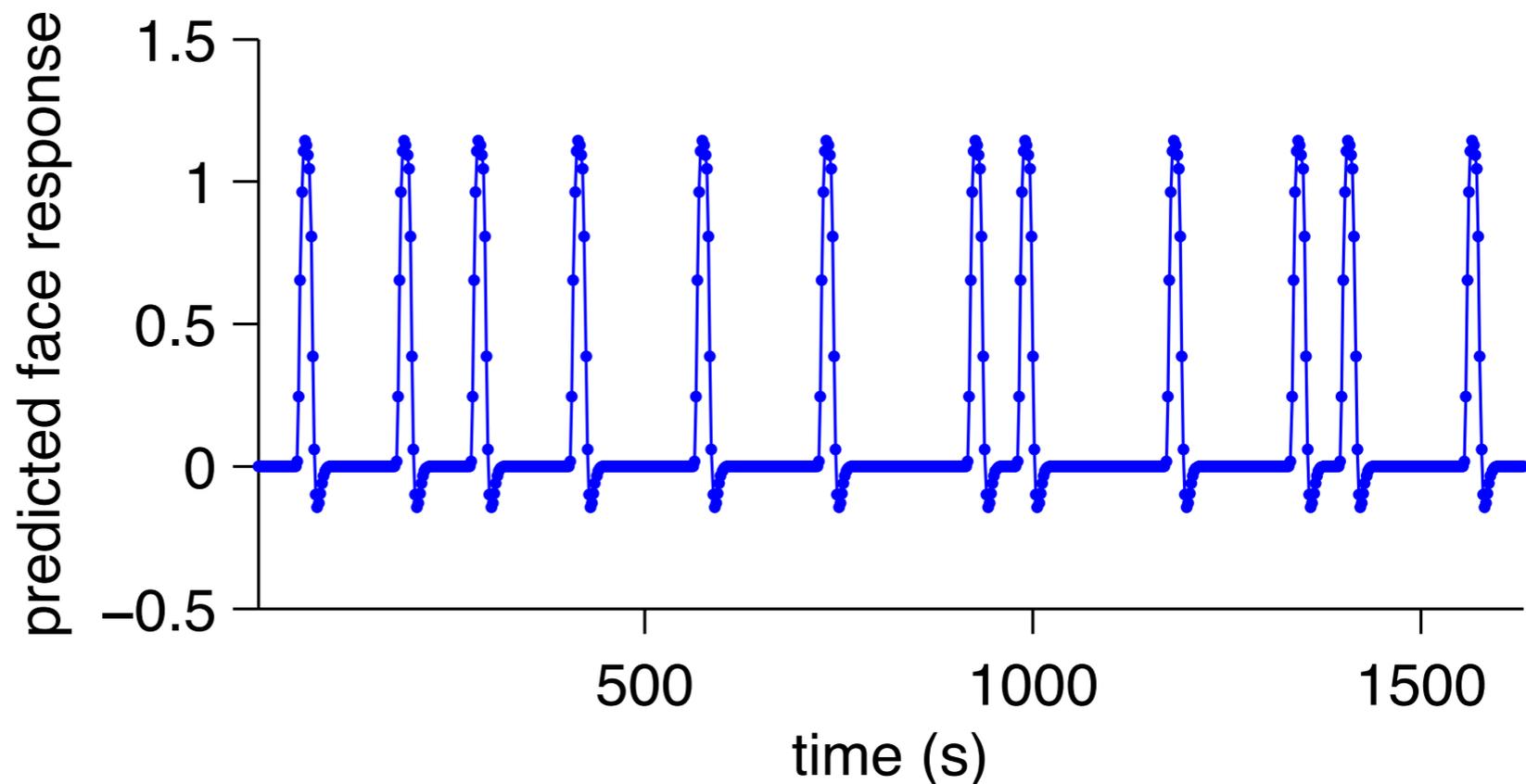between scans?)

lots of signal drift
vs other runs
(head movement
during this scan?)
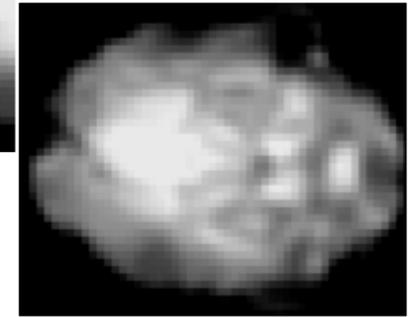
Example voxel - raw data

The (raw) fMRI data

The cognitive model

Not much hope of this working without signal processing

So many problems

- HRF is delayed and temporally smooth

- Signal intensity drifts over time

- EPI images are distorted

- The head is likely to move during the fMRI scan

- Slices within the same image come from different time points (assuming standard 2D EPI)

- Head movements between fMRI scans and structural scans

- Signal is typically spatially extended

- Even if we can correct the above, different people's brains are different shapes, so how do you do group analysis?

So many problems

Solutions

- HRF is delayed and temporally smooth
- Signal intensity drifts over time
- EPI images are distorted
- The head is likely to move during the fMRI scan
- Slices within the same image come from different time points (assuming standard 2D EPI)
- Head movements between fMRI scans and structural scans
- Signal is typically spatially extended
- Even if we can correct the above, different people's brains are different shapes, so how do you do group analysis?

Just model it! Next lecture

Just model it! Next lecture

Use a B0 fieldmap to undistort

Rigid-body motion correction (realign)

Slice timing correction

Coregister headers

Spatial smoothing

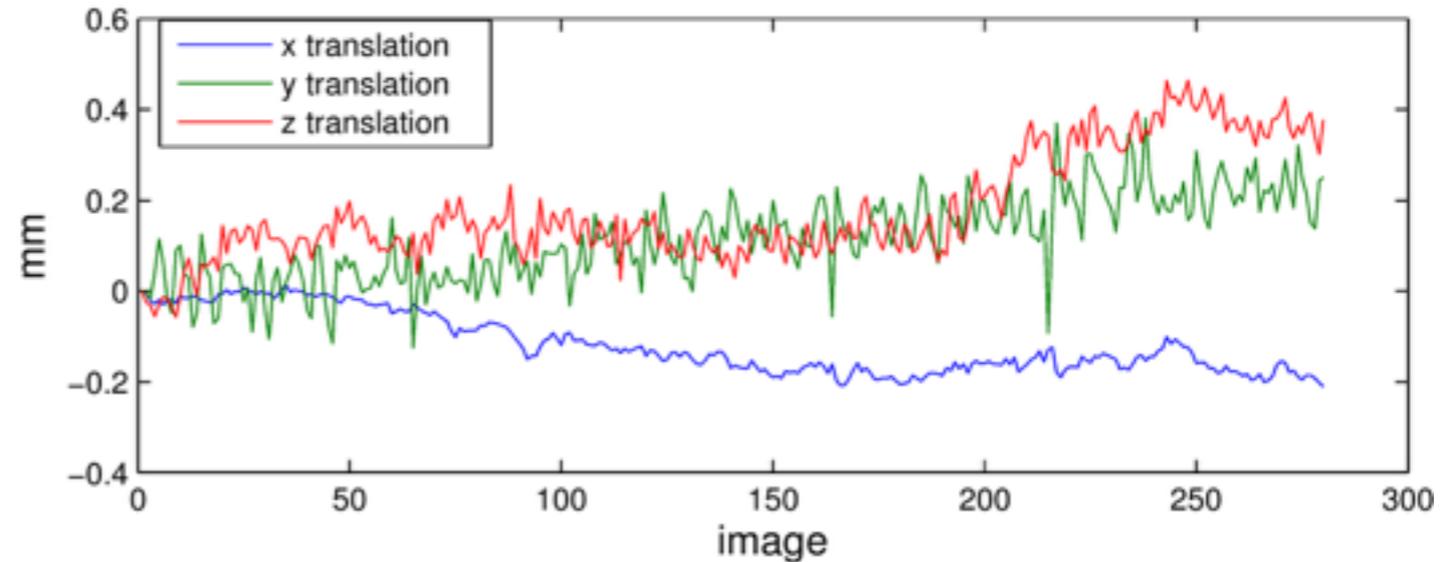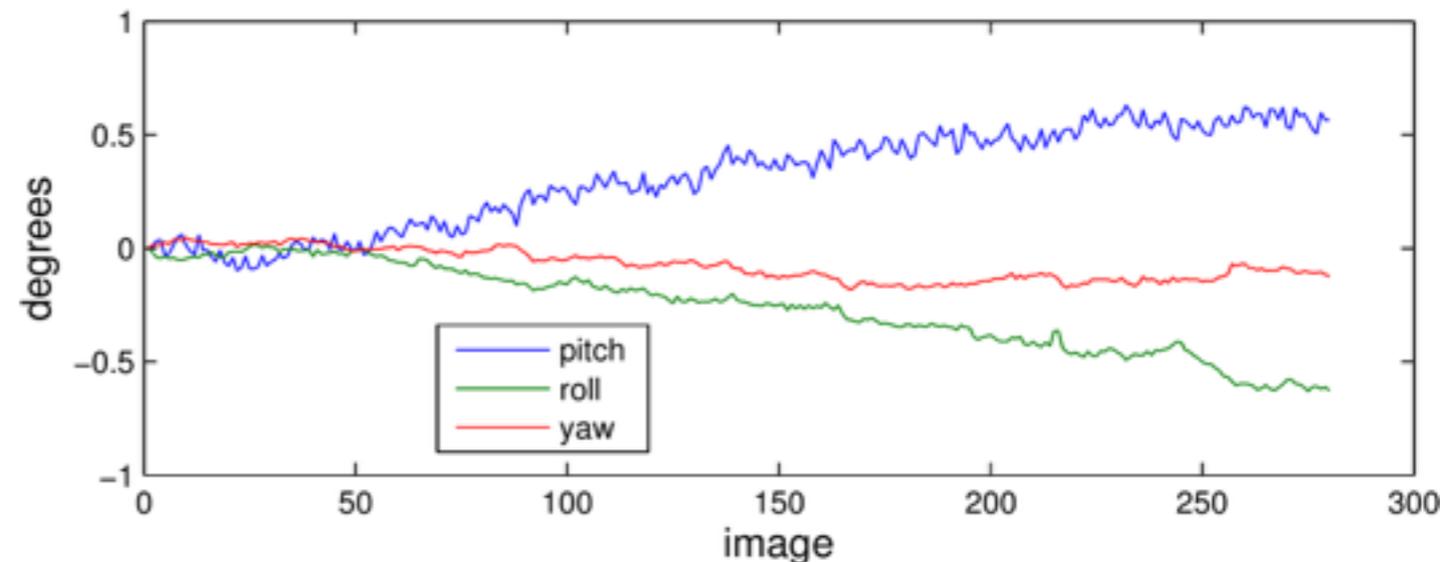Normalisation to template (MNI) brain, or ROI analysis

So many problems

- HRF is delayed and temporally smooth

- Signal intensity drifts over time

- EPI images are distorted

- The head is likely to move during the fMRI scan

- Slices within the same image come from different time points (assuming standard 2D EPI)

- Head movements between fMRI scans and structural scans

- Signal is typically spatially extended

- Even if we can correct the above, different people's brains are different shapes, so how do you do group analysis?
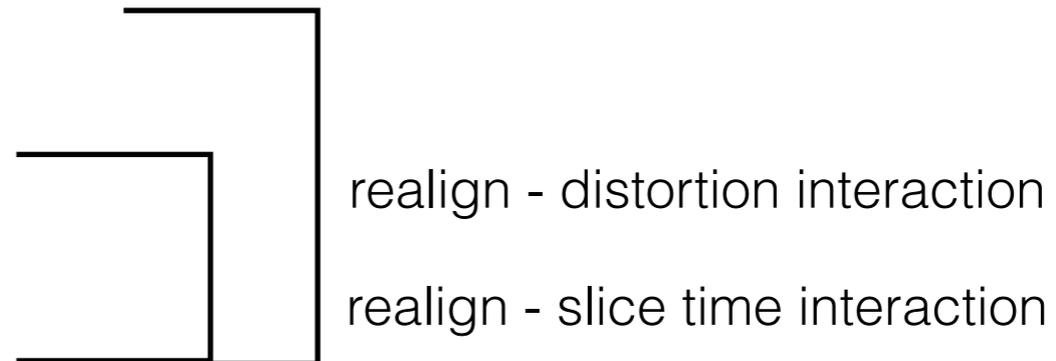
Interactions are harder to fix

realign - distortion interaction

realign - slice time interaction

Preprocessing is no substitute for collecting high quality data

Typical preprocessing pipeline

Images in dicom format

Convert to format used by SPM (NIFTI)

Initial image diagnostics

Normalise structural

Within series processing:
- Spatial realignment
- Undistortion
- Temporal realignment

Coregister EPI to structural

Normalise EPI

Smooth EPI

Single subject stats

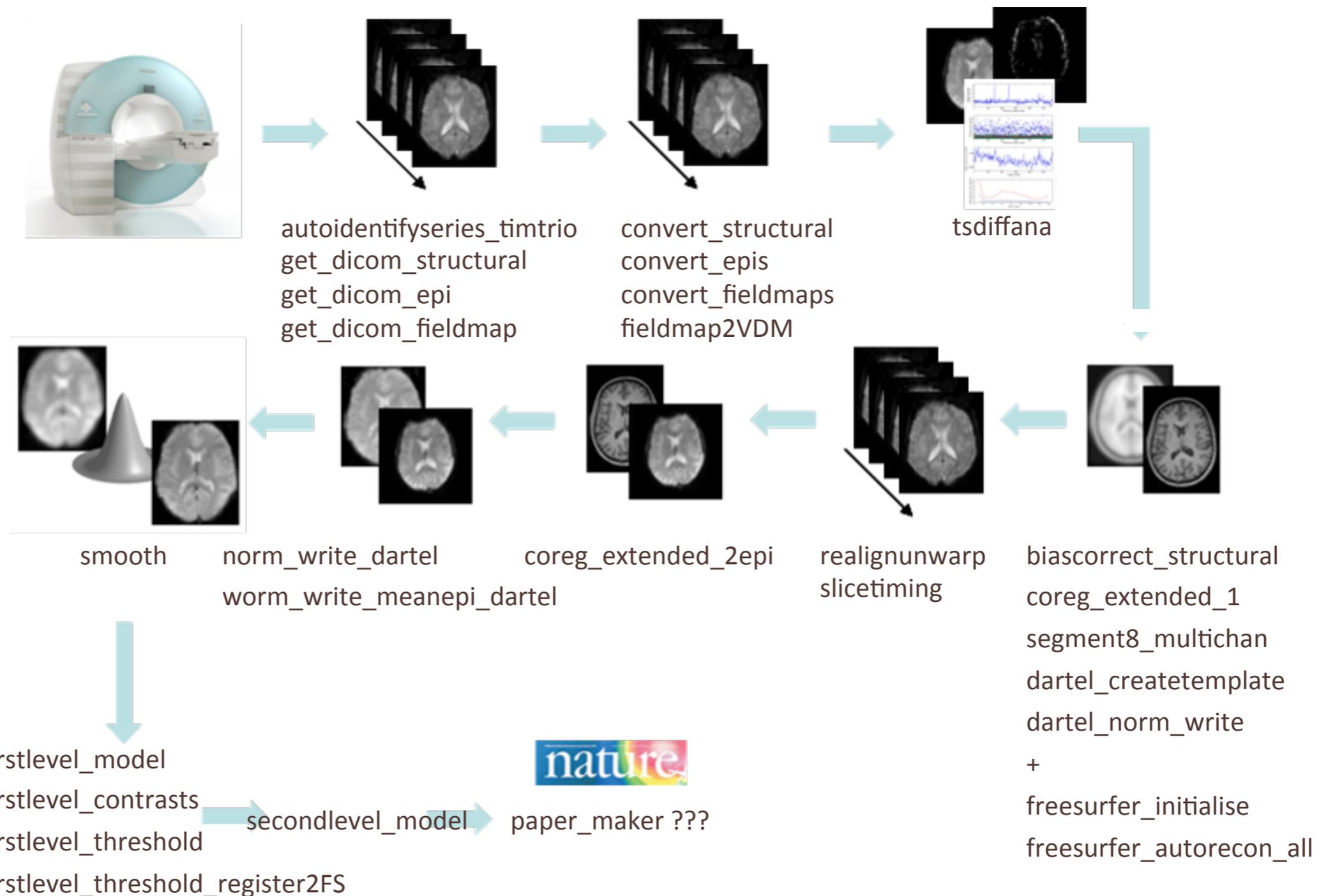Group stats

Publish...

Typical AA pipeline

autoidentifyseries_timtrio
get_dicom_structural
get_dicom_epi
get_dicom_fieldmap

convert_structural
convert_epis
convert_fieldmaps
fieldmap2VDM

tsdiffana

smooth

norm_write_dartel
worm_write_meanepi_dartel

coreg_extended_2epi

realignunwarp
slicetiming

biascorrect_structural
coreg_extended_1
segment8_multichan
dartel_createtemplate
dartel_norm_write
+
freesurfer_initialise
freesurfer_autorecon_all

firstlevel_model
firstlevel_contrasts
firstlevel_threshold
firstlevel_threshold_register2FS

secondlevel_model

nature

paper_maker ???

EPI diagnostics

Mean and variance images:
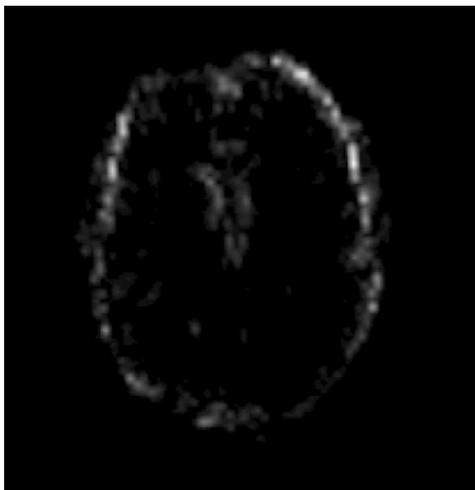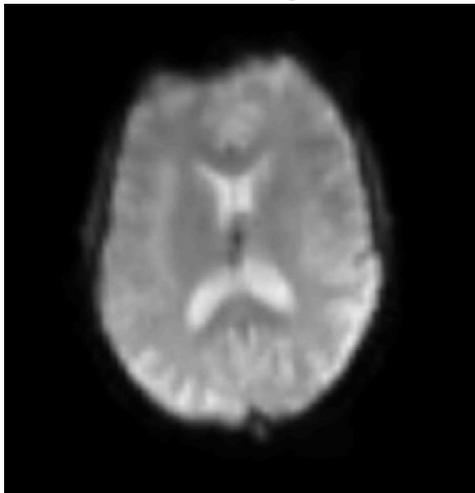
Diagnostic plots:

Scaled variance of difference from the 1st vol.:

- Volumewise

- Slicewise

Descriptive stats:

- Volumewise

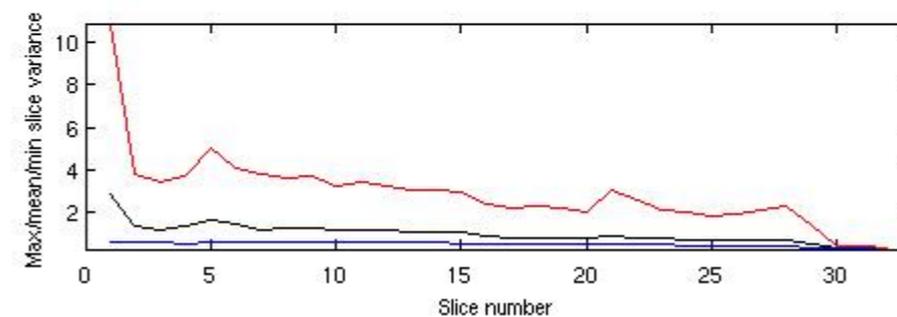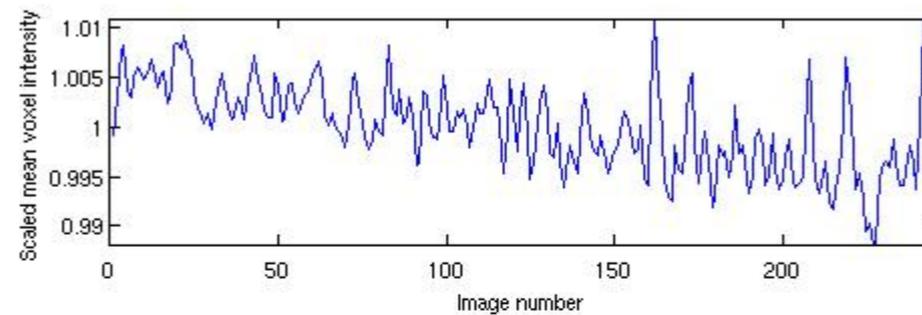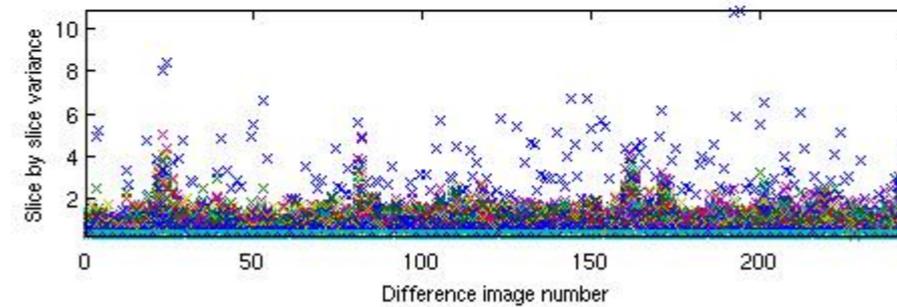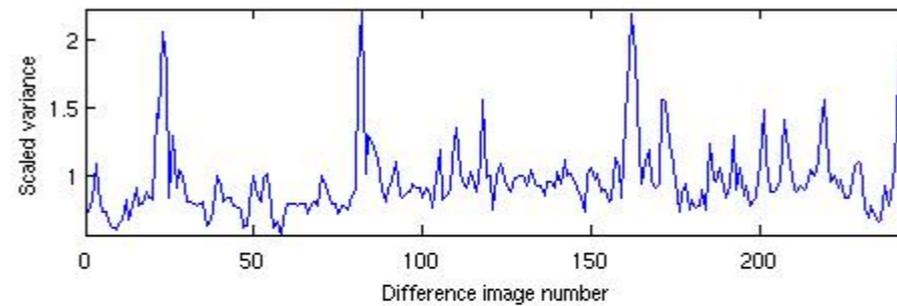- Slicewise

Template brain normalisation

Goal: transforming brain so its shape matches that of a template. Useful for:

- Group analysis

- Cross study comparison, meta analysis

Template: universal space

- Talairach and Tournoux, 1988 – Brainvoyager, AFNI

  - Based on a single subject

- Montreal Neurological Institute: MNI152 – SPM, FSL

  - Averaged from T_1 images of 152 subjects

- Information eXtraction from Images (London): IXI (in SPM12)

  - Also in MNI

  - Fewer subjects, but may be more representative locally

  - More classes (segmentation)

Coordinate systems
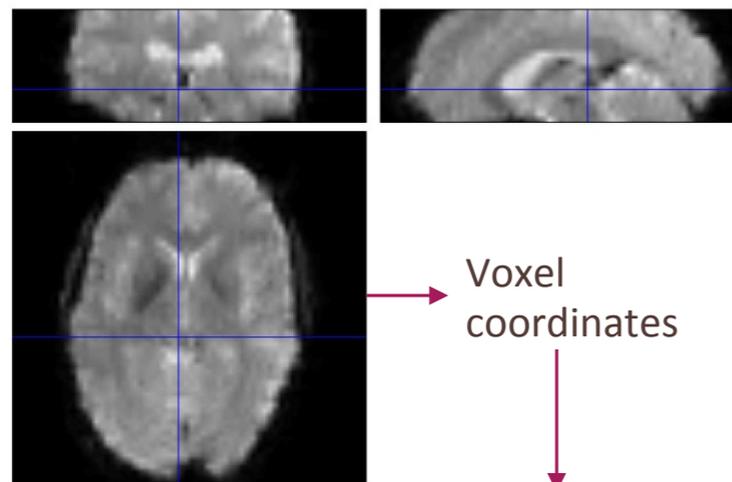
Voxel coordinates

-3.0	-0.2	0.1	107.1
-0.3	2.8	-1.3	-61.7
0	1.0	3.8	-47
0	0	0	1

X

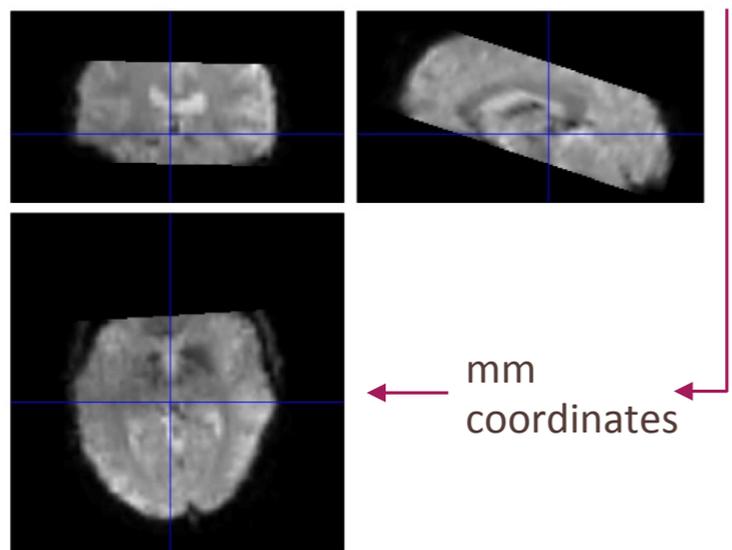| 34 |
|----|
| 28 |
| 5 |
| 1 |

=

0
0
0
1

mm coordinates

- **"Spaces"**
  - "Voxel space": location in the data matrix
  - "World space": meaningful units (mm) from a POO[1]

- **Transformation matrix: relationship between "voxel space" and "world space"**

$$
\begin{matrix}
\text{Translations} & \text{Pitch} & \text{Roll} & \text{Yaw}
\end{matrix}
$$

$$
\begin{pmatrix} 1 & 0 & 0 & X_{trans} \\ 0 & 1 & 0 & Y_{trans} \\ 0 & 0 & 1 & Z_{trans} \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & \cos(\Phi) & \sin(\Phi) & 0 \\ 0 & -\sin(\Phi) & \cos(\Phi) & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos(\Theta) & 0 & \sin(\Theta) & 0 \\ 0 & 1 & 0 & 0 \\ -\sin(\Theta) & 0 & \cos(\Theta) & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos(\Omega) & \sin(\Omega) & 0 & 0 \\ -\sin(\Omega) & \cos(\Omega) & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}
$$

- Changing the transformation matrix[2]
  - ↓
- Changes the relationship
  - ↓
- Transforms the image without having to resample (reslice) it

Coordinate transformations

The transform can describe a transition

* voxel index >> mm (e.g., relative to center of scanner bore)

* mm >> mm (e.g., from scanner to MNI)

Transforms can be

* Linear (ie, same parameters for the entire volume)

  * 'rigid body': 6 df - translation (x,y,z), rotation (pitch, roll, yaw). Used for co-registration between structural and EPI, motion correction

  * 'affine': 12 df - scale (aka 'zoom'), shear. Used as initial stage of normalisation.

* Non-linear (ie, different parameters for different voxels) - for normalisation to template brains
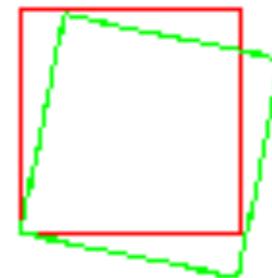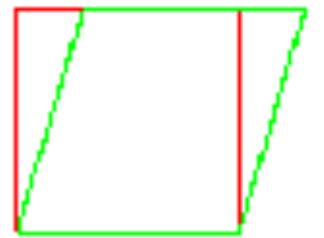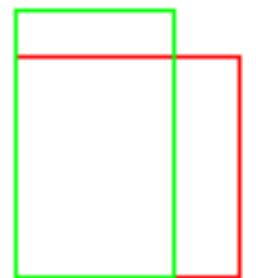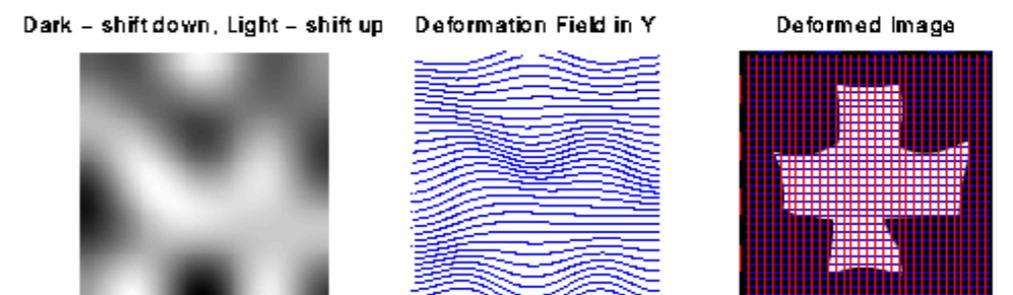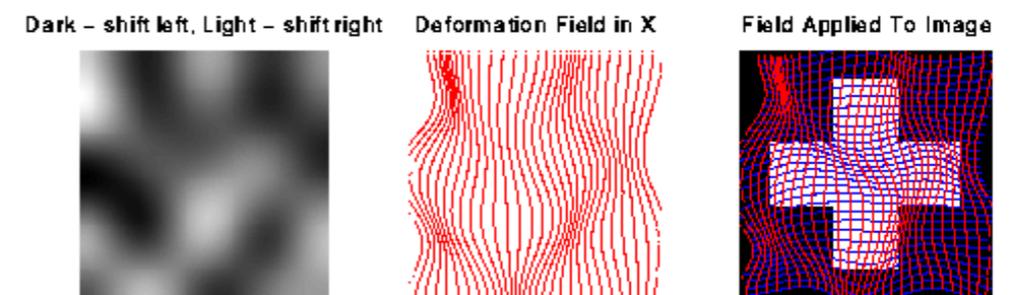
rotation   shear
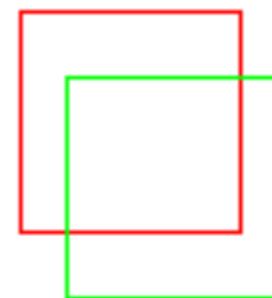
translation   scale

The transform can be applied to

* Header only (e.g., in co-registration)

* To reslice a new, transformed image (e.g., in motion correction, normalisation)

SPM normalisation

- Two steps: first affine registration, then nonlinear registration with regularisation to correct local errors

- Unified segmentation: divide the brain into 3 tissue classes (WM, GM, CSF) and normalise each separately to a template. Much better than whole-image normalisation, if the segmentation is good (effectively another nonlinearity)

- Not expected to work perfectly - SPM assumes you will use spatial smoothing to overcome residual errors in registration

Dark – shift left, Light – shift right   Deformation Field in X   Field Applied To Image

Dark – shift down, Light – shift up   Deformation Field in Y   Deformed Image

Normalization routes

The goal is to bring the fMRI data into a standard space:

- Direct: EPI >> MNI

  - Probably bad idea. Distorted, not optimised for anatomical contrast

- Indirect:

  - Coregister participant's fMRI and structural data (EPI header >> T1 header)

  - Find nonlinear transform to bring participant structural into MNI space (T1 >> MNI)

  - Apply the transform to the EPI data (EPI >> MNI)

- Indirect + study template (DARTEL):

  - EPI header >> T1 header

  - Create study-specific template brain (T1 >> study template)

  - Normalize the study-specific template (study template >> MNI)

  - Apply the concatenated T1 >> study template >> MNI transform to the EPI data
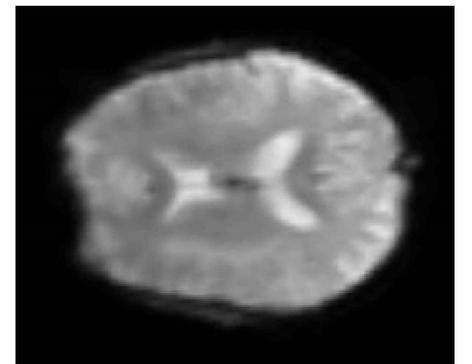
Sidebar - converting between Talairach and MNI

- The 'classic' route for converting between the Talairach *atlas* and MNI is the 'Brett' transform (Brett et al, 2001, NeuroImage - developed here at CBU): http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach

- But if the goal is to convert between MNI and Talairach *volumes* (ie, outputs of a software package such as AFNI), you will probably get a better result with the BrainMap transform, which builds on the Brett transform to improve registration performance (Lancaster et al., 2007, HBM): http://www.brainmap.org/icbm2tal/

Normalisation diagnostics

Segmentation QA
Normalisation is usually
checked manually (e.g.
overlay normalised
images in FSLView)
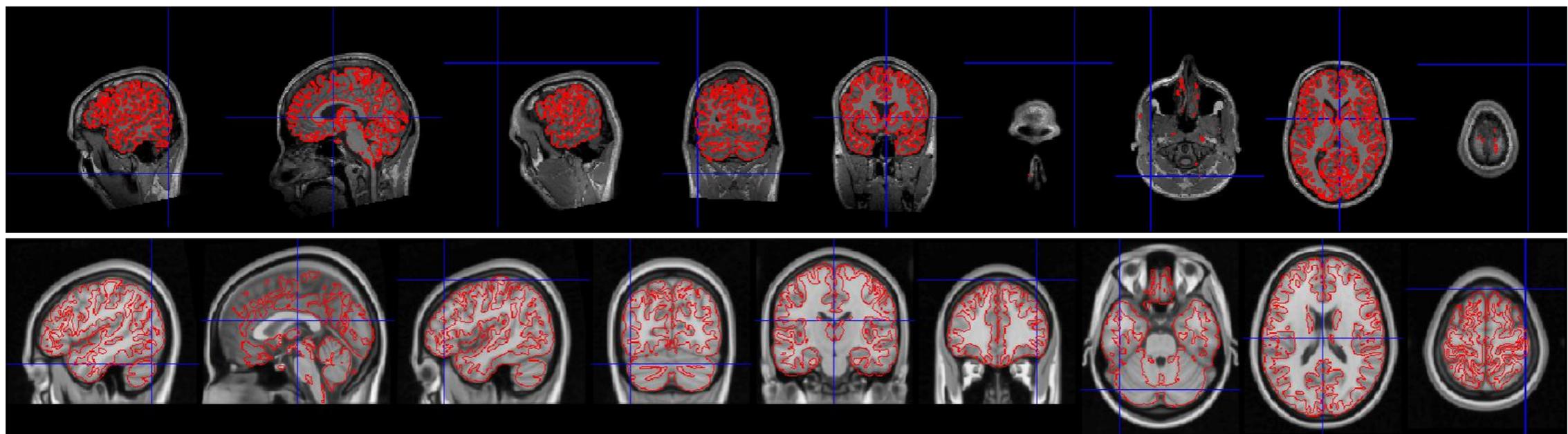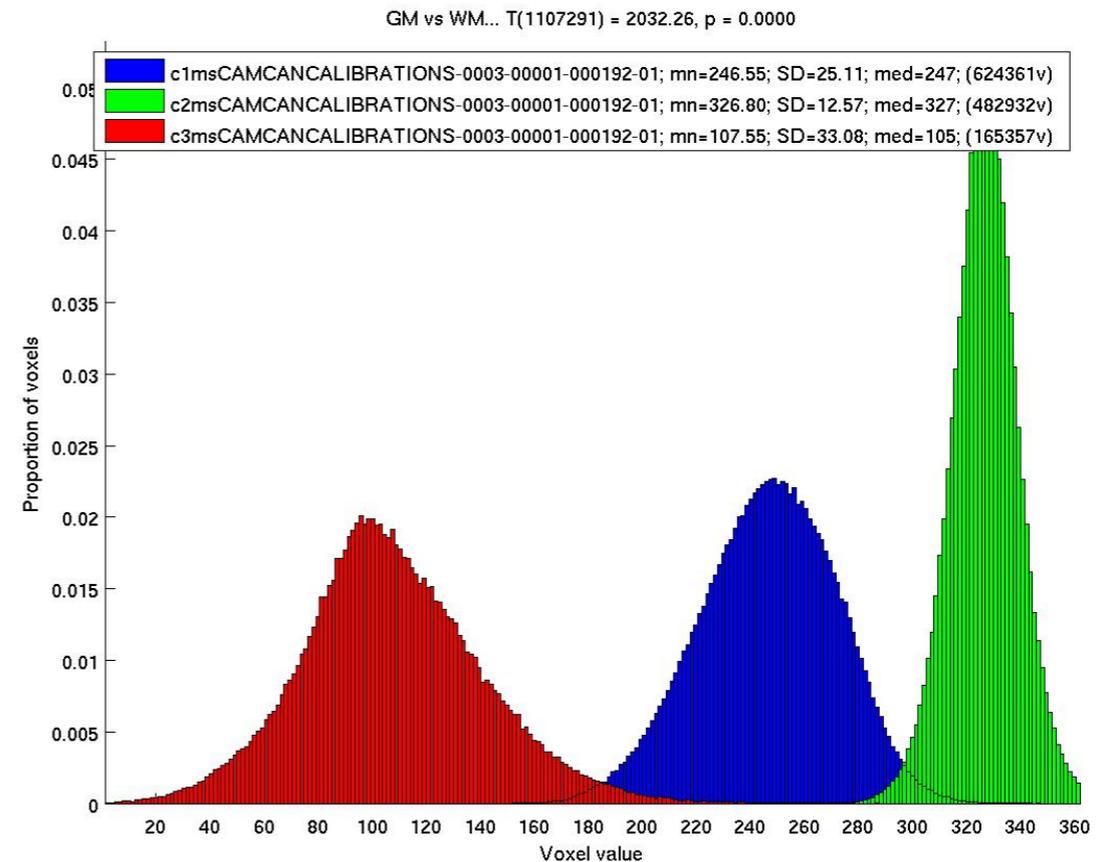
Slice time correction

- Interpolate data to approximate what we would have obtained, had we acquired all slices simultaneously

- Key parameter: reference slice. The only slice that is not interpolated, so pick your favourite, or perhaps the middle (to minimise overall interpolation)

- Be *very* careful to specify the correct slice order! AA helps automate this.
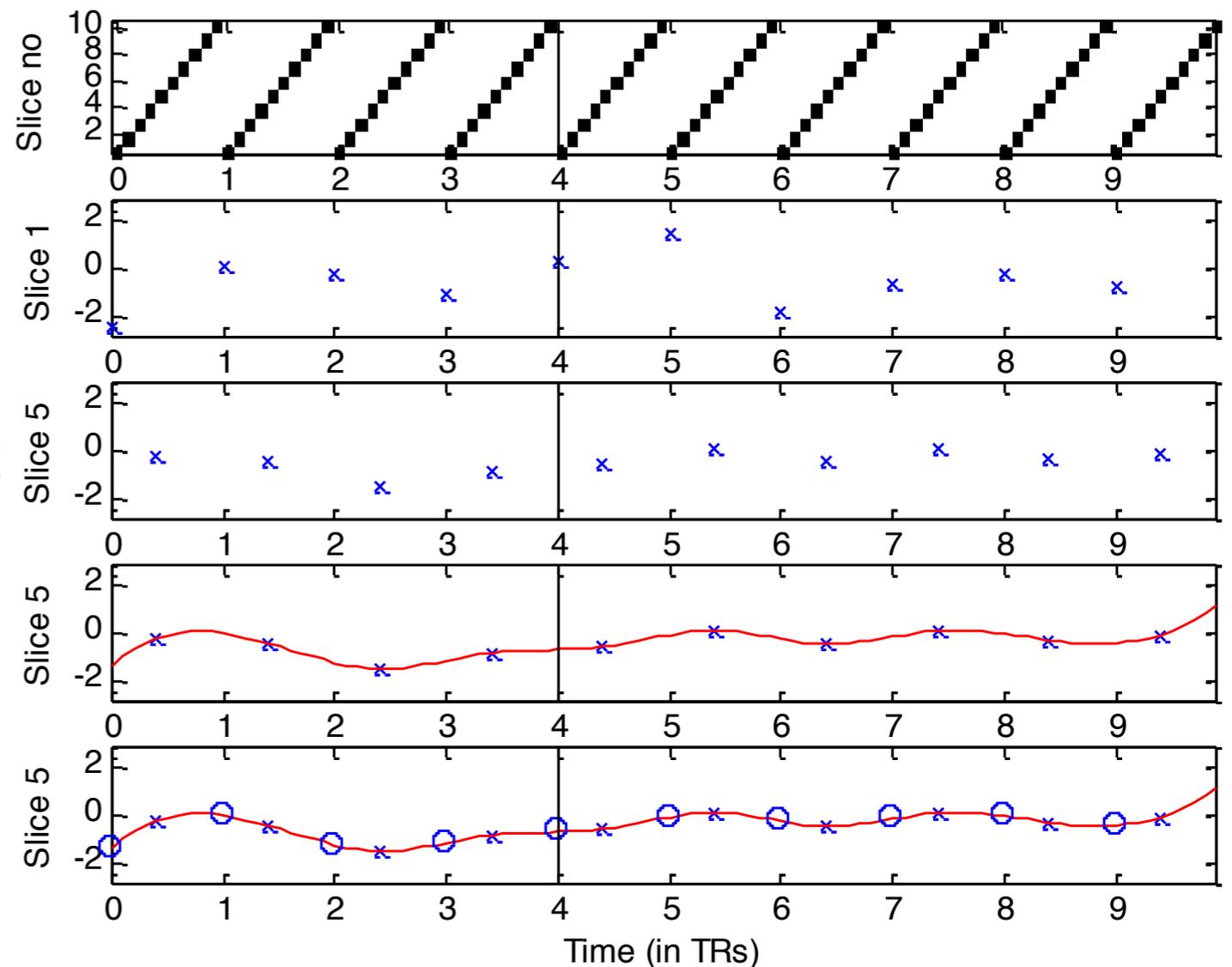
Motion correction (realign)

- A 6-parameter rigid body correction

- Target: the first image of the first run, or the mean image of the first run

- Works perfectly under these assumptions:

  1. The magnetic field is homogeneous

  2. All slices are acquired simultaneously

  3. The images are noiseless (remember, the motion parameters are *estimated* from the EPI images themselves)

- … So motion correction is not expected to work perfectly with real distorted, sequentially acquired, noisy data. But it helps!

- Be suspicious of data with a lot of head movement
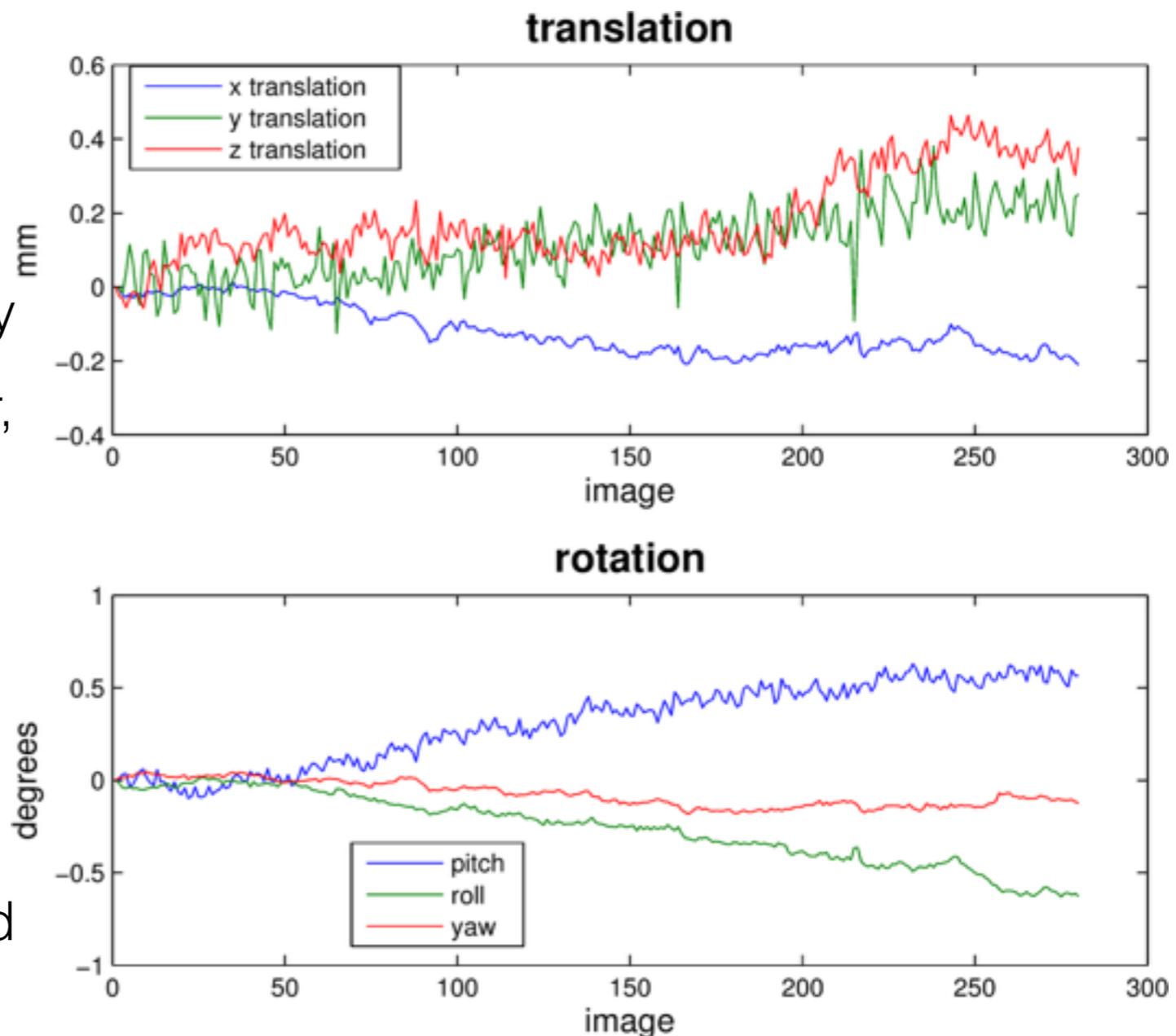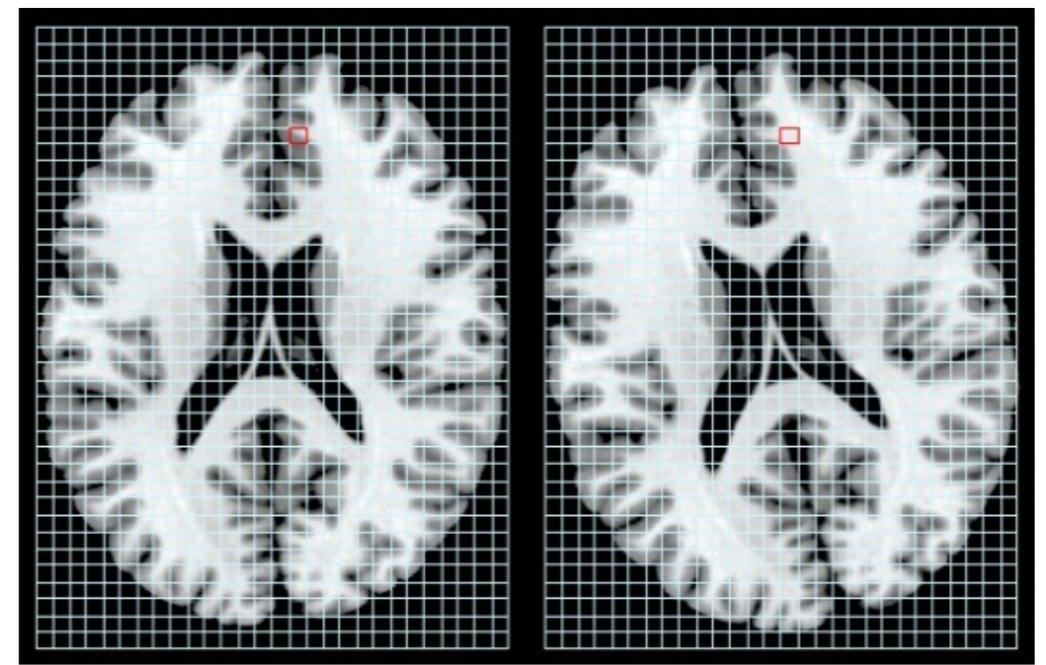
Example voxel - motion corrected

Looks better - especially run 3.

We still need to remove low-frequency scanner drift before the model below makes sense (next lecture).
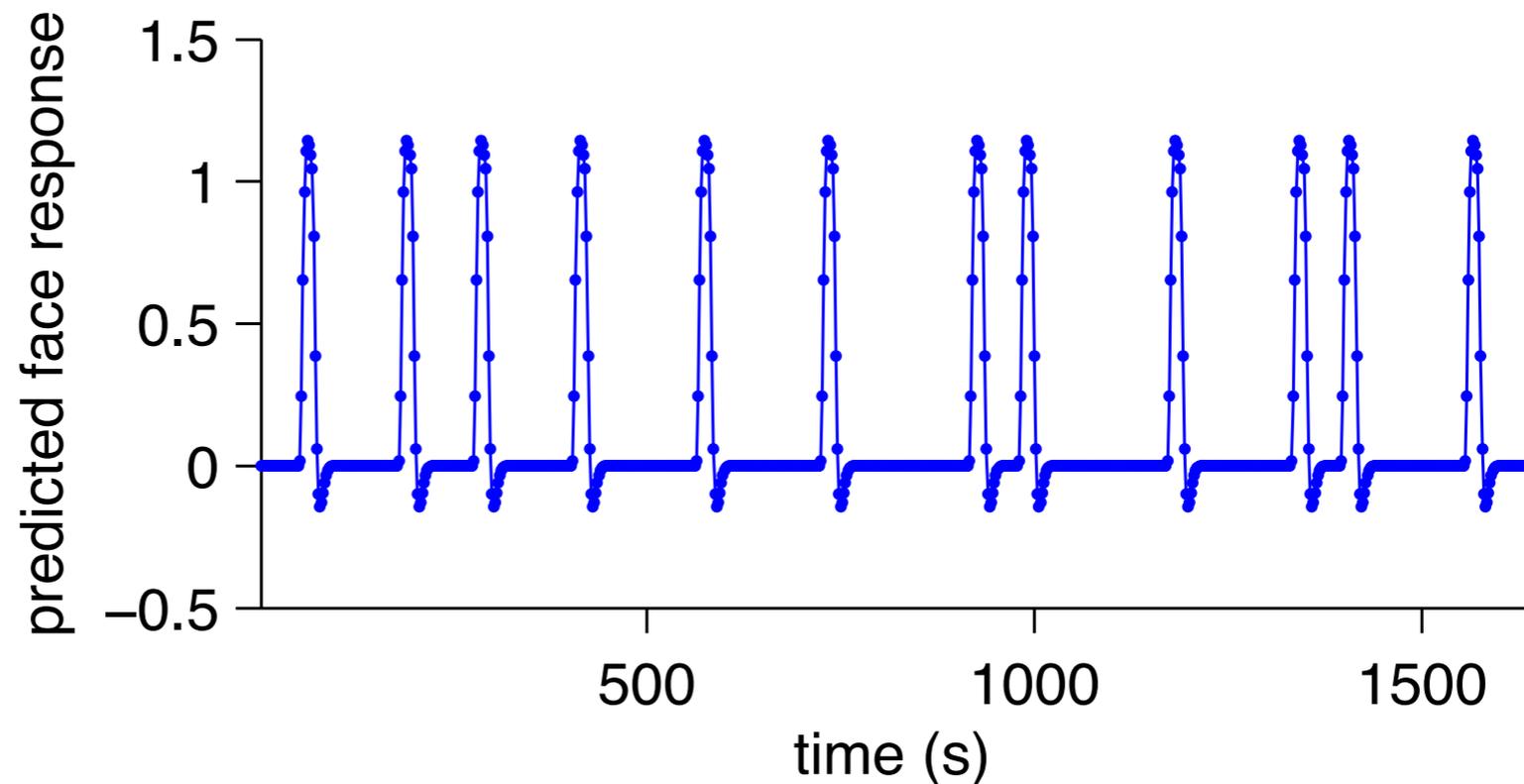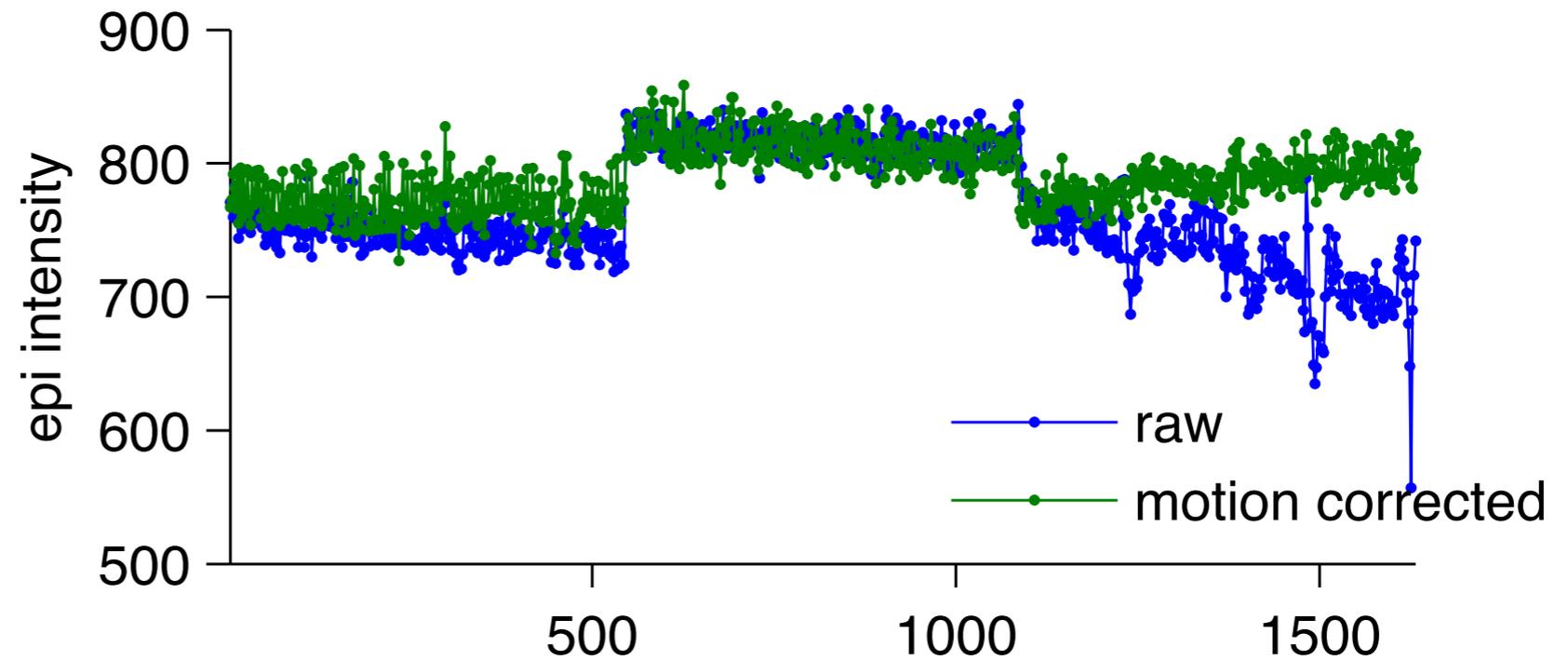
Motion artefacts to look out for: spin history effects

- Movement against slice direction can lead to striping

- Only really a problem with interleaved acquisitions - because if you move up 1 voxel, the slices are excited every 1/2 or 3/2 TR instead of 1/1 as intended

- Basically a movement by slice time interaction - can't correct this, and motion parameters won't show the problem. Need to look at your data!

No motion   Motion

Interleaved

Sequential
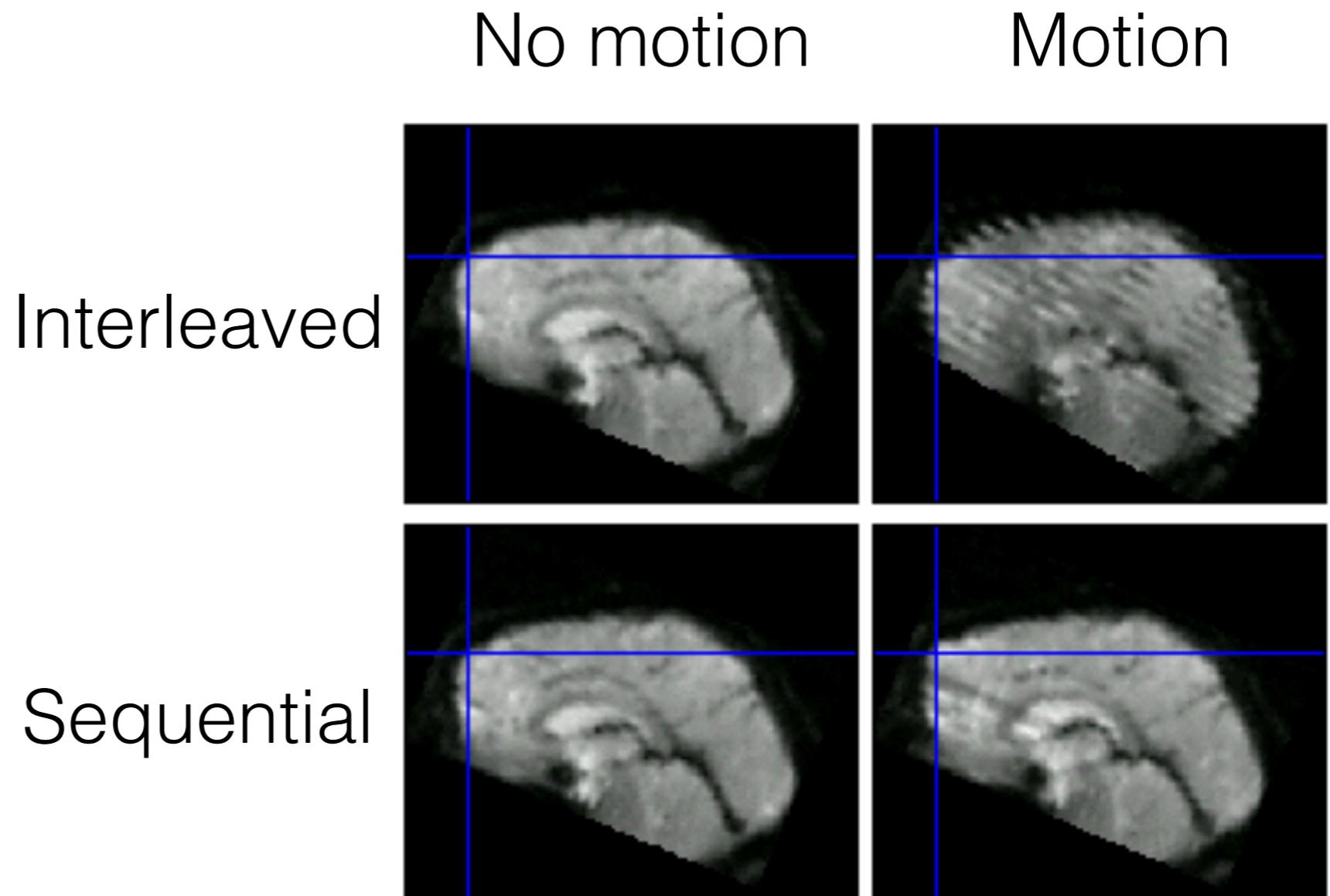
Thanks: Danny Mitchell

Motion artefacts to look out for: magnetic field inhomogeneities

- Large changes to head position (typically from between run movement) can change the apparent shape of the head

- Because motion correction is rigid body, we typically can't accommodate these effects

- Won't show up in motion parameters (but large estimated motion is a hint that something could be going on). Check your data!

First (realigned) volume from each run: Anterior-posterior stretching clearly visible
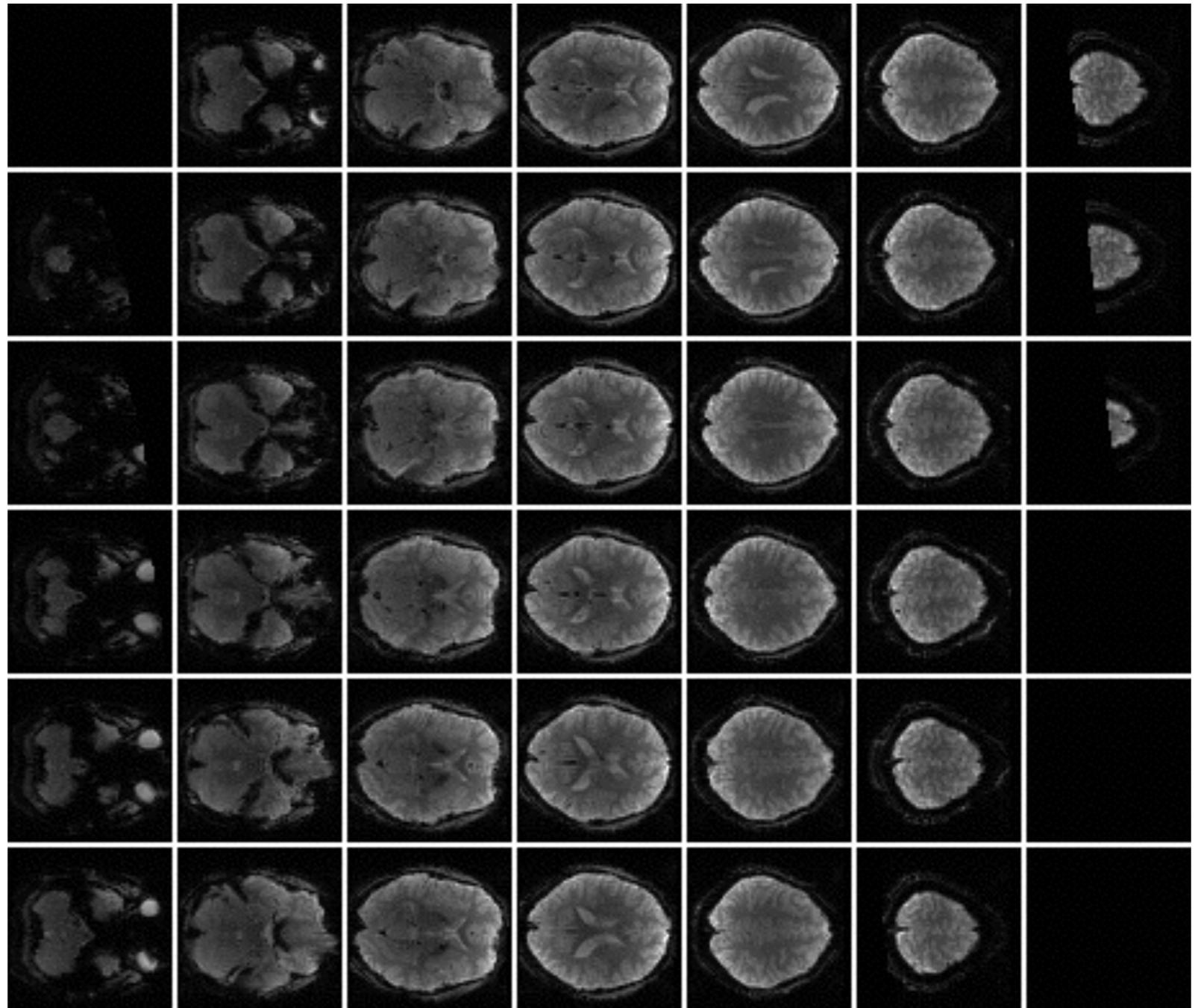
Problematic and non-problematic motion traces
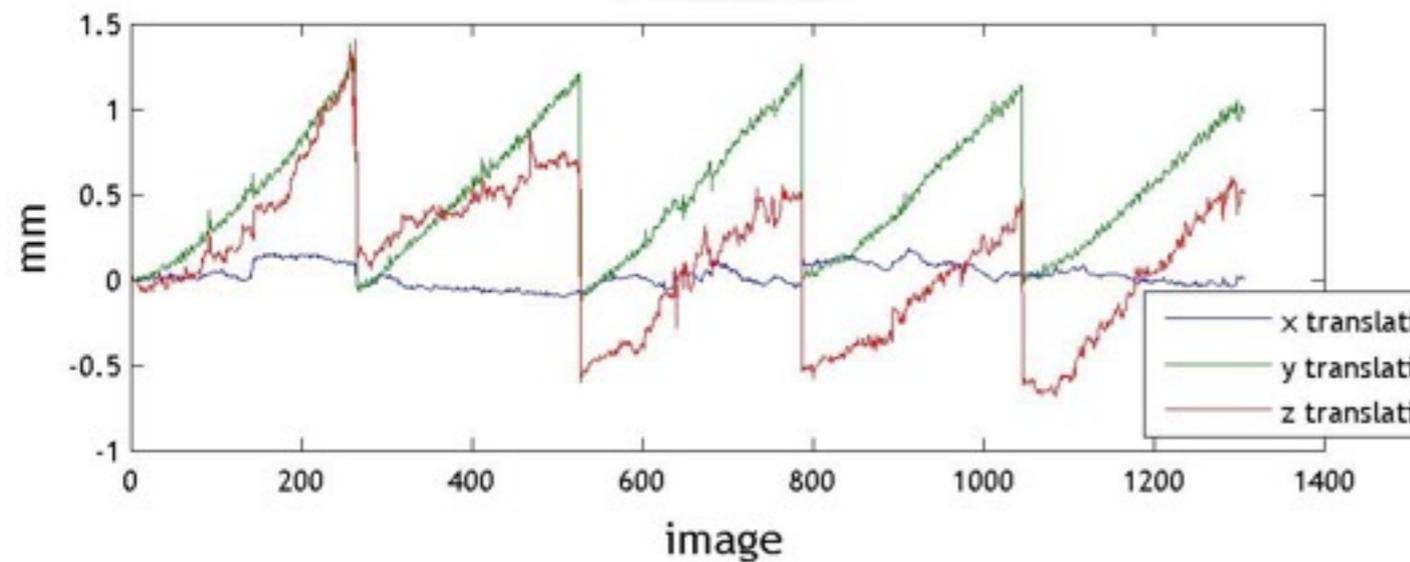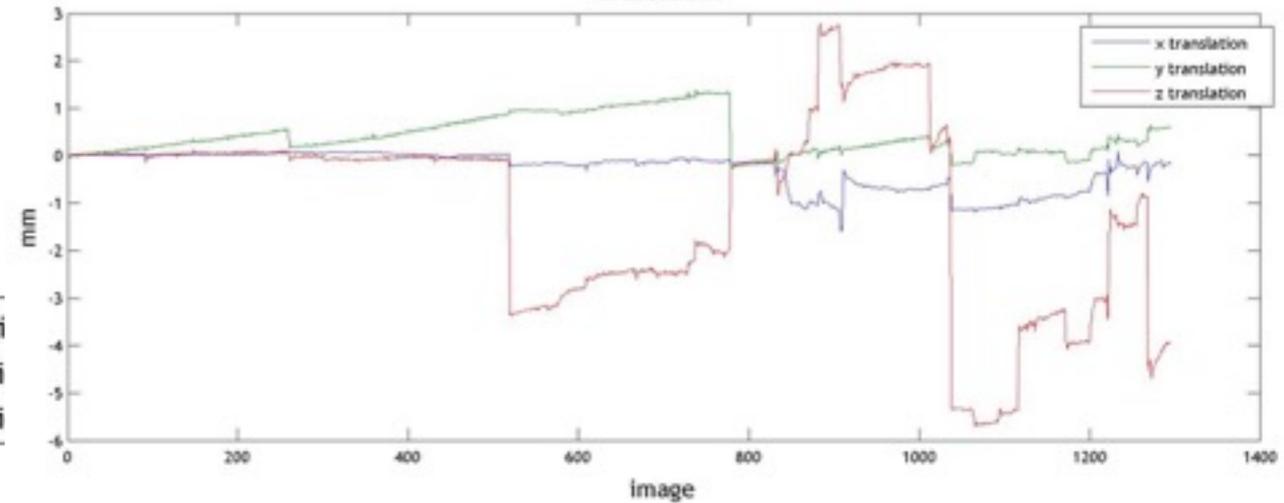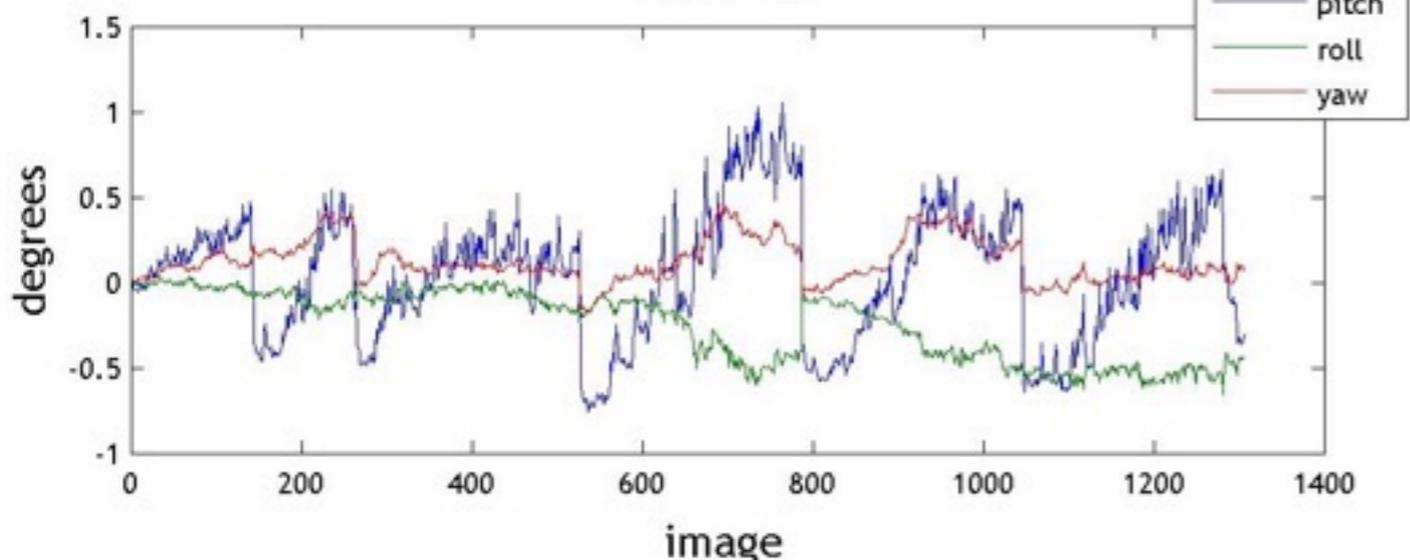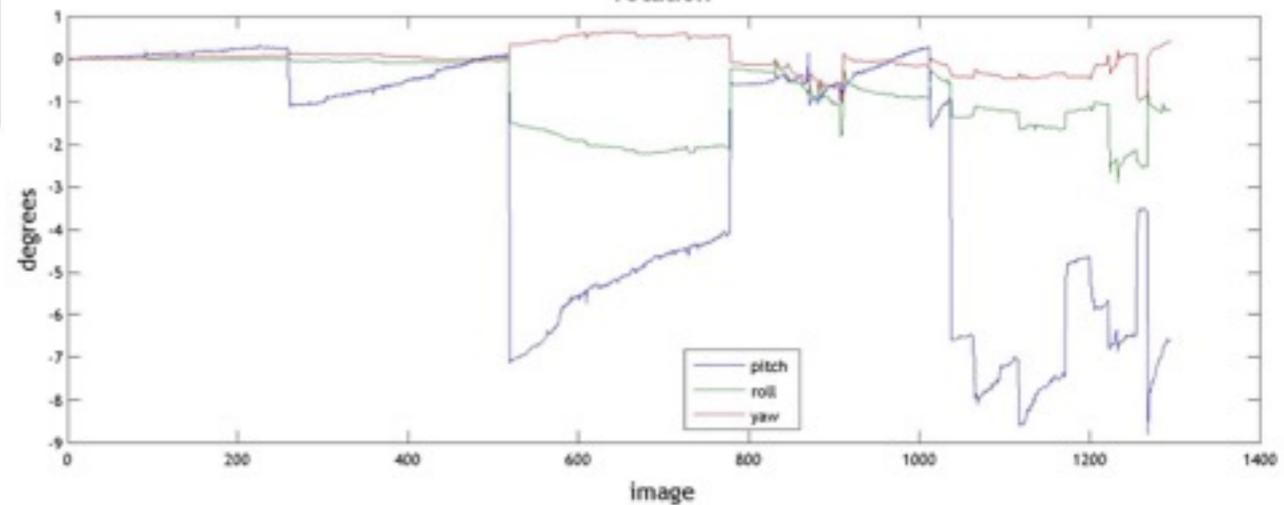
Realign before or after slice time correction?

- Generally it boils down to which preprocessing step you want to prioritise:

  - Slice time first: + slice timing is completely fixed (ish), - non-linear (ie, non-correctable) spatial effects in your data if there is head motion

  - Realign first: + head motion is completely fixed (ish), - slice timings are a little bit wrong sometimes due to head movement

- So realign first if:

  - You use a sequential acquisition - timing errors will be small (slices are ~50ms apart), << CBU standard sequence

- Slice time correct first if:

  - You use an interleaved 2D acquisition - timing errors could be large

- Don't bother with slice time correction if:

  - You acquire the slab at once (3D EPI) or TR is extremely short (e.g., multi-band)

  - If you plan to model HRF shape (FSL solution) - but careful with overfit

Realign & Unwarp or just Realign?

- Unwarp is basically another step on top of realign - first realign, then estimate deformations caused by the interaction between head movement and magnetic field

- So instead of a static undistortion step (applied equally to all images in the time series), estimate a continuous correction over time as a function of head movement

- Sounds good, but does not always help in practice (it's only an estimate, after all!). Standard realign is still the default for most.

- If you are really worried about distortion - head movement interactions, perhaps better to collect one fieldmap per run and undistort each run separately

Coregistration

- Rigid-body align *between modality*

- Similar to realign, but:

  - different algorithm to accommodate differences in image contrast

  - typically only applied to the structural *header*

- Why not reslice the structural? a) you'd be reslicing to the EPI resolution, b) reslicing will happen when we normalise anyway, c) you don't need to reslice to overlay structural and functional in SPM results viewer or MRICron (FSLView will require reslicing though).

- Diagnostics? spm_check_registration (see right)
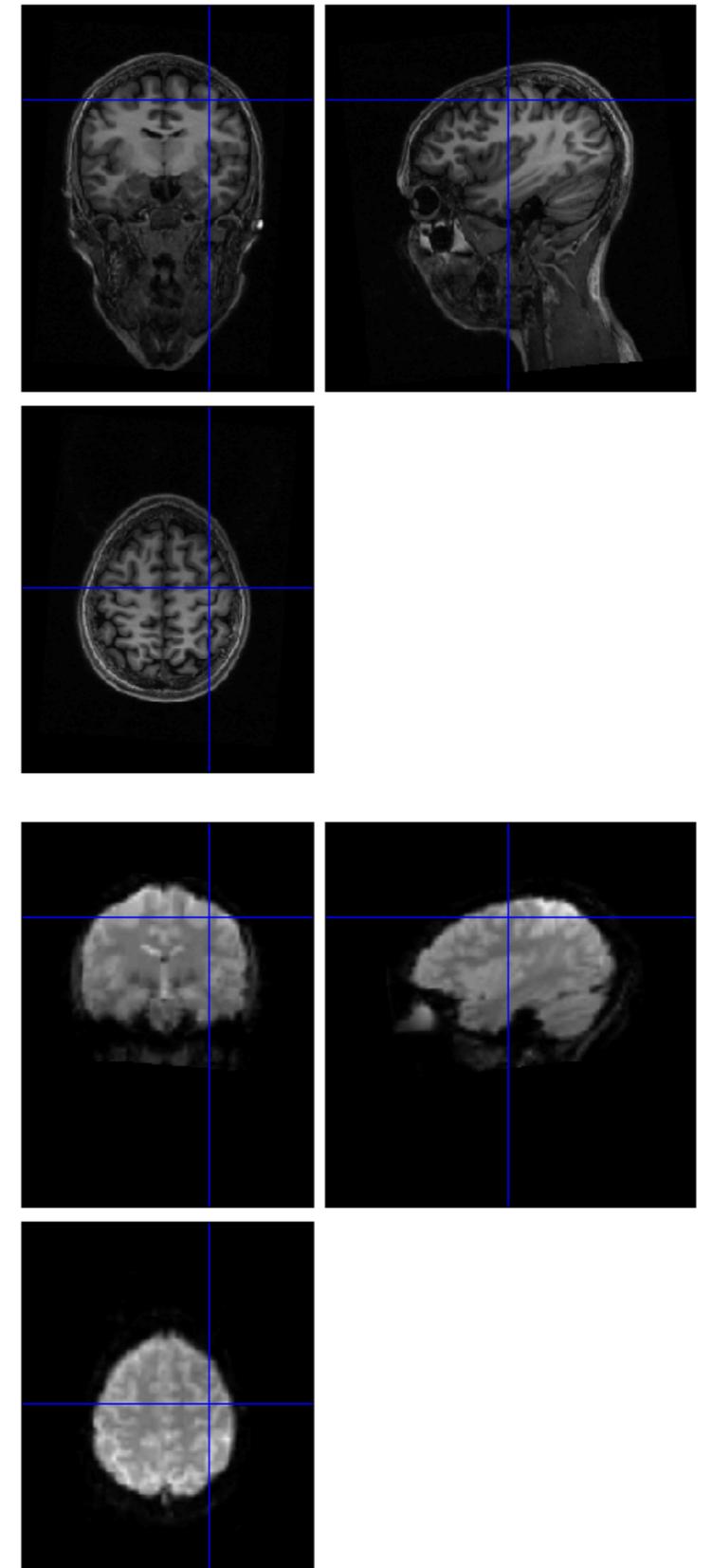
Smoothing

- Necessary for validity of multiple comparisons correction with random field theory (full width at half max > 3x voxel size)

- Helps make residual errors in previous spatial preprocessing stages less problematic (e.g., imperfect normalisation, motion correction)

- Improves functional contrast-to-noise ratios for effects matching the size of the filter (matched filter theorem) - but do you have an a priori prediction for this?

Workshop time

Setup (if running in your own time)

- Open a terminal:

  - cd /imaging/[yourusername]

  - scp -r /imaging/jc01/Workshop/aa_preprocessing ./

  - cd aa_preprocessing

  - matlab_r2012b (NB NOT guaranteed to work on other versions)

- In Matlab:

  - addpath /imaging/local/software/spm_cbu_svn/releases/spm12_latest

  - addpath /imaging/local/software/AA/release-5.4.0/

  - edit aa_user_fmri

Common AA files

- aa_user_fmri - User master script (you will definitely need to adapt to your study)

- aap_parameters_defaults_CBSU.xml - default options (probably no need to change - but your user master script is likely to override several of these settings)

- aap_tasklist_fmri.xml - pipeline definition (you will probably write your own)

- aap_prov.png - graph of the pipeline. Very useful for working out what each module folder contains

Standard QA checks

1. raw data - tsdiffana.

2. motion corrected data - movement parameters, overlay images in FSLVIEW

3. normalisation - segmentation, spm_check_registration, AA report

4. coregistration - spm_check_registration, AA report