



MRC Cognition
and Brain
Sciences Unit



UNIVERSITY OF
CAMBRIDGE

Functional Magnetic Resonance Imaging



GitHub https://github.com/dcdace/fMRI_training

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February 2026

Outline

- Introduction
- Experimental design
- Data management
- **Pre-processing**
- Statistical analysis
- Practical demo

✓ Environment



Data
Organise & Manage

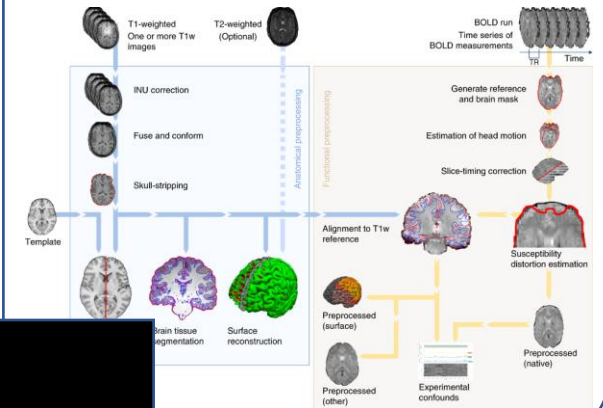
Pre-process

Collect the data



Why can't we analyse right away?

Pre-process & Analyse

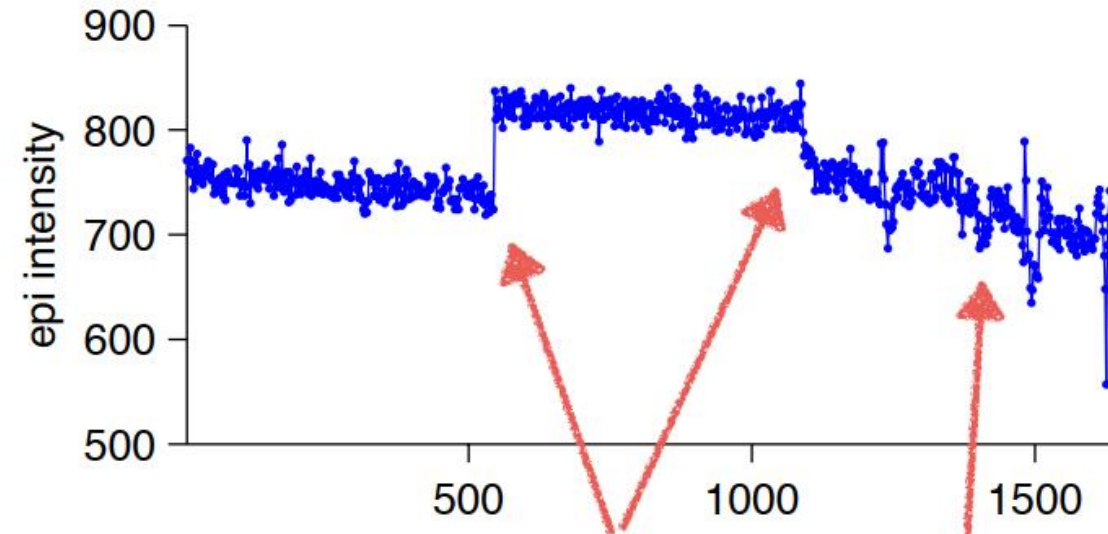


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    1208200617178_22_7328.dcm  
    1208200617178_22_9264.dcm  
    1208200617178_22_9967.dcm  
    1208200617178_22_3894.dcm  
    1208200617178_22_3899.dcm  
  1208200617178_23/  
  1208200617178_24/  
  1208200617178_25/
```



```
my_dataset/  
  participants.tsv  
  sub-01/  
    anat/  
      sub-01_T1w.nii.gz  
    func/  
      sub-01_task-rest_bold.nii.gz  
      sub-01_task-rest_bold.json  
    dwi/  
      sub-01_dwi.nii.gz  
      sub-01_dwi.json  
      sub-01_dwi.bval  
      sub-01_dwi.bvec  
  sub-02/  
  sub-03/  
  sub-04/
```

Raw data in example voxel

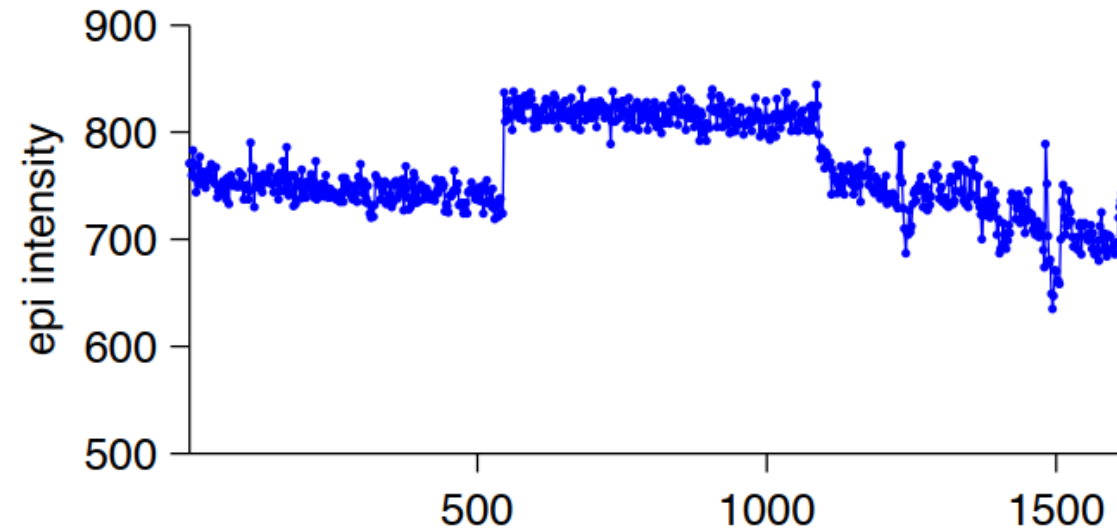


run transitions
(head movement
between scans?)

lots of signal drift
vs other runs
(head movement
during this scan?)

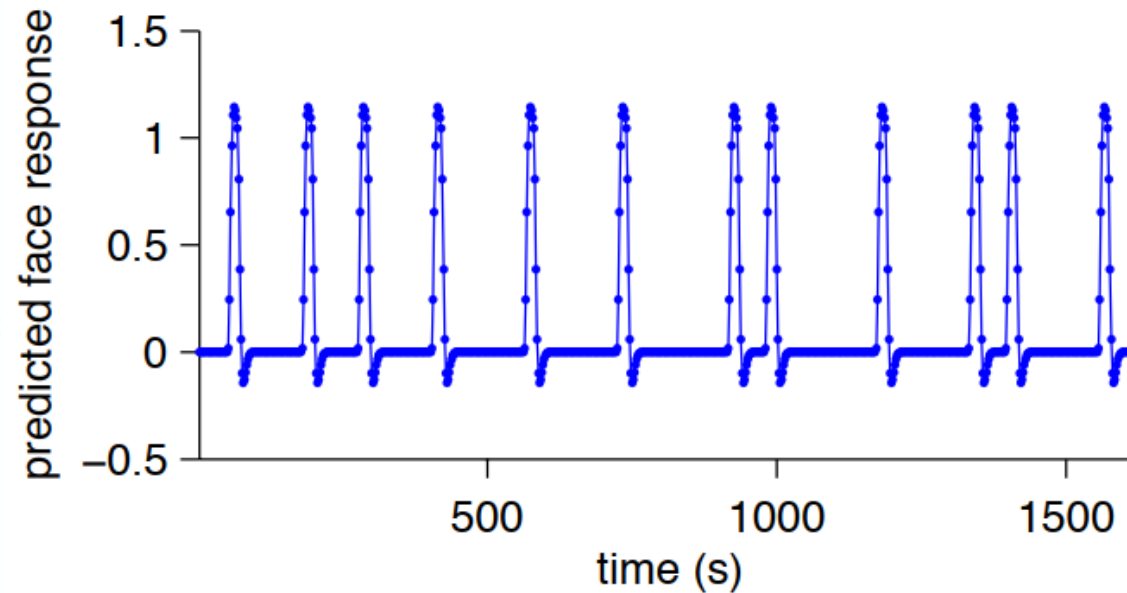
Raw data in example voxel

The (raw) fMRI data

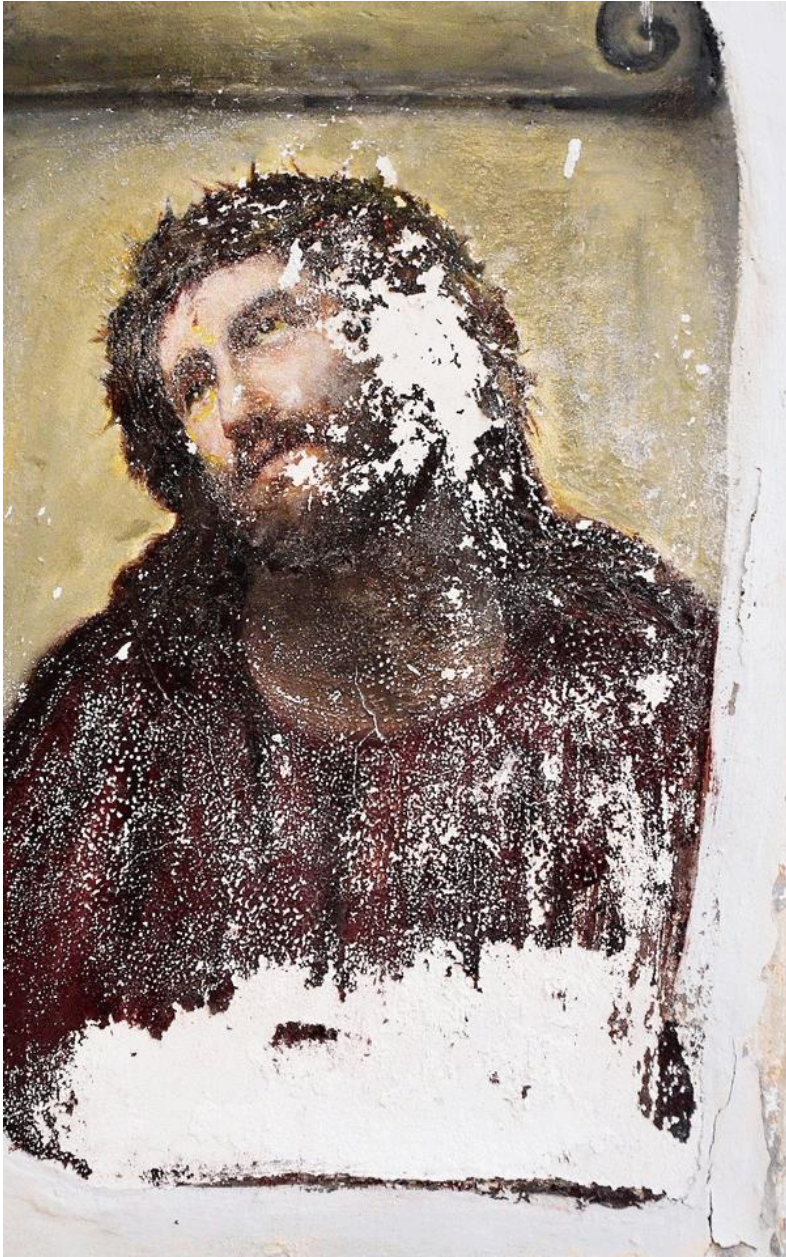


The cognitive model

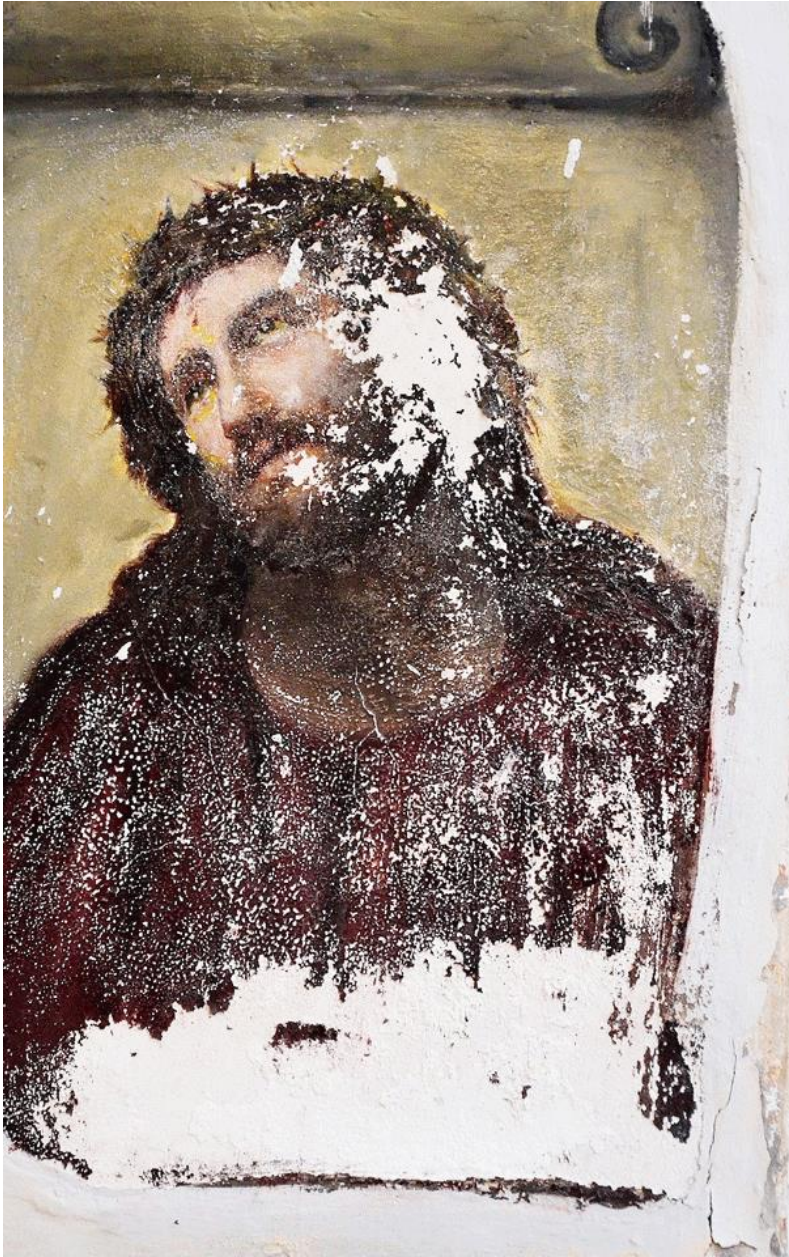
Not much hope of
this working
without signal
processing



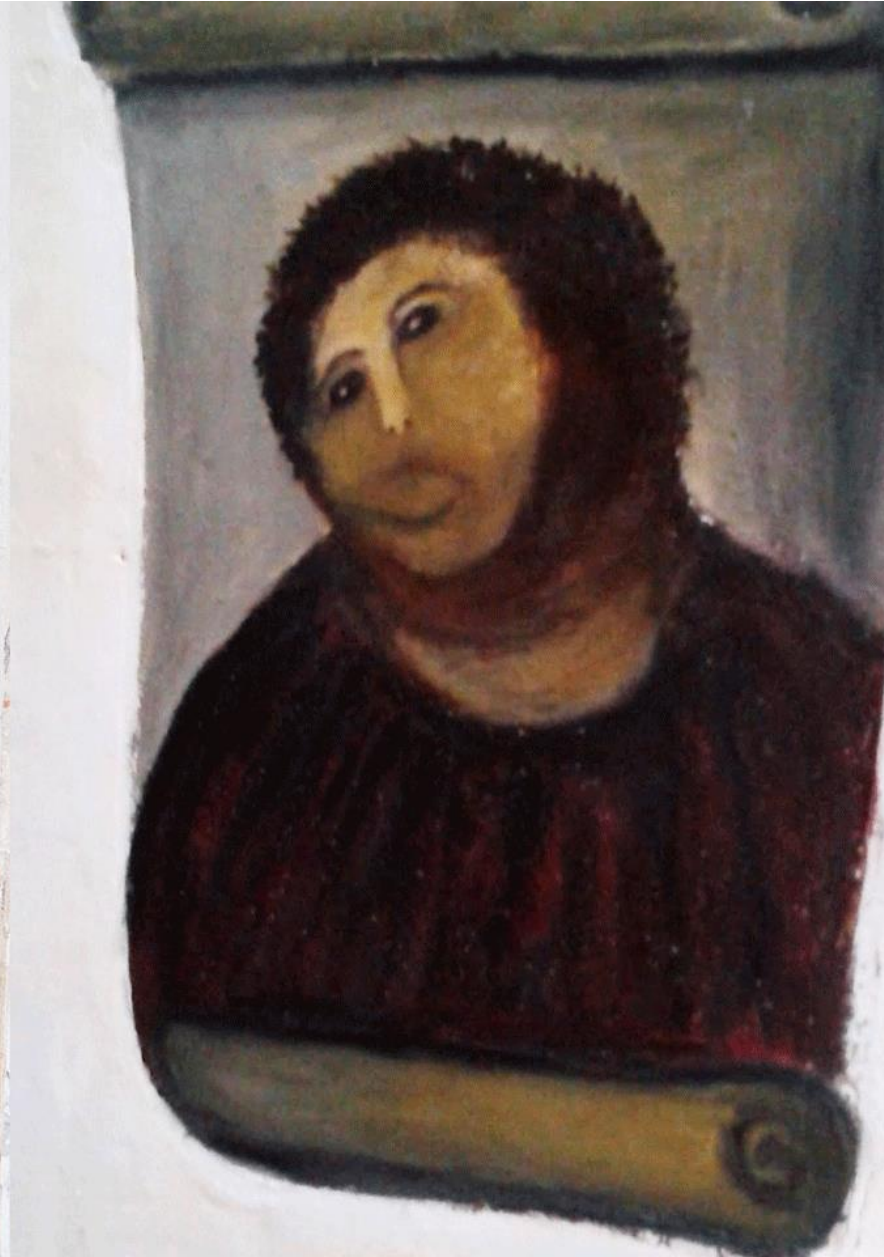
raw



raw



pre-processed



Problems with fMRI data

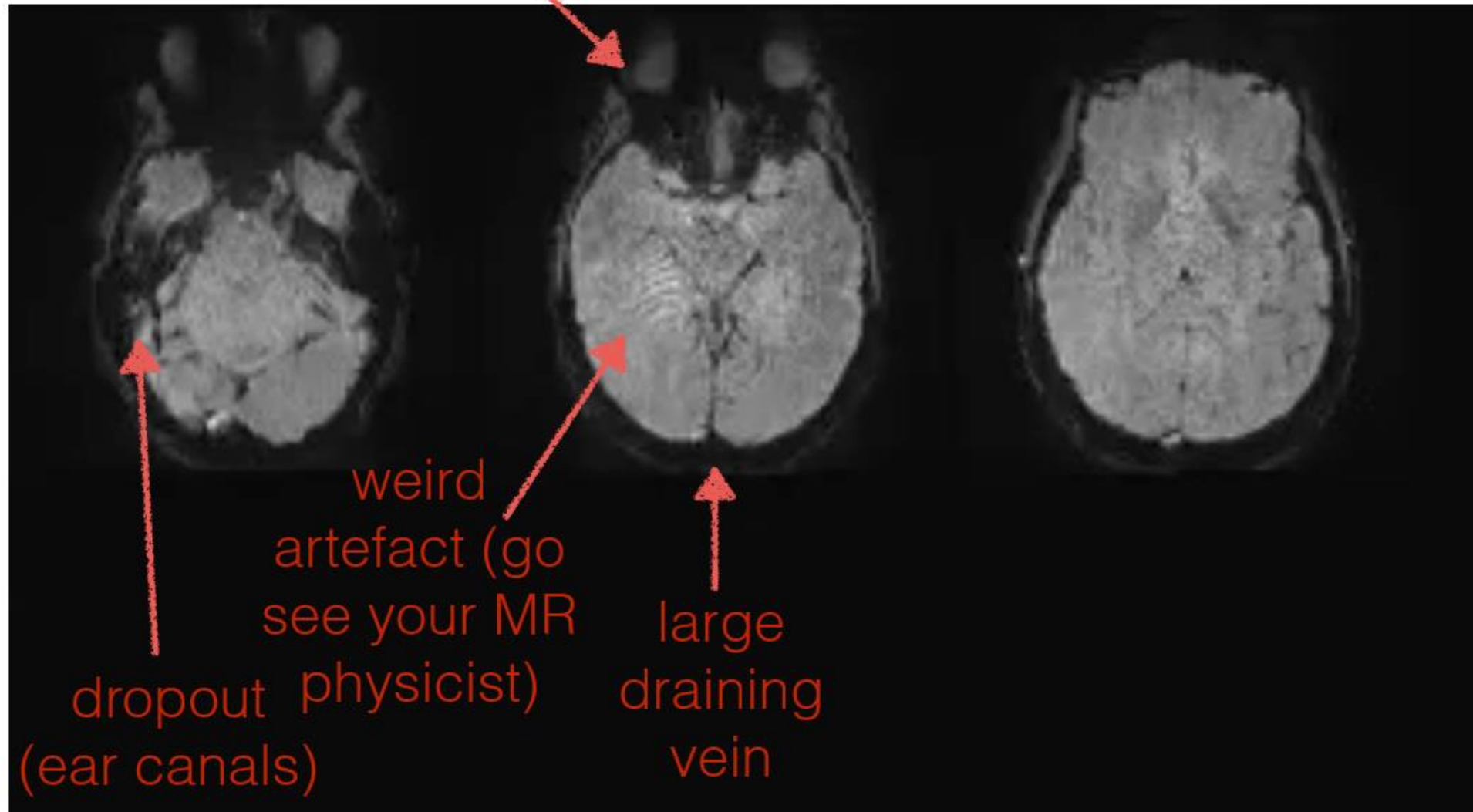
- Artefacts
- Head motion
- Slice timing
- Brain differences
- Noise
- ... and many others

Problems with fMRI data

- Artefacts
- Head motion
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- Brain differences
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- ... and many others

Artefacts

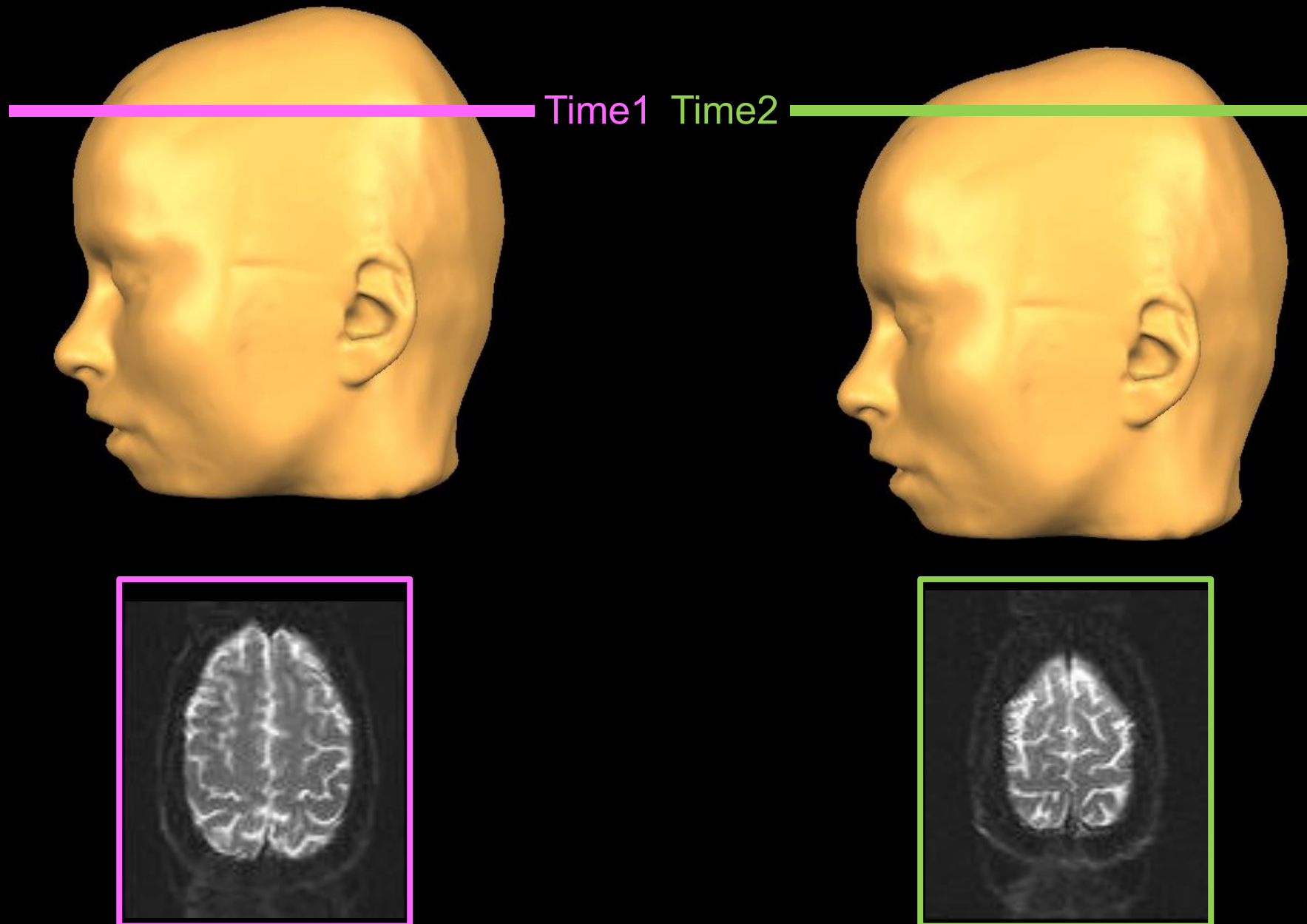
eye blink / movement effect
(not just in eye balls!)



Problems with fMRI data

- Artefacts
- Head motion
- Slice timing
- Brain differences
- Noise
- ... and many others

Head motion



Head motion correction

- Prevention is the best remedy
- Tell your subjects how to be good subjects
- Make sure the subject is comfortable going in
- Discourage any movements that would displace the head between scans



Bite bar



Thermoplastic mask

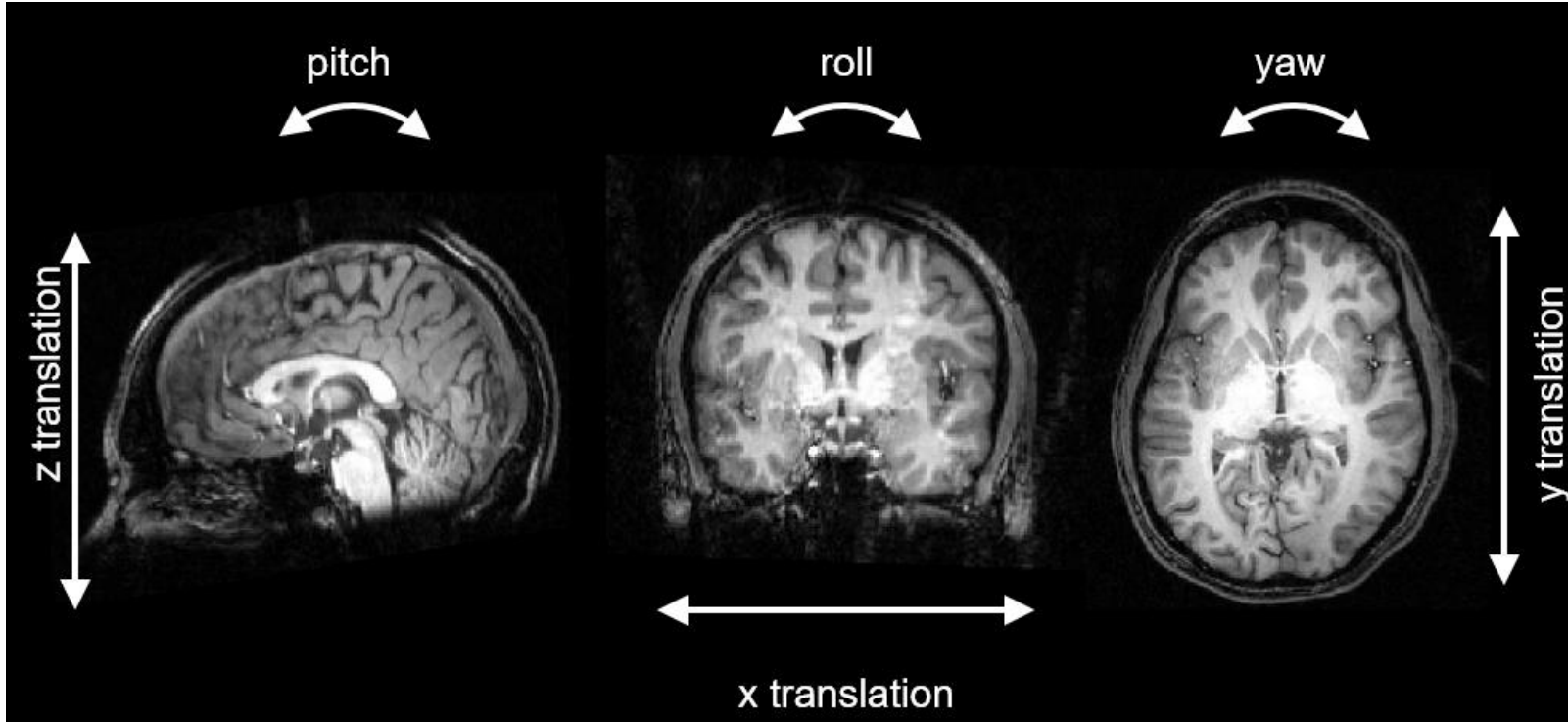


Vacuum pack

Often a bunch of foam padding works as well as anything

Head motion correction

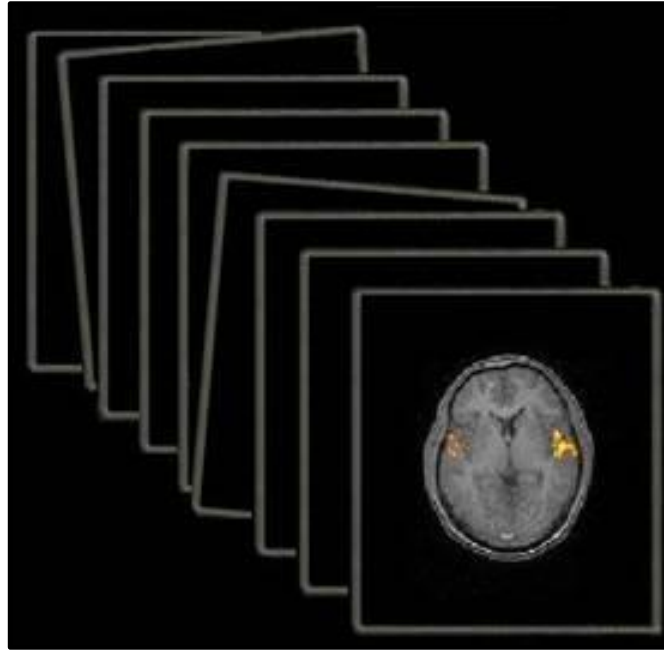
- Spatial realignment



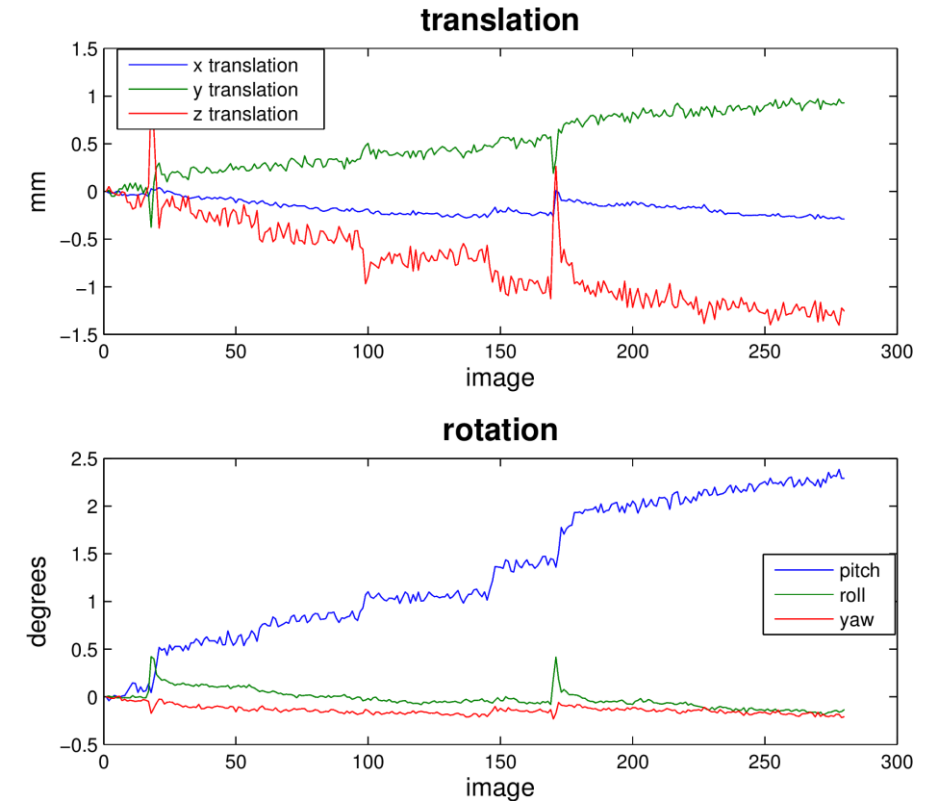
- Most algorithms assume a rigid body (= the brain doesn't deform with movement)
- Align each volume of the brain to a **target volume** using **6 parameters**: 3 translations and 3 rotations
- Target volume: e.g., the mean image of the first run

Head motion correction

- Spatial realignment
 - Not expected to work perfectly, but it helps
 - Be suspicious of data with a lot of head movement!



Translation (mm)			Rotation (rad)		
x	y	z	Pitch	Roll	Yaw
0.3417	0.3348	1.8892	0.0182	0.0065	0.001
0.2733	0.418	1.5832	0.0165	0.0063	0.0061
0.8953	0.4925	0.8524	0.0234	0.0123	0.0269
1.8179	1.5353	1.8285	0.0327	0.0222	0.0939
1.0054	0.3014	0.7574	0.0043	0.0197	0.0094
0.737	0.9508	1.0428	0.026	0.0171	0.0164



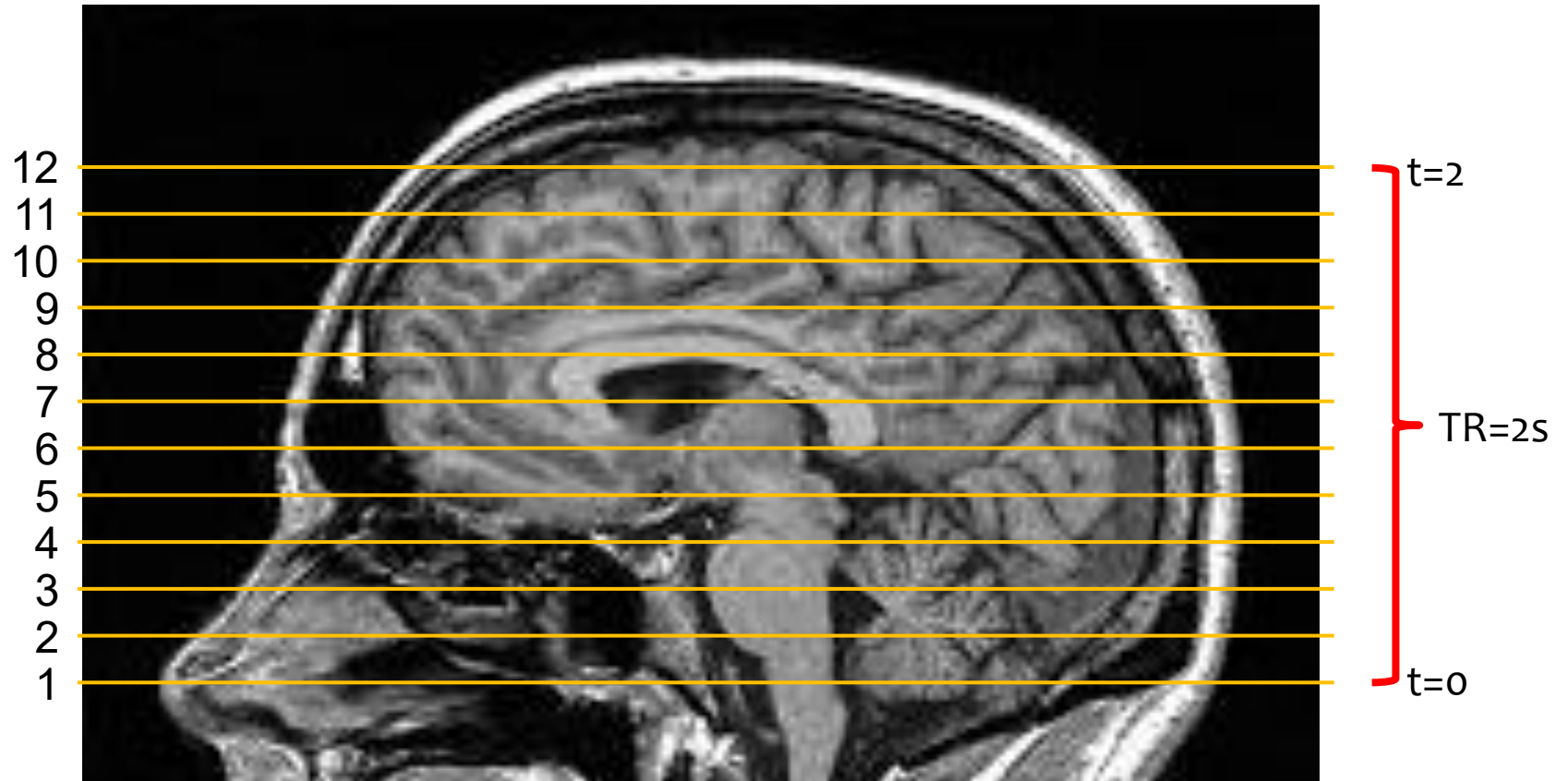
Problems with fMRI data

- Artefacts
- Head motion
- Slice timing
- Brain differences
- Noise
- ... and many others

Slice timing

Typically, the fMRI data are acquired slice-by-slice – not the whole brain all at once

Order: **Ascending**



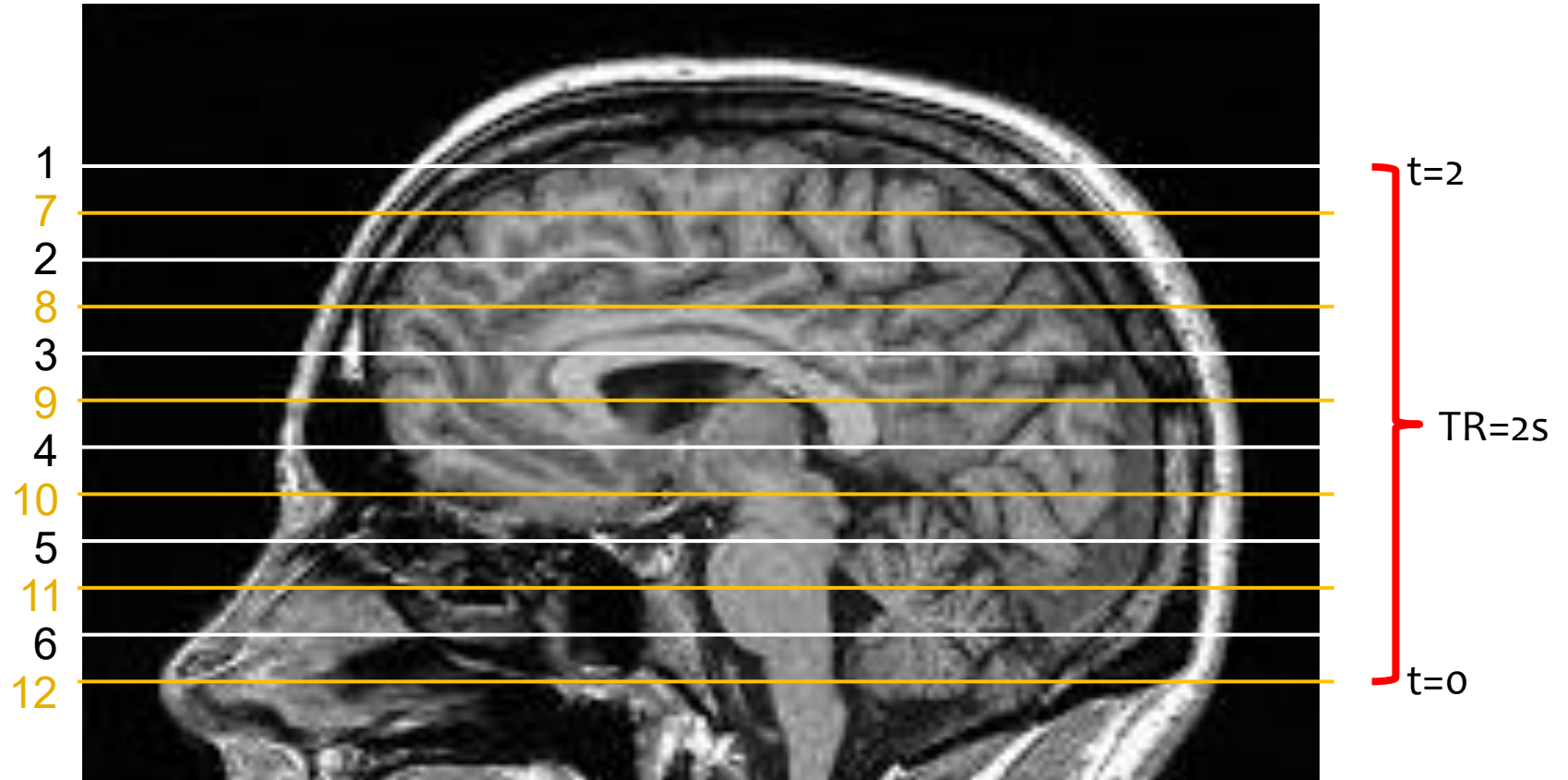
- The first slice is collected almost 2s before the last slice!
- Excitation of one slice may carry over to next slice!
 - Can be solved by **interleaved** acquisition



Slice timing

Typically, the fMRI data are acquired slice-by-slice – not the whole brain all at once

Descending-Interleaved

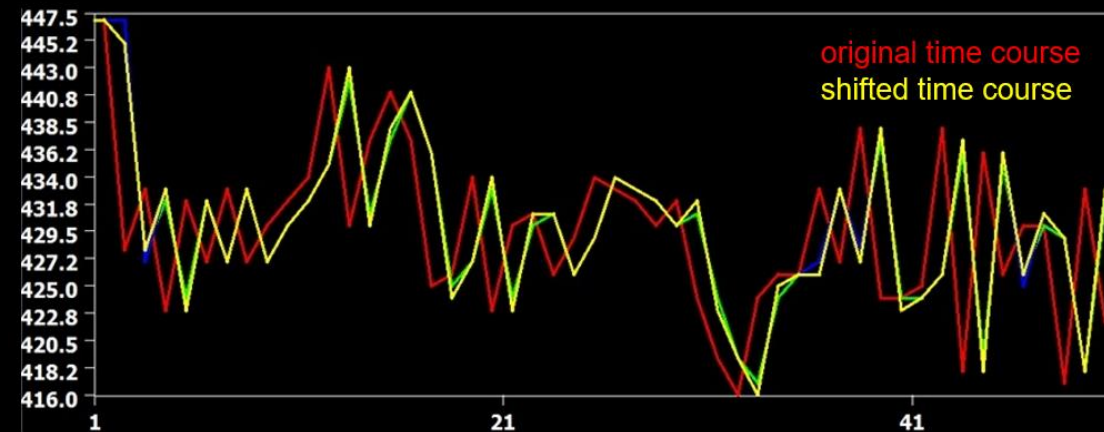
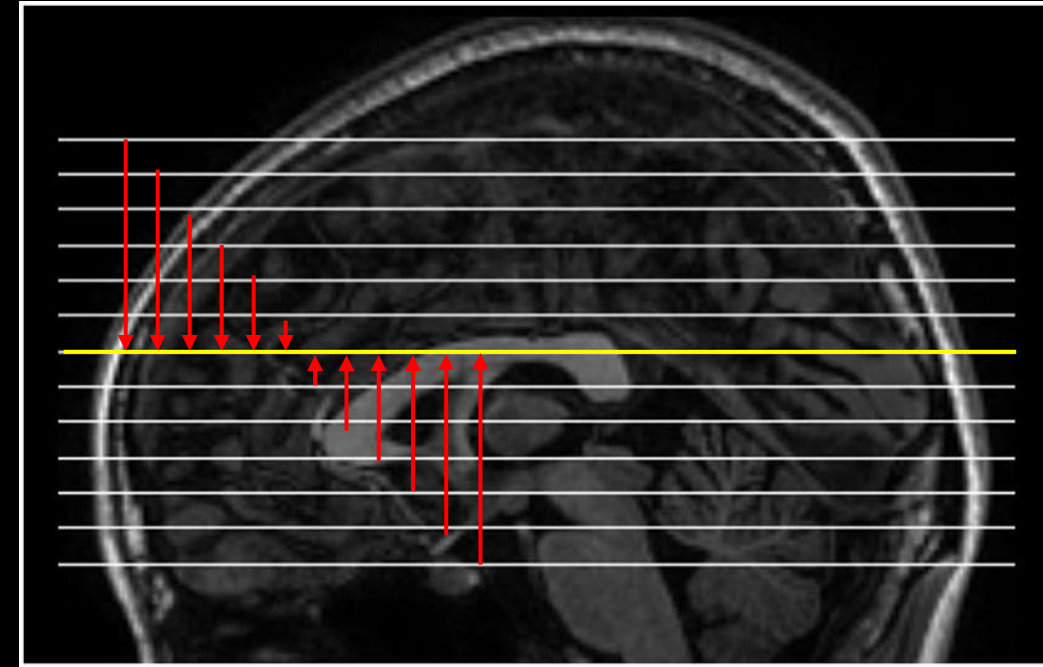


- The first slice is collected almost 2s before the last slice!



Slice time correction

- **Temporal interpolation**
 - Adjusts the timings of the slices so that it is **as if they had been collected simultaneously**
 - Uses information from nearby time points to **estimate the amplitude of the MR signal** at the onset of each TR
- **Key parameters**
 - **Reference slice**
 - The only slice that is not interpolated
 - Typical choice is to use the middle slice
 - **Slice order**
 - **TR**
- No need to slice time correct if TR is very short (e.g., multi-band: multiple slices at the same time)

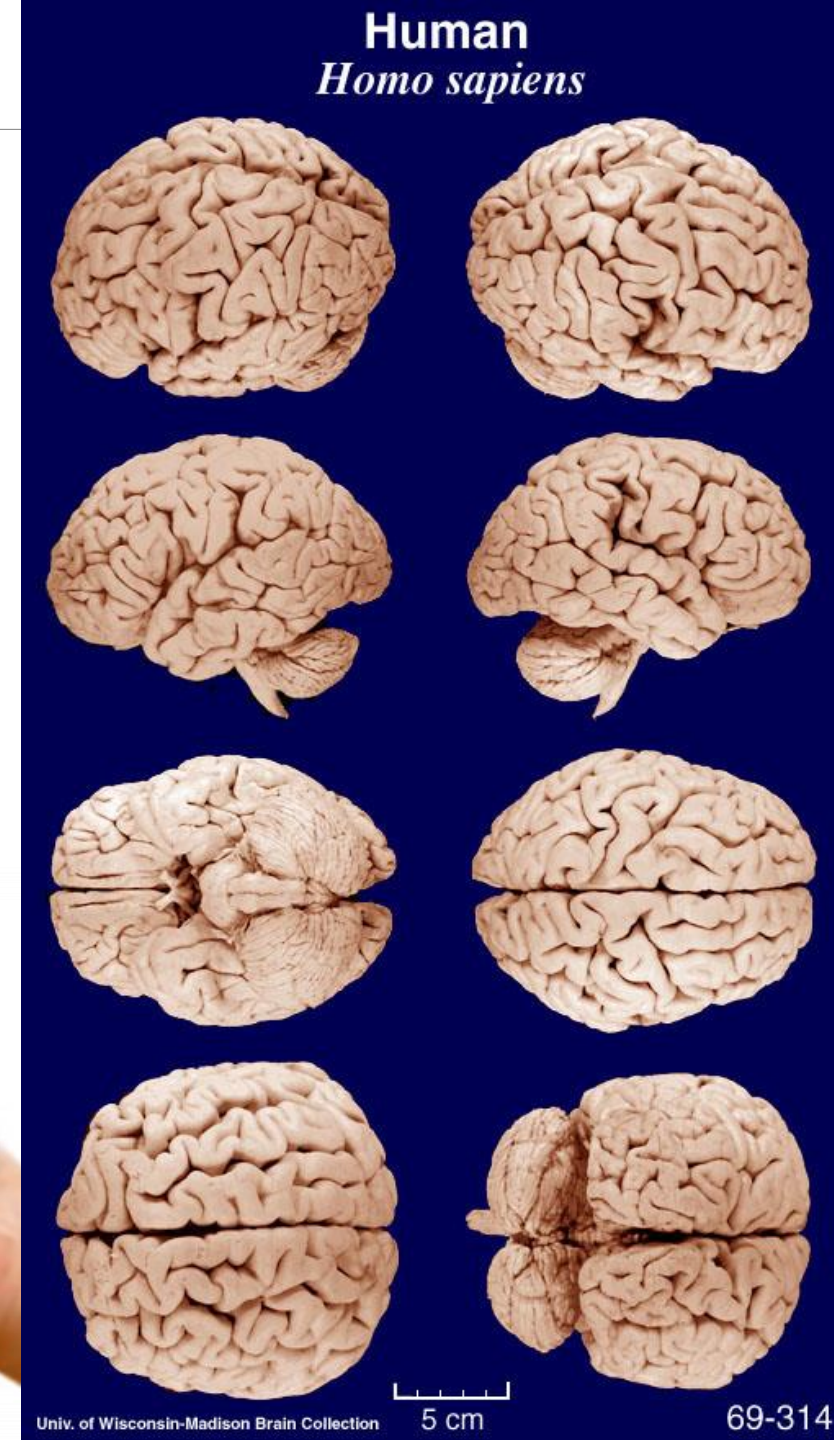


Problems with fMRI data

- Artefacts
- Head motion
- Slice timing
- Brain differences
- Noise
- ... and many others

Brain differences – between subjects

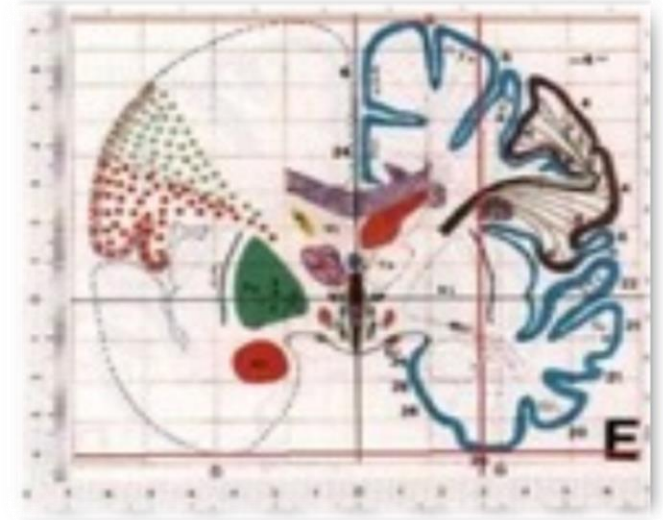
- Brain size can differ (up to 30%)
- Brain shape can differ
- Solution: **normalise to a standard template**
 - stretching, squeezing and warping each brain to the “standard brain”



Standard brain template

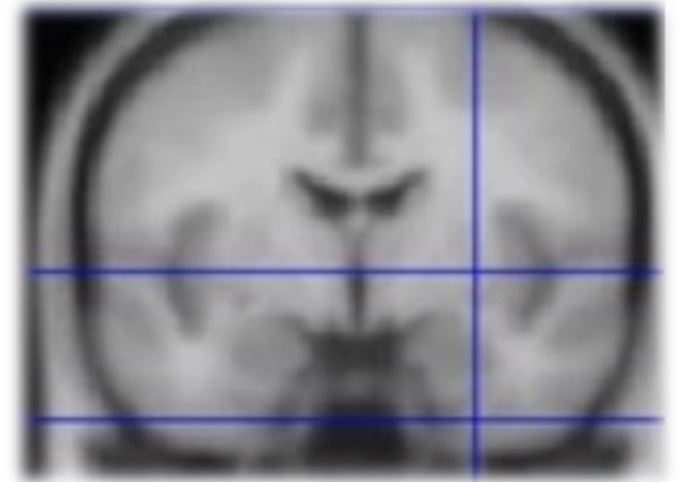
- **Talairach space**

- From atlas of Talairach and Tournoux (1988)
- Based on **single subject (60y, Female, Cadaver)**



- **MNI – Montreal Neurological Institute**

- Average scan of **152 ‘normal’ right-handed subjects**
- Approximated to Talairach space
- Slightly larger



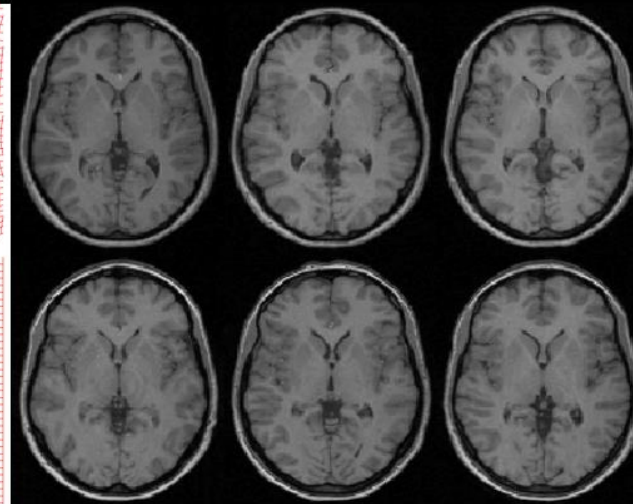
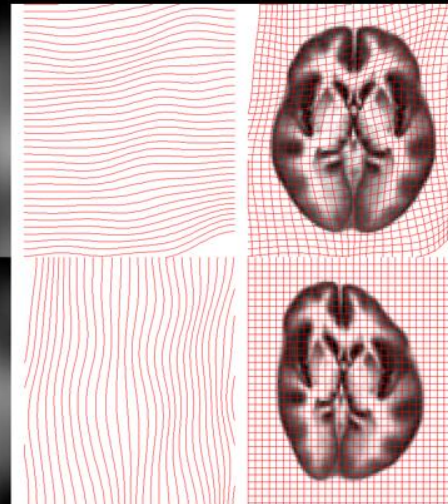
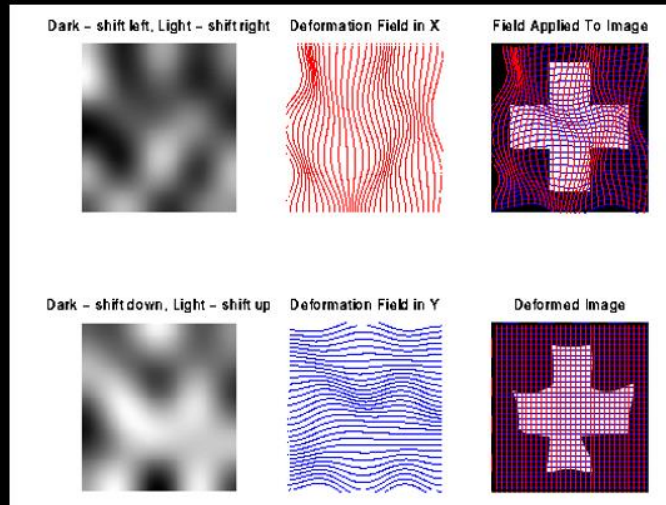
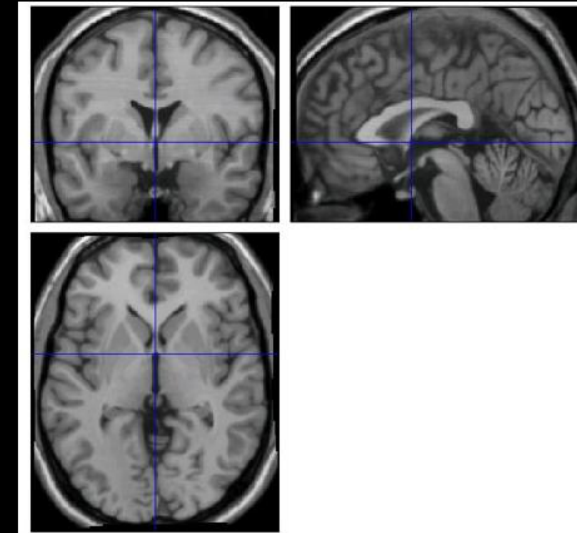
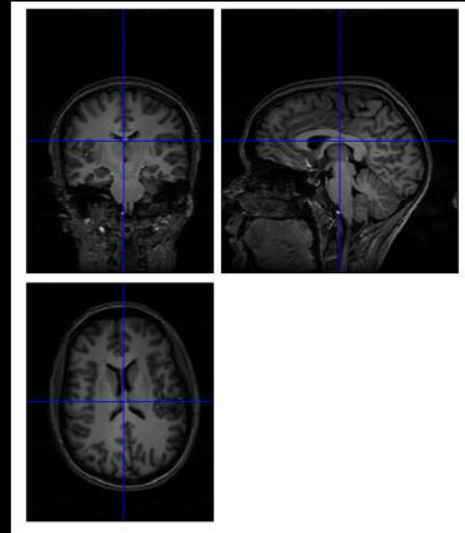


About the MNI space(s)

<https://www.lead-dbs.org/about-the-mni-spaces/>

- **MNI305**: 305 normal MRI brains were linearly coregistered (9-param) to 241 brains that had been coregistered (roughly) to the Talairach atlas. This was the first MNI template. It is T1 only.
- **Colin27 original**: Colin Holmes, a lab member of the MNI, was scanned 27 times. This was used as the standard template in SPM96. This template was matched to the MNI305. In the original release, only a T1 template was available.
- **MNI152 linear**: 152 normal images were linearly coregistered (9-param) to the 305 space. This was adopted to define standard anatomy by the International Consortium of Brain Mapping (ICBM) and is used by SPM from version 99 on. Only a T1 template is available.
 - **SPM**: Note that in later iterations, SPM defined its own “space” based on scans acquired within the **IXI dataset**, leveraging on the concept of segmentation-based normalizations (as applied in the **Unified Segmentation**, **DARTEL** and **SHOOT** approaches). This space, **referred to as the IXI549Space** is largely similar to MNI152 and of similar resolution (where it's likely safe to say that differences do not matter as much for most applications). Along the same lines, both spaces are unsuitable for use in DBS imaging, in our opinion. **More info here.**
- **MNI152 NLIN 6th generation**: Here, the 152 brains were nonlinearly registered into 305 space. Again, only a T1 template is available.
 - **FSL**: The FSLR is an adapted version of this space but in its asymmetric flavor (MNI152NLIN6Asym, hence different to the official **one provided here**). The template also provides surface coordinates references. **More info here.**
- **Colin27 hires T1/T2 version (2008)**: The MNI also released a high-resolution version of the Colin27 space.
- **MNI152 NLIN 2009**: Finally, in 2009, the MNI released an updated version after again nonlinearly co-registering the 152 acquisitions. This template exhibits the best resolution and detail to date and is available in T1, T2, PD and T2-relaxometry versions. It has not (yet) been adopted by SPM or FSL though and it's anatomy is slightly different in direct comparison to the 6th generation templates. Moreover, it comes in three versions (two of which are explicitly mentioned here) that each have a symmetric and asymmetric subversion:
 - **MNI152 NLIN 2009a**: Probably the official new template in $1 \times 1 \times 1$ mm resolution. It comes in T1, T2, PD and T2-relaxometry versions. There is a symmetric and an asymmetric version (latter not featuring T2-relaxometry).
 - **MNI152 NLIN 2009b**: The only of the novel templates available in $0.5 \times 0.5 \times 0.5$ mm resolution. It is available in a T1, T2 and PD version. Due to the high resolution of this template, **it has been adopted by Lead-DBS as the primary anatomy template**. Lead-DBS uses the asymmetric version of this template.

Normalisation



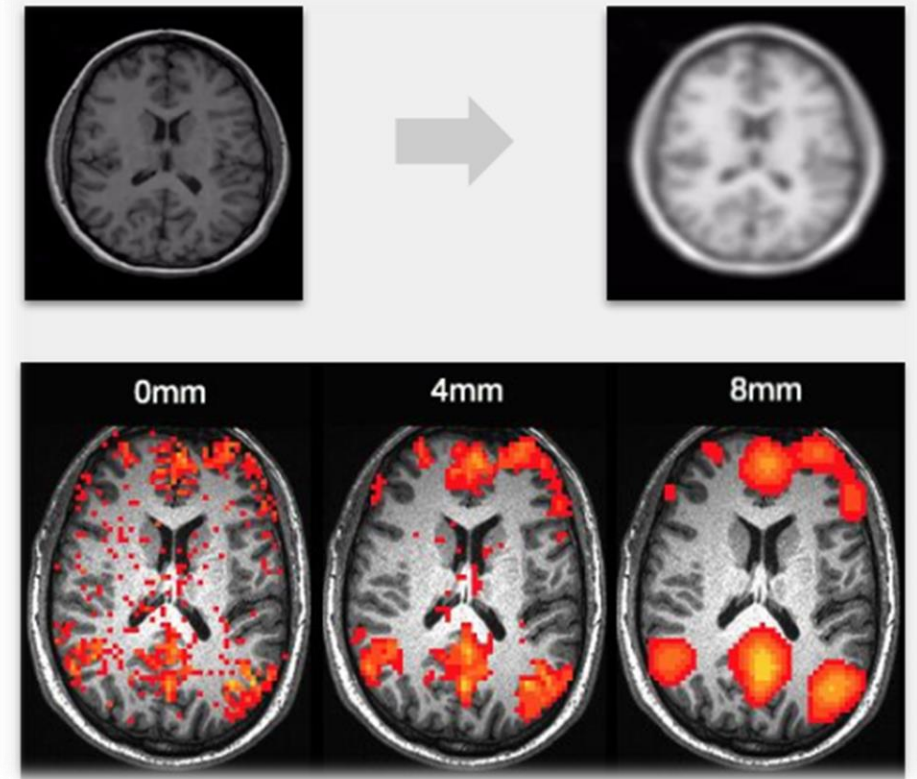
Non-linear spatial transformations



FMRI 4 NEWBIES .COM

Spatial smoothing

- Helps make residual errors in previous spatial pre-processing stages less problematic (e.g., imperfect normalisation, motion correction)
- Can increase signal-to-noise ratio
- Necessary for validity of multiple corrections within random field theory
- But it reduces the image resolution

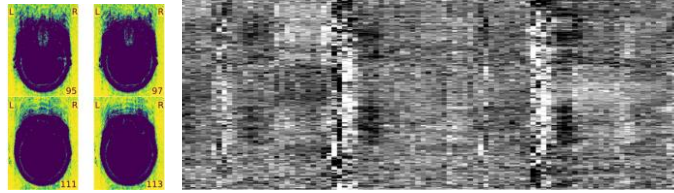


Problems with fMRI data

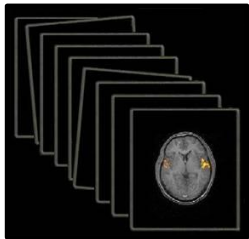
- Artefacts
- Head motion
- Slice timing
- Brain differences
- Noise – can be modelled in GLM
- ... and many others

Typical fMRI pre-processing pipeline

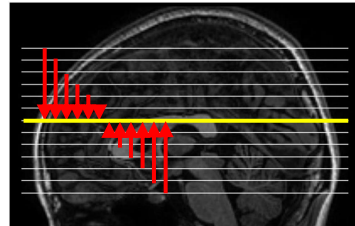
Data quality
assessment



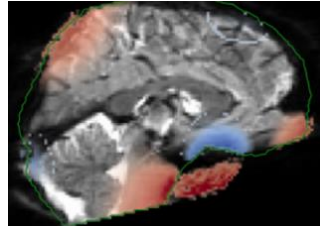
Motion-
correction



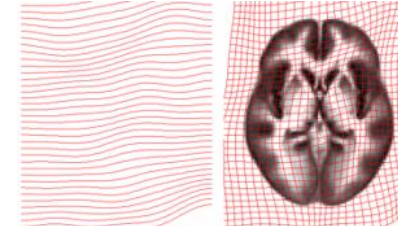
Slice-time
correction



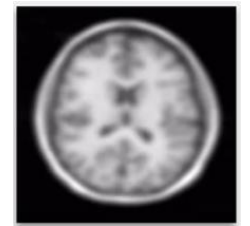
Distortion
correction



Normalisation to
MNI space

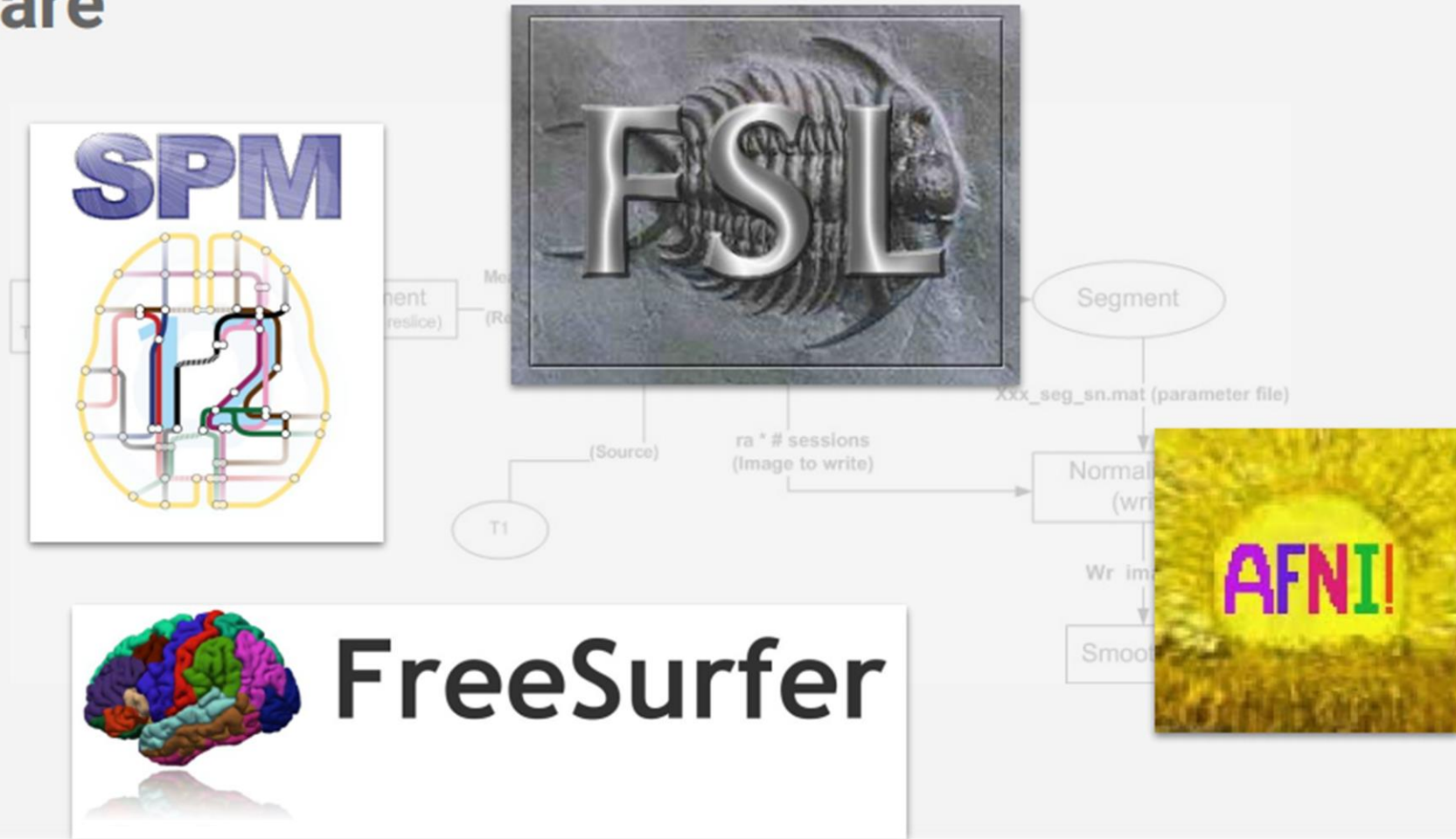


Spatial
smoothing

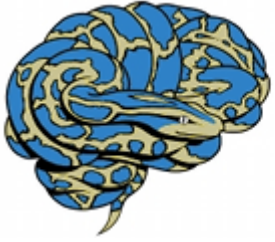


Pre-processing tools

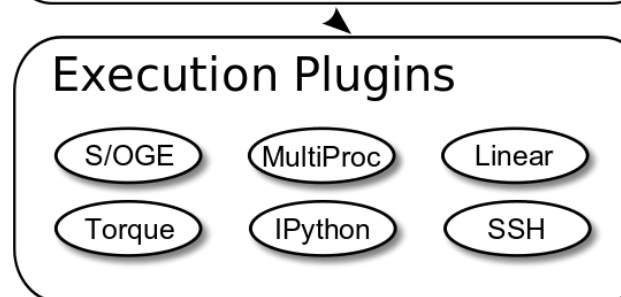
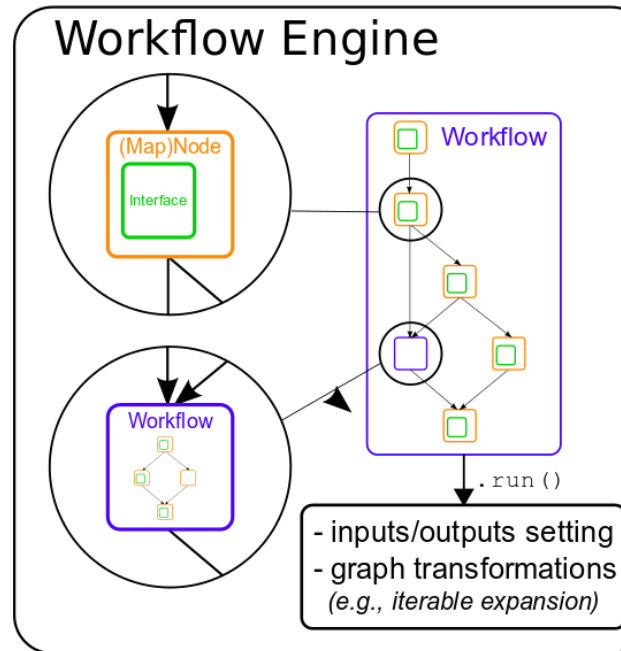
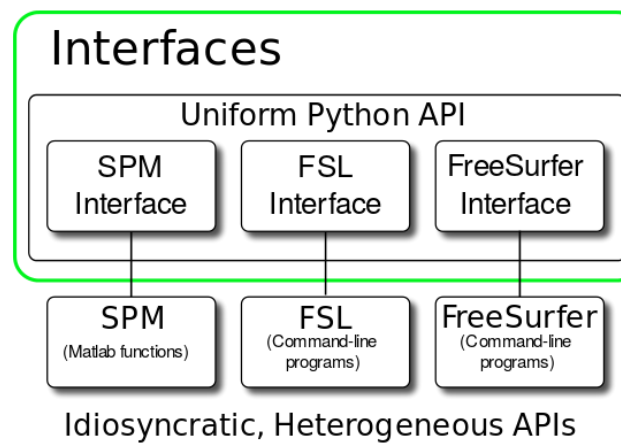
Software



Pre-processing tools



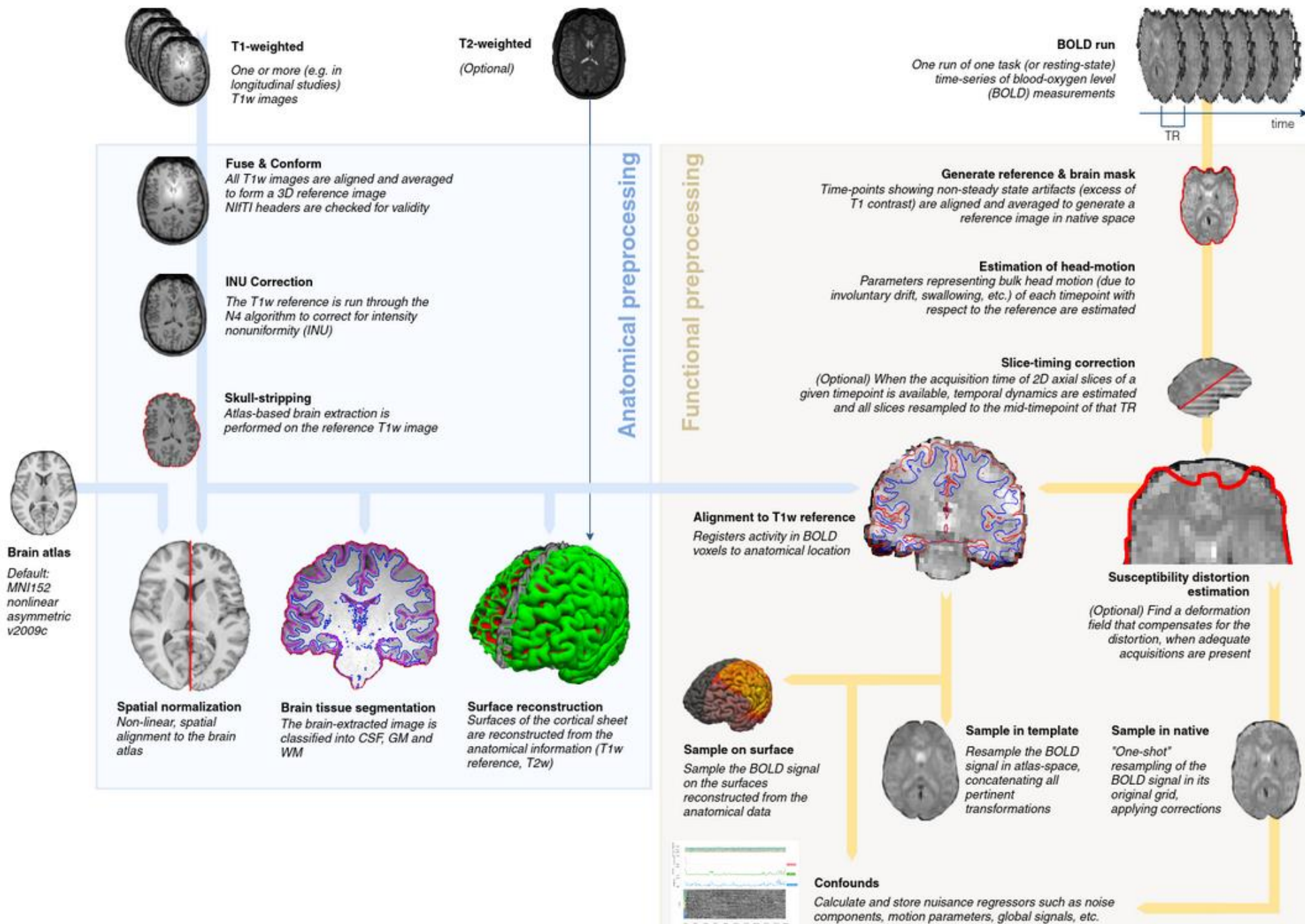
Nipype: Neuroimaging in Python Pipelines and Interfaces



Pre-processing tools

- **fMRIPrep** <https://fmriprep.org/en/stable/>
 - Fully automated fMRI data pre-processing tool
 - The workflow is based on [Nipype](#) and encompasses a large set of tools from well-known neuroimaging packages, including [FSL](#), [ANTs](#), [FreeSurfer](#), [AFNI](#), and [Nilearn](#). This pipeline is designed to provide the best software implementation for each state of pre-processing.
 - **Robustness** - The pipeline adapts the pre-processing steps depending on the input dataset and should provide results as good as possible independently of scanner make, scanning parameters or presence of additional correction scans (such as fieldmaps).
 - **Ease of use** - Thanks to dependence on the BIDS standard, manual parameter input is reduced to a minimum, allowing the pipeline to run in an automatic fashion.
 - **“Glass box” philosophy** - Automation should not mean that one should not visually inspect the results or understand the methods. Thus, fMRIPrep provides visual reports for each subject, detailing the accuracy of the most important processing steps.

fMRIPrep



fMRIprep

<https://fmripiprep.org/en/stable/usage.html>

```
usage: fmripiprep [-h] [--skip_bids_validation]
                  [--participant-label PARTICIPANT_LABEL [PARTICIPANT_LABEL ...]]
                  [--session-label SESSION_LABEL [SESSION_LABEL ...]]
                  [-t TASK_ID] [--echo-idx ECHO_IDX]
                  [--subject-anatomical-reference {first-lex,unbiased,sessionwise}]
                  [--bids-filter-file FILE] [-d PACKAGE=PATH [PACKAGE=PATH ...]]
                  [--bids-database-dir PATH] [--nprocs NPROCS]
                  [--omp-nthreads OMP_NTHREADS] [--mem MEMORY_MB] [--low-mem]
                  [--use-plugin FILE] [--sloppy] [--anat-only]
                  [--level {minimal,resampling,full}] [--boilerplate-only]
                  [--reports-only]
                  [--ignore {fieldmaps,slicetiming,sbref,t2w,flair,fmap-jacobian} [{fieldmaps,slicetiming,
                  [--force {bbr,no-bbr,syn-sdc,fmap-jacobian} [{bbr,no-bbr,syn-sdc,fmap-jacobian} ...]]
                  [--output-spaces [OUTPUT_SPACES ...]]
                  [--longitudinal LONGITUDINAL]
                  [--bold2anat-init {auto,t1w,t2w,header}]
                  [--bold2anat-dof {6,9,12}] [--force-bbr FORCE_BBR]
                  [--force-no-bbr FORCE_NO_BBR]
                  [--slice-time-ref SLICE_TIME_REF] [--dummy-scans DUMMY_SCANS]
                  [--fallback-total-readout-time FALLBACK_TOTAL_READOUT_TIME]
                  [--random-seed _RANDOM_SEED]
                  [--me-t2s-fit-method {curvefit,loglin}]
                  [--output-layout {bids,legacy}] [--me-output-echos]
                  [--aggregate-session-reports AGGR_SES_REPORTS]
                  [--medial-surface-nan] [--project-goodvoxels]
                  [--md-only-boilerplate] [--cifti-output [{91k,170k}]]
                  [--msm | --no-msm] [--return-all-components]
                  [--fd-spike-threshold REGRESSORS_FD_TH]
                  [--dvars-spike-threshold REGRESSORS_DVARS_TH]
                  [--skull-strip-template SKULL_STRIP_TEMPLATE]
                  [--skull-strip-fixed-seed]
                  [--skull-strip-t1w {auto,skip,force}] [--fmap-bspline]
                  [--fmap-no-demean] [--use-syn-sdc [{warn,error}]]
                  [--force-syn FORCE_SYN] [--fs-license-file FILE]
                  [--fs-subjects-dir PATH] [--submm-recon | --no-submm-recon]
                  [--fs-no-reconall] [--fs-no-resume] [--track-carbon]
                  [--country-code COUNTRY_CODE] [--version] [-v] [-w WORK_DIR]
                  [--clean-workdir] [--resource-monitor] [--config-file FILE]
                  [--write-graph] [--stop-on-first-crash] [--notrack]
                  [--debug {compcor,fieldmaps,pdb,all} [{compcor,fieldmaps,pdb,all} ...]]
                  bids_dir output_dir {participant}
```

Limitations and reasons not to use fMRIPrep

- **Very narrow FoV images** oftentimes do not contain enough information for standard image registration methods to work correctly.
- fMRIPrep may also underperform for **particular populations** (e.g., infants) and non-human brains, although appropriate templates can be provided to overcome the issue.
- If you really **want unlimited flexibility** (which is obviously a double-edged sword).
- If you **want students to suffer** through implementing each step for didactic purposes, or to learn shell-scripting or Python along the way.
- If you are trying to **reproduce some in-house lab pipeline**.

✓ Environment



Data
Organise & Manage



Notebook: [nb03_Quality-Control-and-Preprocessing.ipynb](#)

Pre-process

Outline

- Introduction
- Experimental design
- Data management
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- **Statistical analysis**
- Practical demo