MR Methods for Faculty II

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Internal Reproducibility

You should be able to effortlessly reproduce your own analysis

— Version Control
— Data provenance
— Automated, reproducible computations
— Documentation
— Replicable computational environments

Review

Internally reproducible research

— Organize your data (BIDS)

— Use scripts

— Use version control (git)

— Options for making reproducible software environments (singularity]

Review

fMRI task design

— Block vs event designs

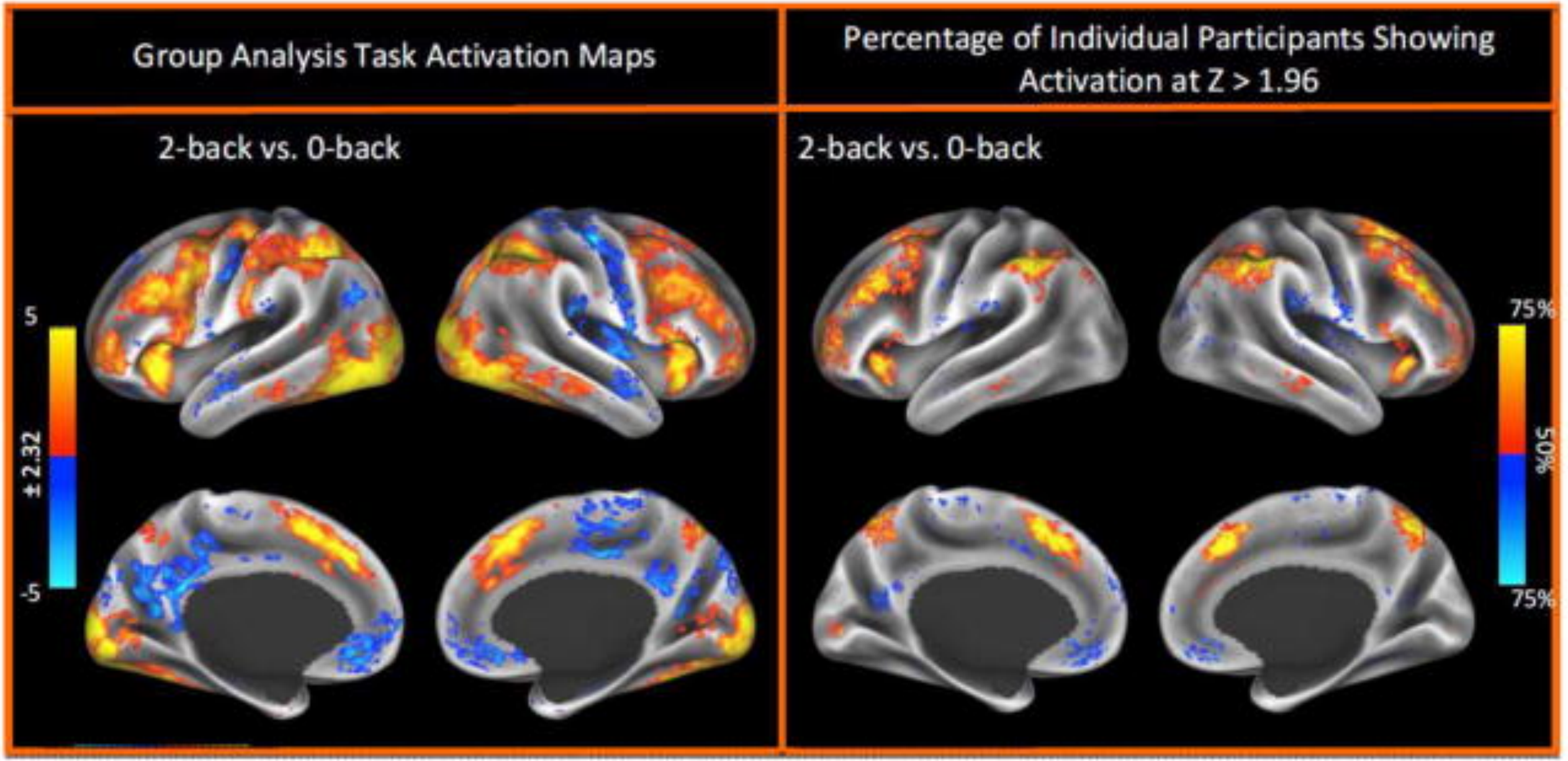
— Detection vs estimation efficiency

— Design optimization is important

Review

Resources for design optimization

- `RSFgen` (AFNI)
- `make_random_timing.py` (AFNI)
- `optseq2` (MGH/FreeSurfer)
- Genetic algorithms psych.colorado.edu/~tor/Software.htm
- m-sequences cfn.upenn.edu/aguirre/wiki/public:m_sequences


Group Analysis Task Activation Maps
Percentage of Individual Participants Showing Activation at Z > 1.96
2-back vs. 0-back
2-back vs. 0-back
5
±2.32
-5
75%
50%
75%

Group vs Individual Activation

— Group average data does not reflect individuals

— Group analyses may not be reliable if the underlying activation is highly variable

Low Within Subject Reliability

- Test-retest fMRI reliability is poorly characterized
  - 10s of thousands of publised task fMRI studies
  - 63 with test-retest measures (Bennet et al., 2010)
  - Low test-retest reliability (mean ICC = .5; mean overlap = 29%)

Limitations of Reliability

Poor reliability limits scientific value

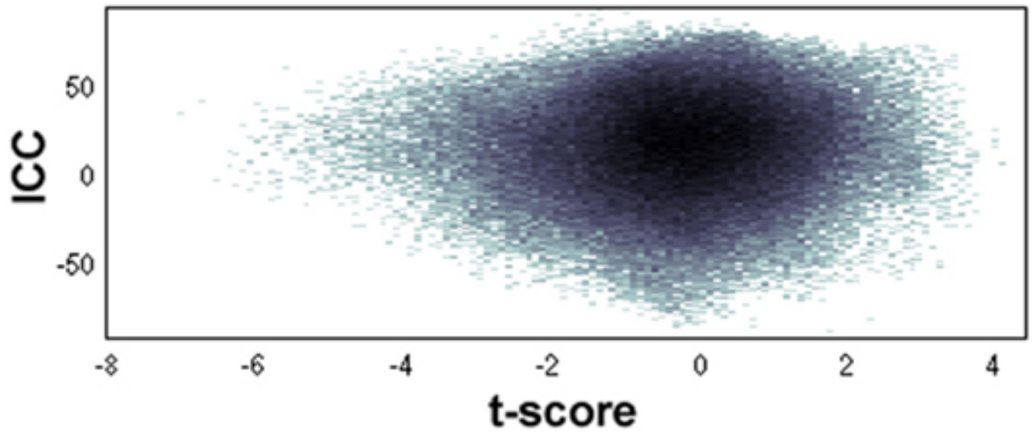
— Between group analyses
— Brain-behavior correlations
— Neurogenetics
— Functional localizers
— Databasing

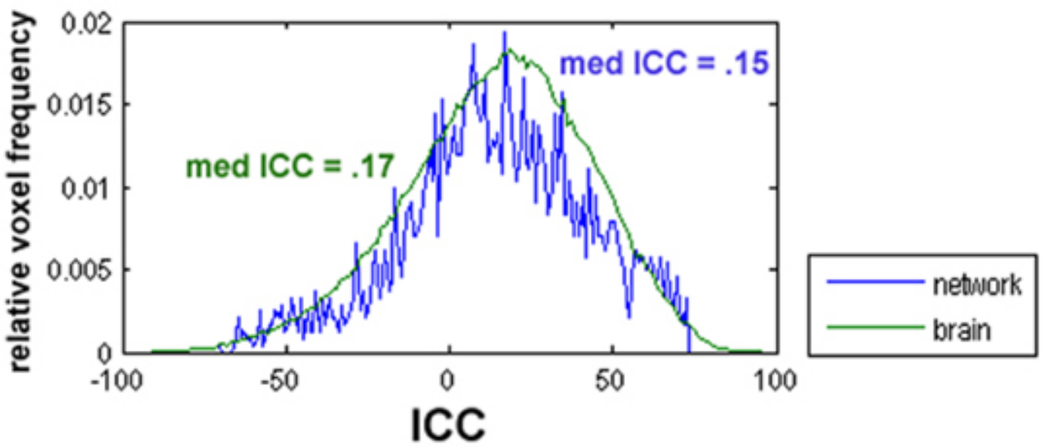
Improving Reliability

- Increase SNR
- Optimize design power
- Minimize confounds (time of day, attention, practice)
- But fMRI is fundamentally noisy
- Select tasks with high reliability and/or do test-retest on your own data

A

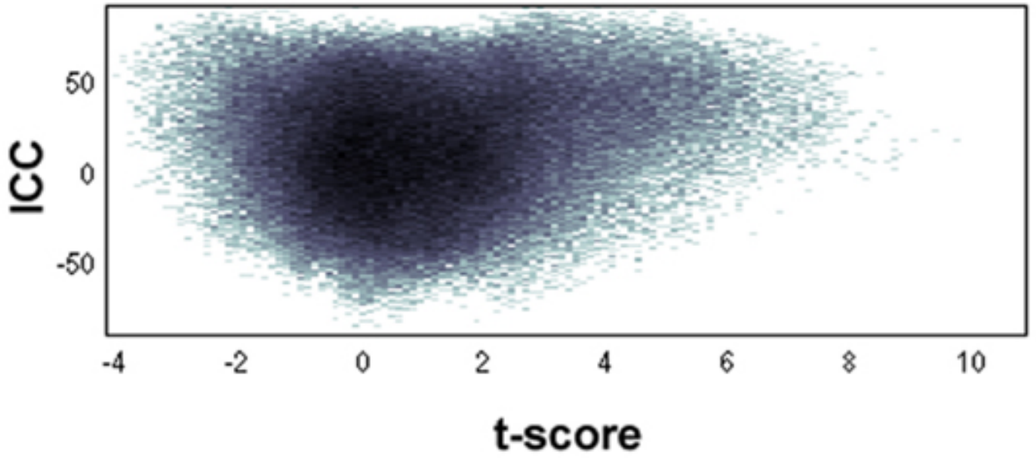
Words

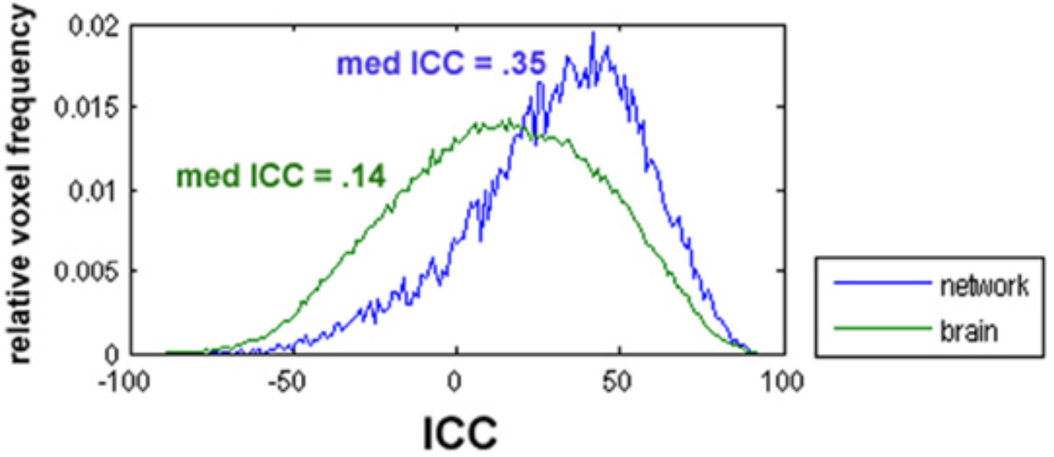




B

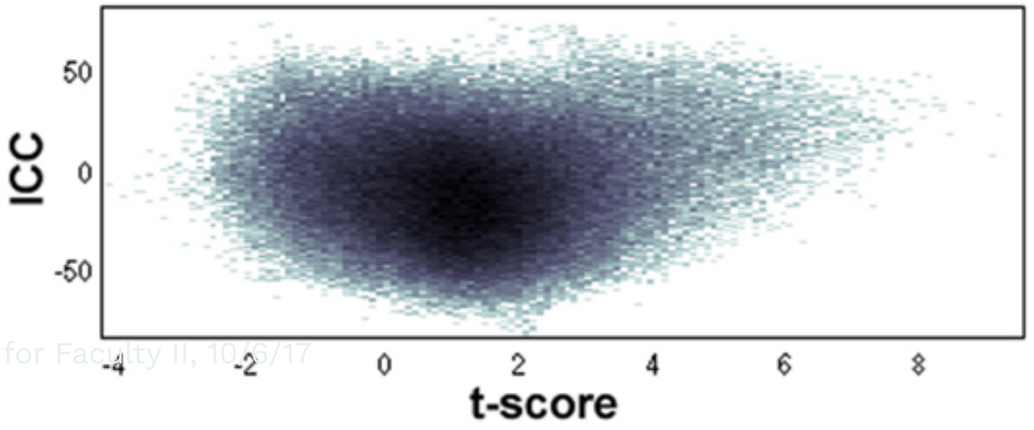
Scenes

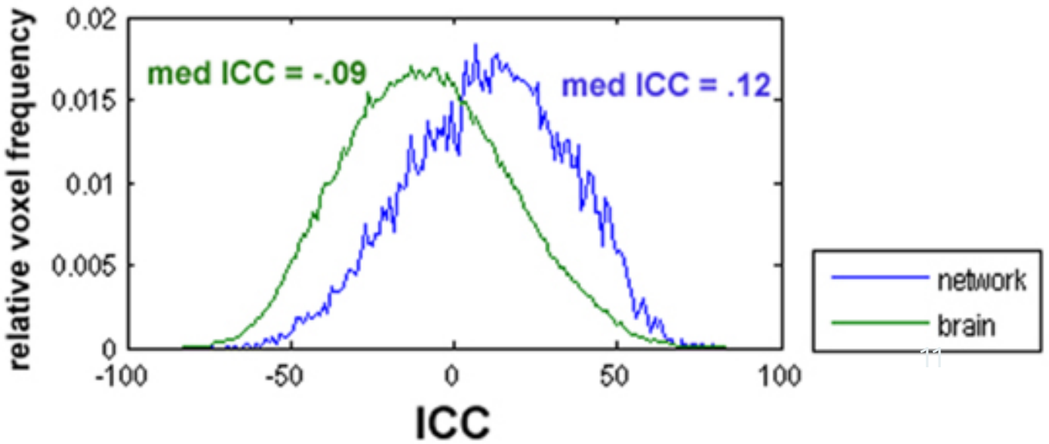




C

Fractals





Today

— Data acquisition
— Preprocessing for volumetric analysis
— Single subject statistics (mass univariate)

Implementing Your Task

— Use your preferred stimulus presentation software
— Check that timing is relatively consistent
— Target output: event or block onset times, temporally aligned with BOLD data
— Use the scanner TTL pulse to align your fMRI data

fMRI Scan Sequence

Nominal setup at BIRC; other sequences are possible

1. Researcher preps the experiment on stimulus PC
2. Operator starts the BOLD sequence
3. Dummy volume collection
4. Scanner sends a trigger pulse
5. Experiment starts

Scanner Pulses

- The scanner sends a 5 keystroke at the beginning of each volume that is kept
- Wait for a 5 response to start the experiment
- Offset event times based on the initial 5 response
- More sophisticated timing setups are possible

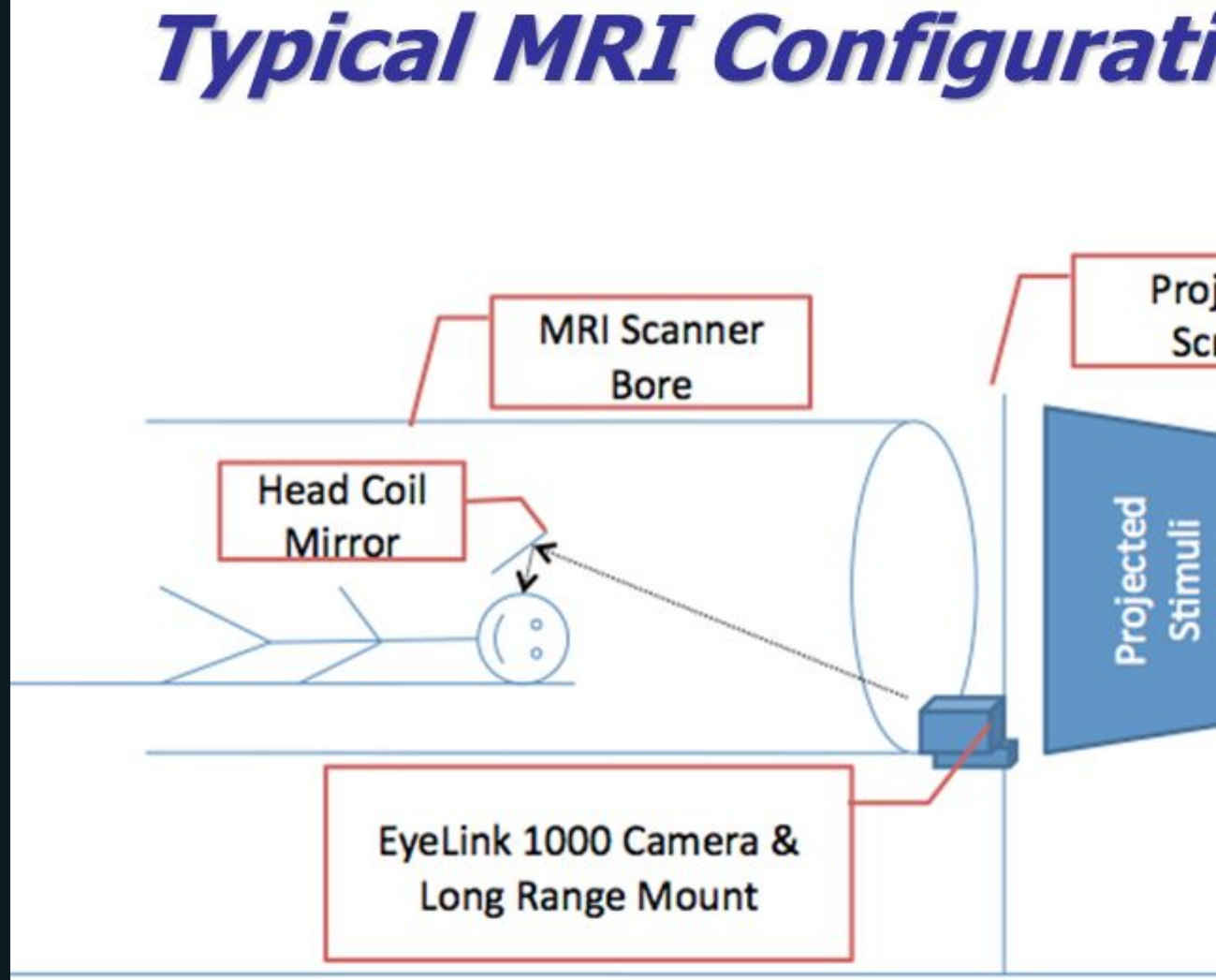
Testing your Experiment

Before scanning, check that

— Your event timing is consistent between runs
— You understand the timing variables
— You understand how to align your events with fMRI data

BOLD Display

See the MRI Display article on the BIRC wiki for visual angle calculations



MRI Protocol

- Develop a general idea of the scan parameters you want
  - Consider existing literature
  - Major projects: ADNI, HCP
- Special considerations:
  - Specialized analysis methods
  - Unusually high temporal or spatial resolution
  - Challenging brain regions

Parameters

Spatial resolution:

- 2-3 mm^3 for typical fMRI and DWI
- Spatial resolution vs SNR ($2mm^3$ is a ~70% reduction in SNR from $3mm^3$)
- Spatial resolution vs acquisition time
- How big is your primary structure of interest?
- Do you have a high movement population?

Parameters

Temporal resolution:

- Typically one sample every few seconds
- Faster is better...
  - Less motion between samples
  - Less physiological aliasing
  - More degrees of freedom
- ... to a degree

Parameters

Temporal resolution:

Definitely choose the fastest unaccelerated sampling possible.

If you need more speed:

- Partial imaging (iPAT/GRAPPA/ASSET/SENSE)
  - Fills in part of the MR signal
  - SNR cost (√2 or more)

Parameters

Temporal resolution:

- Simultaneous multislice (SMS/multiband)
  - Minimal SNR cost
  - Some increased motion sensitivity in some cases
  - <1s sampling possible
  - Also works for DWI

Parameters

Other considerations:

— Do you need whole brain coverage (partial coverage is faster)?

— Are you interested in regions prone to signal loss (vOFC, amygdala, temporal regions)?

Hardware Options

BIRC has a 20-channel head coil and 64-channel head/neck coil

64-channel:

— Better SNR, especially at the surface
— Necessary for SMS or high acceleration
— Smaller
— More heterogeneity

Flip Angle

- Flip angle partially determines how much signal you get
- Maximum signal at 90º for an unexcited sample
- For partially excited samples, maximum at the Ernst angle
- Maximum tSNR in BOLD at lower flip angles

TE

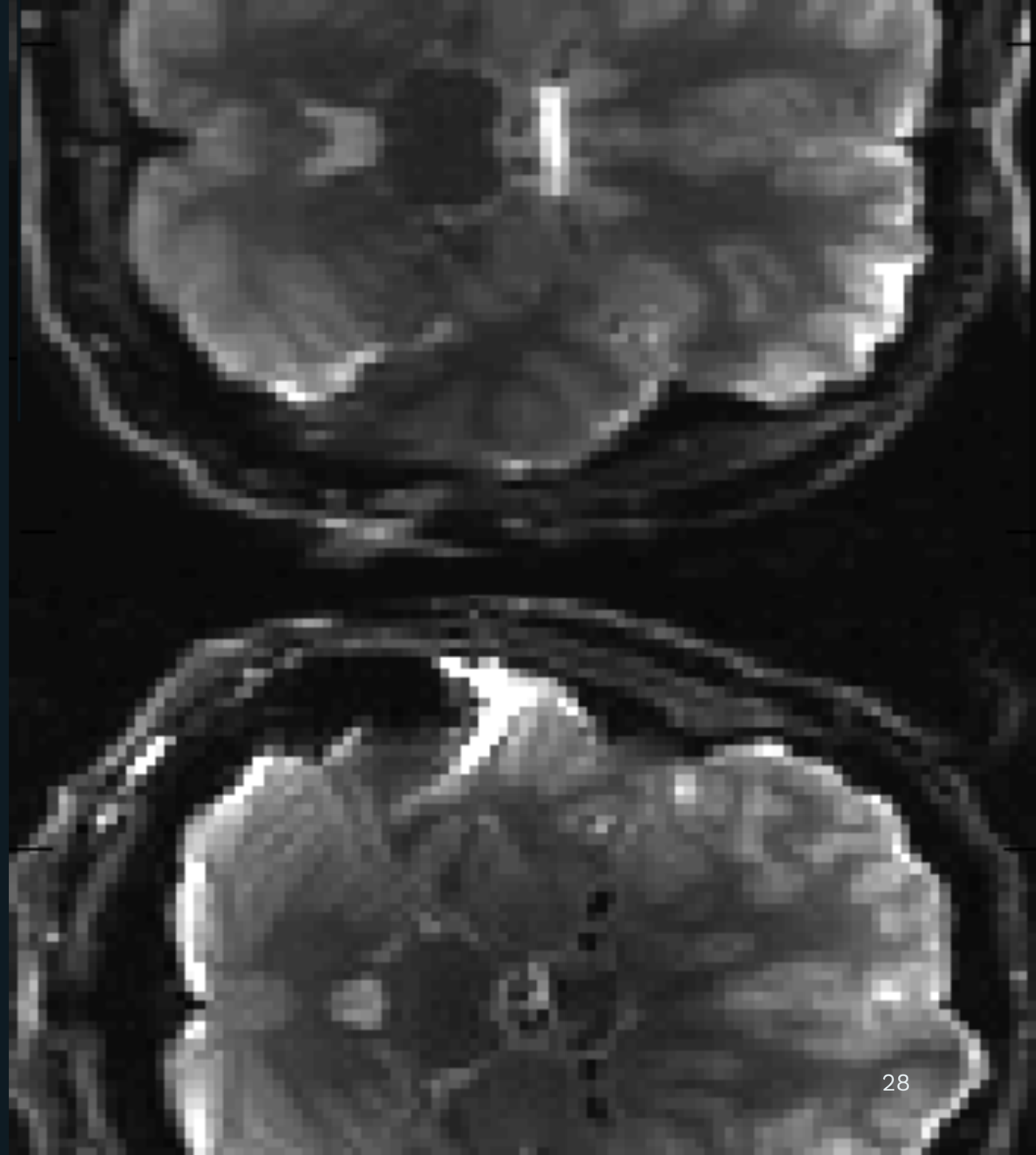
- Optimal signal when TE matches tissues $T2^*$
- Optimal TE varies across the brain, ~20-40ms
- Regions with signal loss (temporal, vOFC) have shorter $T2^*$ (<30ms)
- Regions with good signal (occipital cortex) have longer $T2^*$ (~40ms)
- Slices take longer to acquire with longer TE

Bias Correction

- Receive coil channels have different spatial sensitivities
- Can be corrected online (Prescan Normalization)
- Or offline
- Some sequences save corrected and uncorrected data

Selecting Parameters

- There is no set of universally best parameters
- Consider
  - Your brain regions of interest
  - The expected level of subject movement
  - Your hypotheses and analysis needs
- Pilot and use tSNR as a guide



Time Management

— Prep and setup: ~10 min
— Scout, T1, fieldmap: ~6-8 min
— Cleanup: ~5 min
— Checkin/instructions/setup between scans: ~1 min
— ~35-40 minutes for fMRI in a 1 hour booking

After the Scan

— Data appears in NiDB
— Download DICOM data
— Convert to BIDS
— Preprocessing and analysis

fMRI Processing and Analysis

1. Quality control
2. Minimal preprocessing
3. Quality control
4. Subject level statistics
5. Group level statistics

Quality Control 1

Make sure you have the expected data:

— Files for each expected MRI series
— Behavioral log files
— Do data volumes have the correct dimensions?
— Were the correct scan parameters used?
— BIDS-validator can help

Quality Control 2

Check fMRI data for

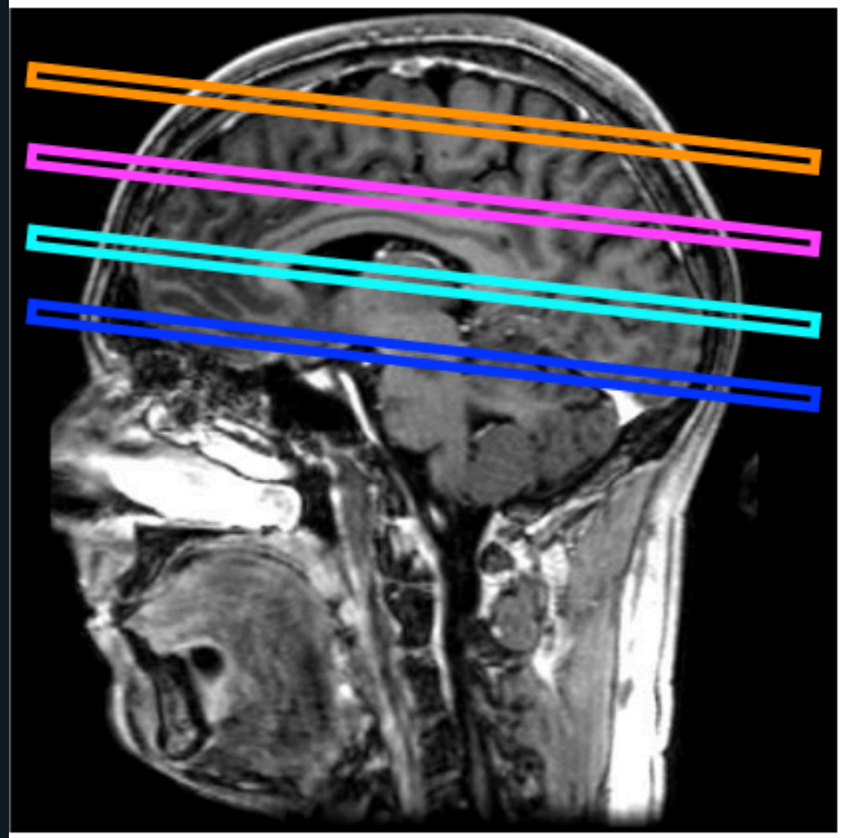
- Ghosts (signal outside the brain)
- tSNR
- Large initial intensity
- Use QAP or mriqc
  - BIDS compatible!

Minimal preprocessing (fMRI)

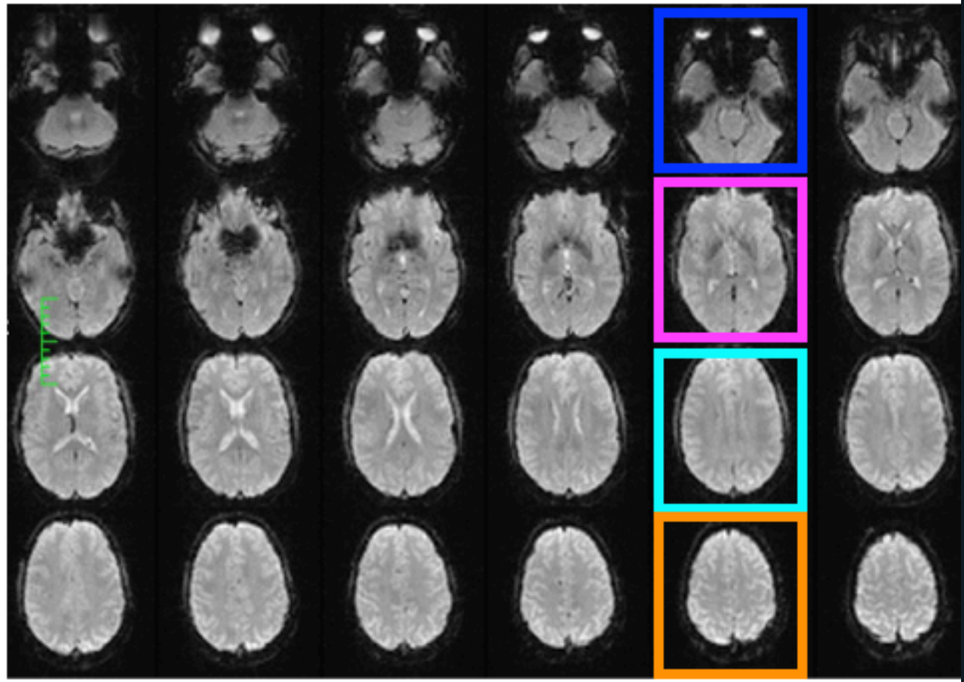
— Slice time correction
— Motion correction
— Distortion correction
— Co-registration

Slice Acquisition

- EPI images are acquired in 2D slices spread over the TR…



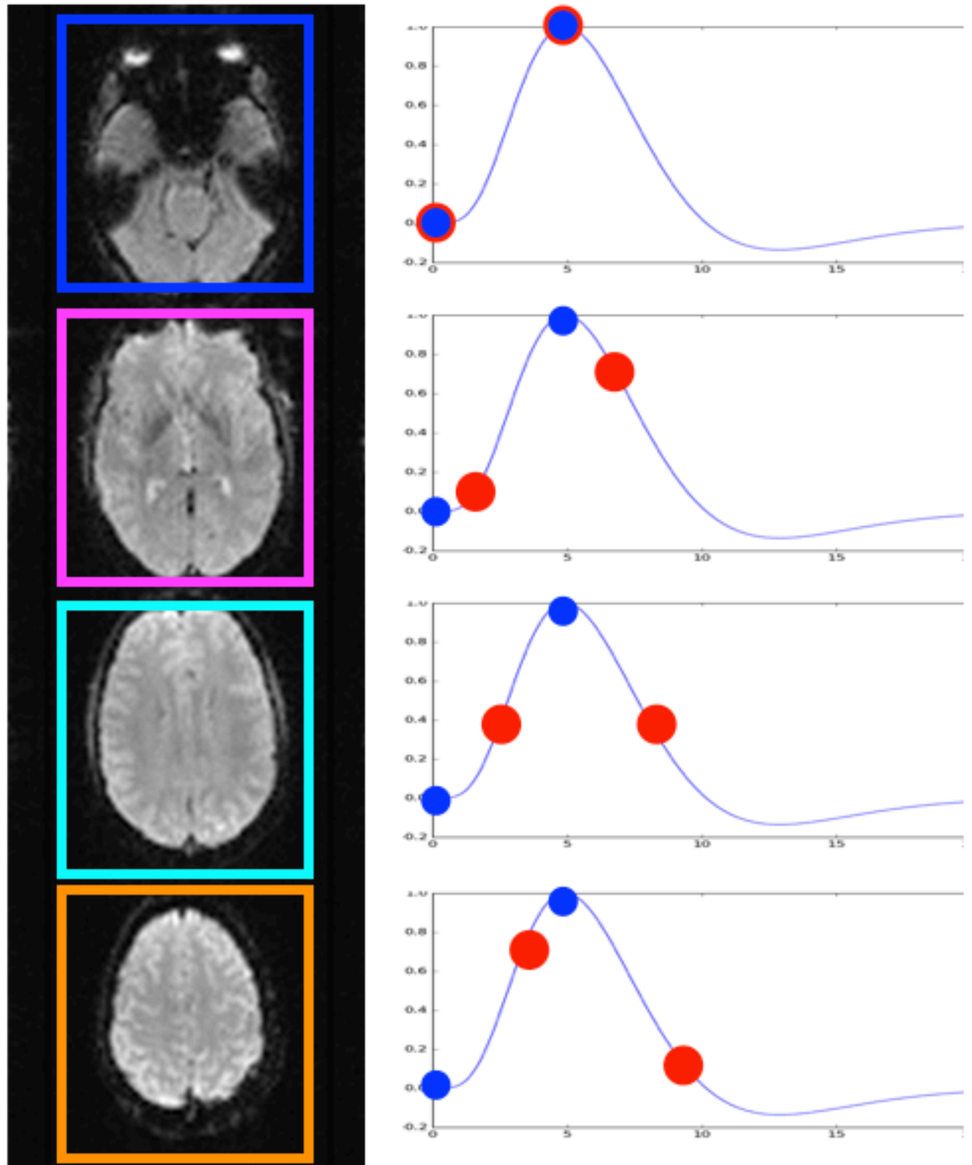
Slice Rx



Slice Mosaic DICOM

But our mass univariate model assumes the data are consistent in time

The model is only correct for this slice →



● Expected sampling point
● Actual sampling point

Slice Time Correction

- Interpolate the time series from each voxel to effectively align the data to a common time point
- Alternative solutions
  - Ignore (for short TRs)
  - Model derivatives of the HRF

Processing Order

There are different approaches to slice time correction:

- Not at all
- Before motion correction
  - Head movements can shift voxels in and out of the head-bad for interpolation
- After motion correction
  - Motion correction can shift voxels into adjacent slices at different timepoints-particularly bad for

Recommended Processing Order

- Needed for effective connectivity
- Always helps detection (Sladky et al, 2011)
  - but maybe not much if TR is short

1. Denoise the data (spikes spread during interpolation)
2. Correct for timing before motion correction if slices are interleaved

Slice Order

When were the slices acquired?

Varies by sequence and manufacturer:

— ascending or descending
— sequential or interleaved
— starting from first or second slice

Or something more complicated, e.g. SMS

Determining Slice Order

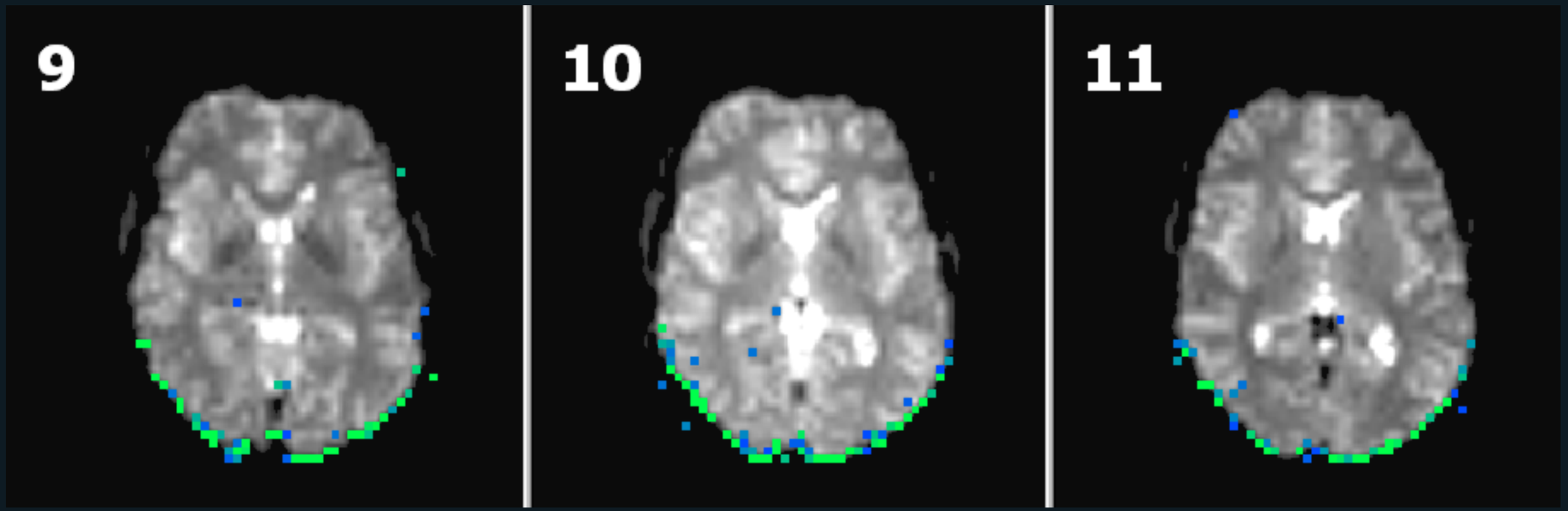
- Check the raw data (e.g. DICOM images)
  - Always start with the raw data if you are unsure of scan parameters or don't trust processed headers
- Inspect NIfTI headers (fslhd, nifti_tool) or .HEAD (3dinfo)
- Usually `alt+z2` (even # of slices) or `alt+z` (odd) here

Physics of Motion

Motion **irreparably** affects your data

- Motion rotates the brain though regions of variable B0 inhomogeneity
  - Can alter correlations between brain regions
  - Introduce regions of signal loss
- Moves regions of the brain between excitations
  - Introduces regions of changing signal intensity

Motion Artifact



Minimize motion

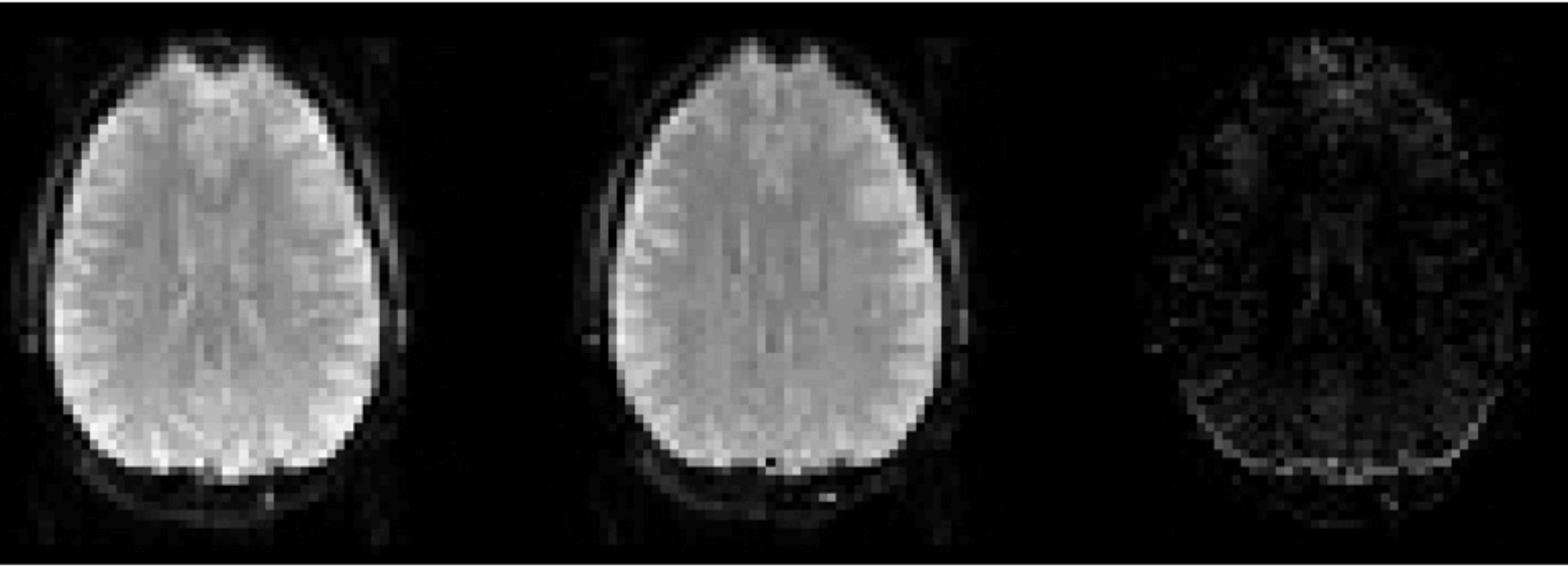
— Train subjects in a mock scanner
— Use padding or restraints
— Emphasize importance of staying still
— Monitor compliance

Realignment

Goal: put voxels in the same place throught the scan

- Spatially correct for movements from volume to volume in an EPI time series
- 6 degrees of freedom (DOF)
  - rotation (roll, pitch, yaw)
  - translation (x, y, z) shifts
- Interpolate voxels to a fixed grid

Reference volume



For every other volume….

Minimize the difference from reference

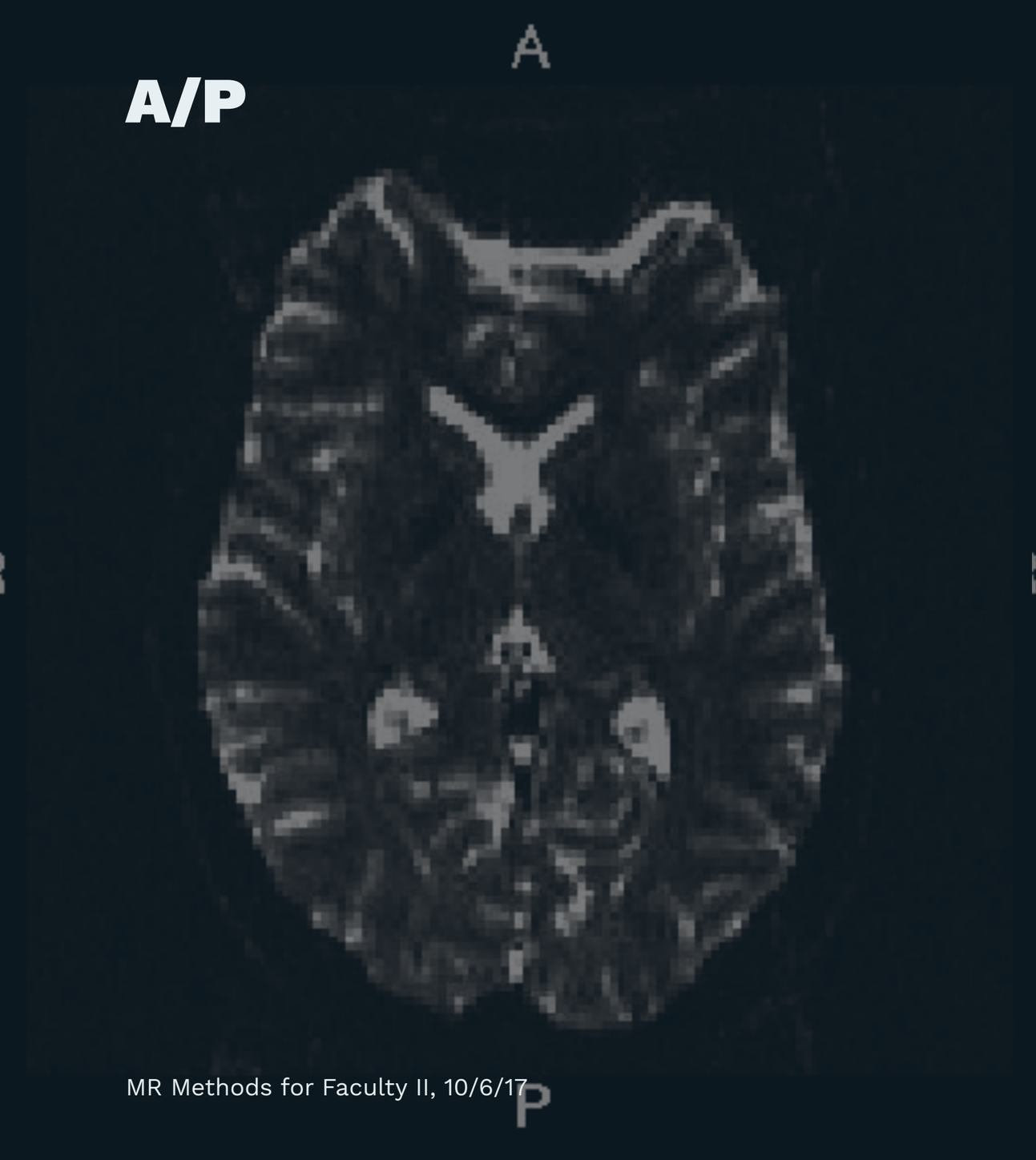
Choices

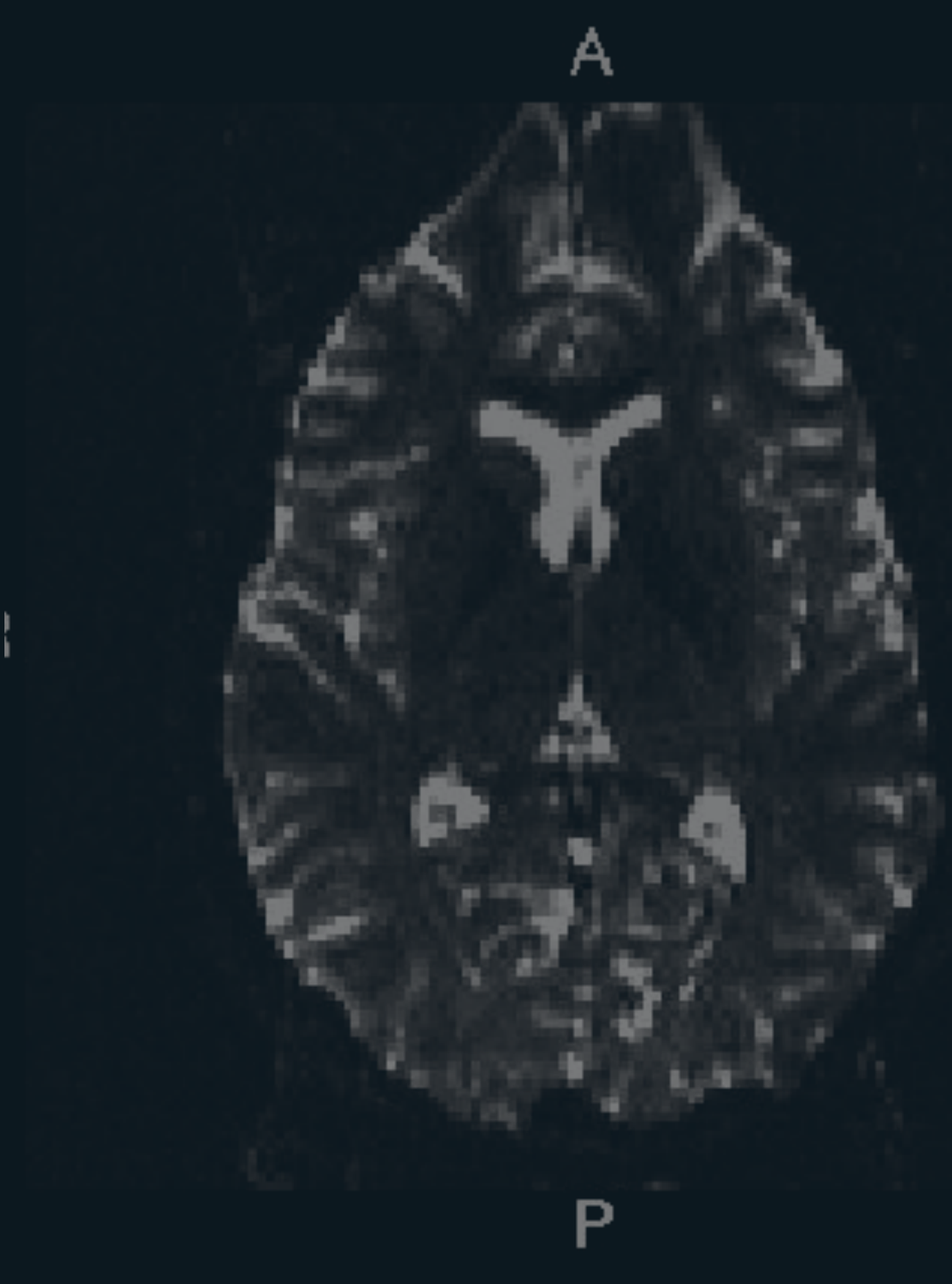
- Another b0 volume that will be used with anatomical alignment
  - For example the reference image from a multi band time series
- First volume-maybe higher signal
- Third volume-maybe a better match to the rest of the time series
- Middle volume-minimize interpolation distance
- Min outlier volume-a volume with minimal artifacts

EPI distortion

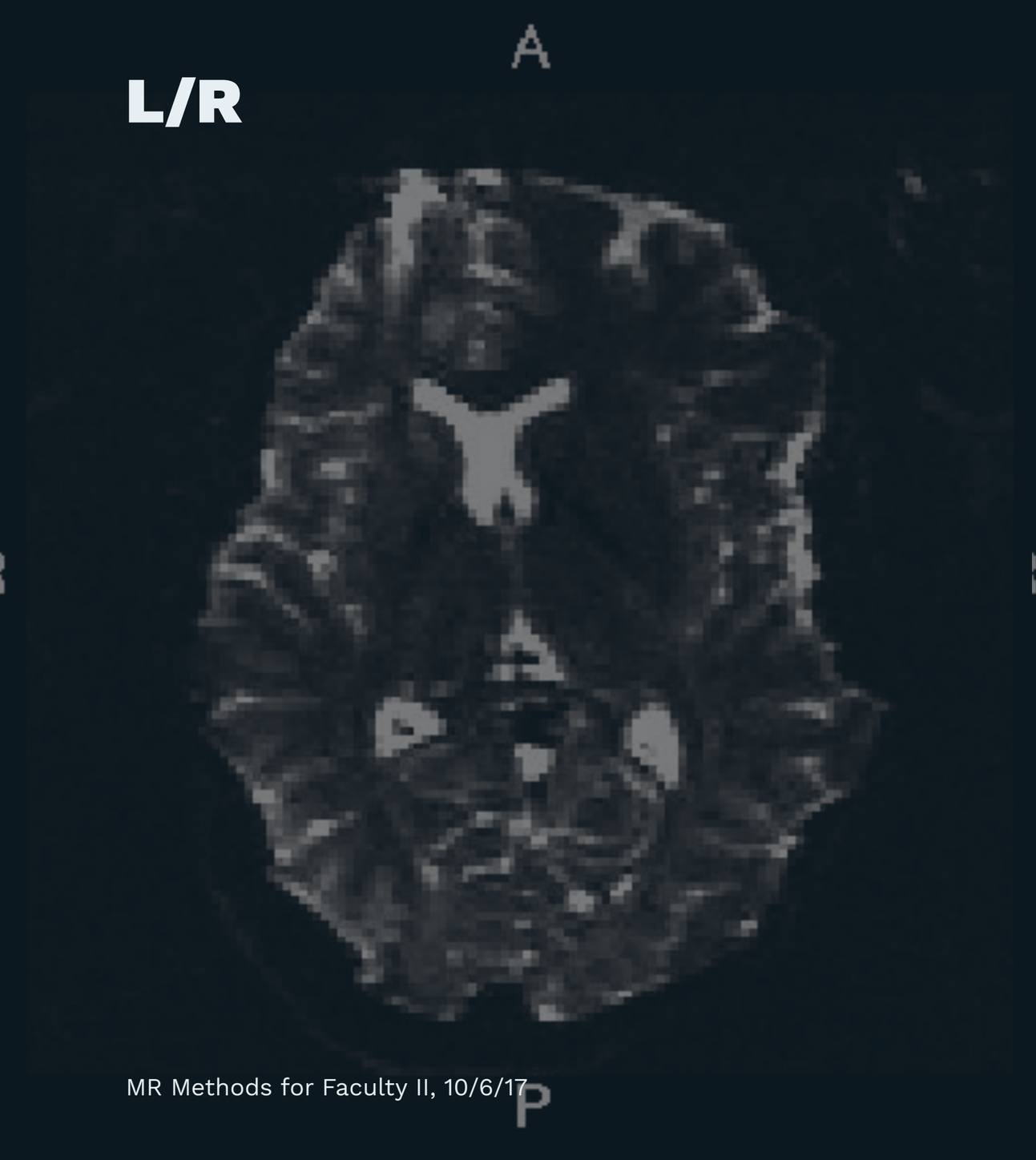
- Field inhomogeneity distorts EPI along the phase encode axis
- Particularly problematic for DWI
- Ideally correct for this using a fieldmap and/or nonlinear alignment

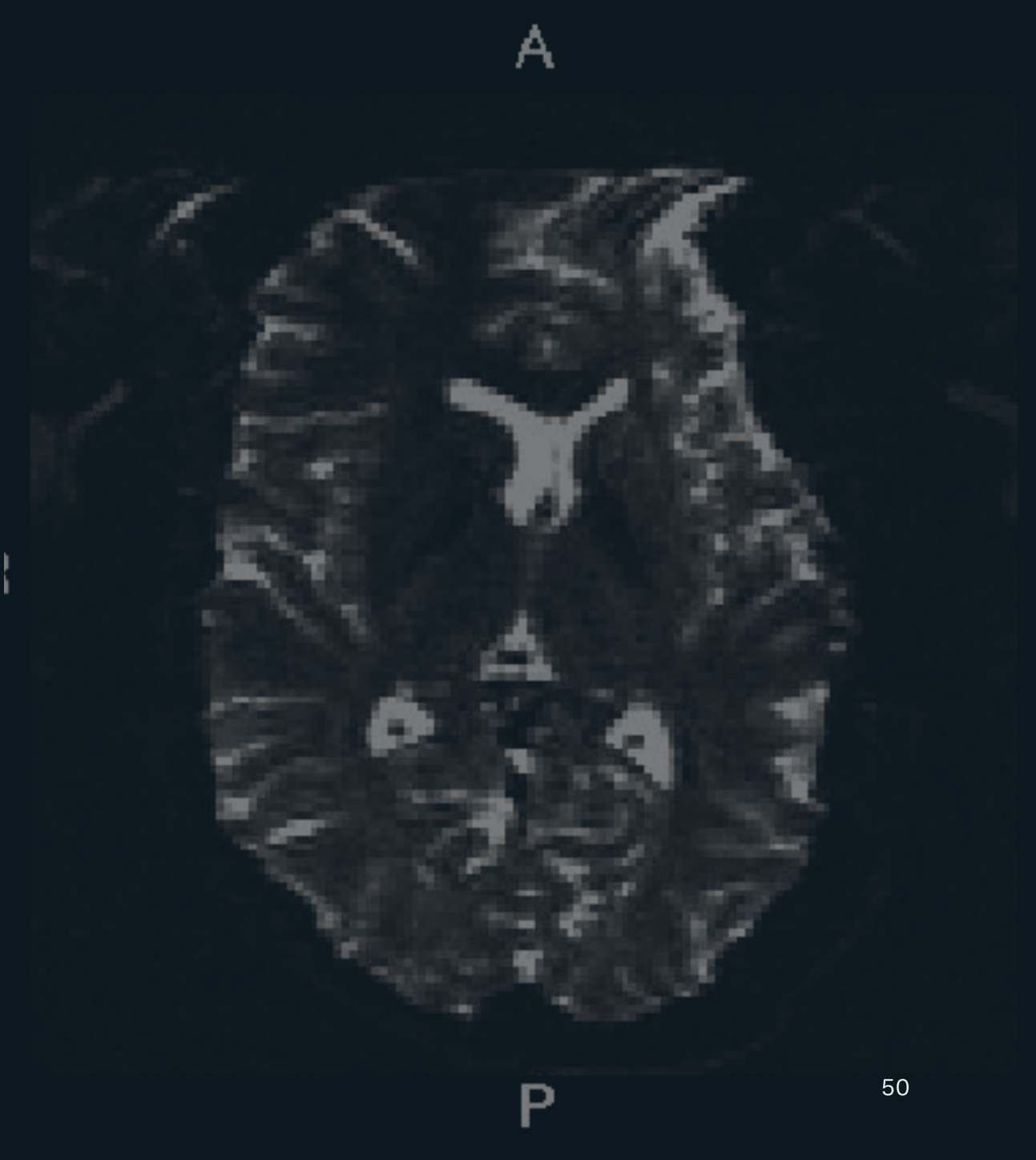
A/P





L/R





Approaches

— Collect a 'real' fieldmap
— Collect multiple scans with flipped PE direction
— Nonlinear warping

Distortion correction

1. Calculate a field map
2. Align the fieldmap and EPI
3. Unwarp the EPI distortion
4. Best done with motion correction

FSL tools: `fugue` and `topup`

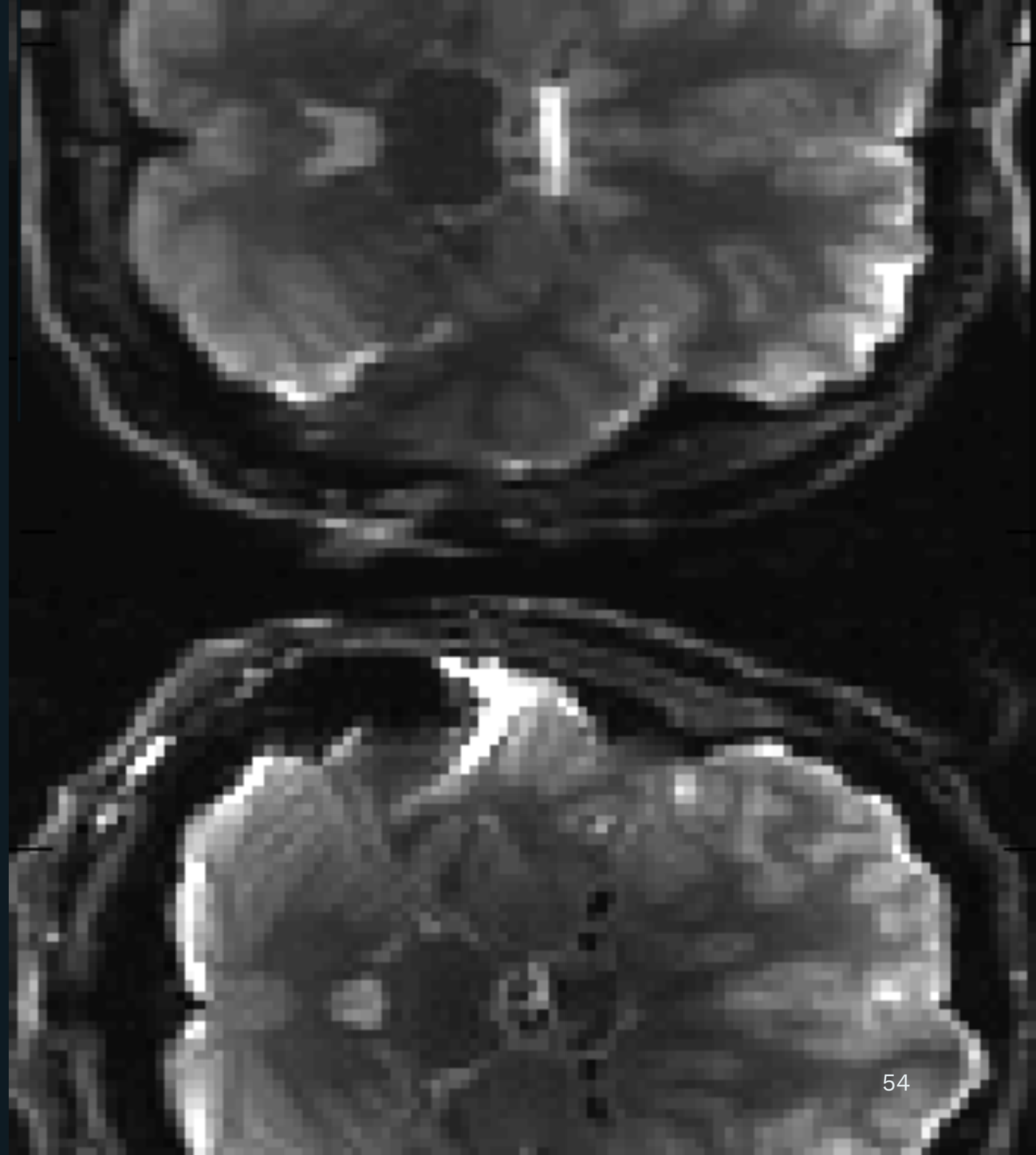
Co-registration

Goal: Align the fMRI data to another dataset

— Typically a T1-weighted anatomical volume
— The T1 (and aligned fMRI) can then be aligned to a template

Co-registration options

- Rigid body
  - Not ideal between modalities
- Affine transformation
  - Also adjusts shearing and scaling
  - Doesn't address geometric distortion
- Non-linear
  - Addresses distortion
  - Recently recommended



Preprocessing Pipelines

- AFNI and FSL do some or all steps
- fmriprep
  - Also generates images for review

Quality Control

- Establish acceptable criteria before analysis
- Mix of visual inspection and quantitative mettics
- Visual
  - Inspect registration
- Quantitative
  - Motion
  - tSNR

Quality Control Tools

— mriqc
— QA

Statistics

- Smoothing to increase SNR
- High pass filtering (.01-.02 Hz) to remove slow drifts
  - Filtering needs to be considered during design
- Scaling
- Single subject GLM

Motion Regressors

- Effort to account for motion-relate signals
- Realignment produces 6 (translation and rotation on 3 axes) motion parameters
- Motion effects extend over time
- Include derivatives or other expanded parameter sets

Motion Metrics

- RMS: absolute volume displacement
- FD (framewise displacement): volume to volume displacement
- DVARS: volume to volume changes in intensity

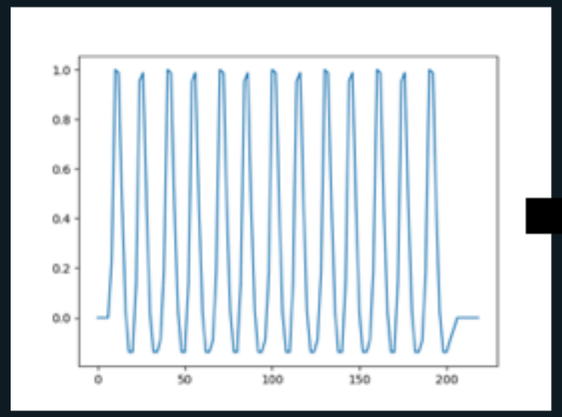
Censoring

- aka scrubbing
- Remove motion contaminated volumes from analysis
- Possibly some successive or prior volumes
  - Delete data (affects filtering and model)
  - Regressors
  - Interpolation (affects df)

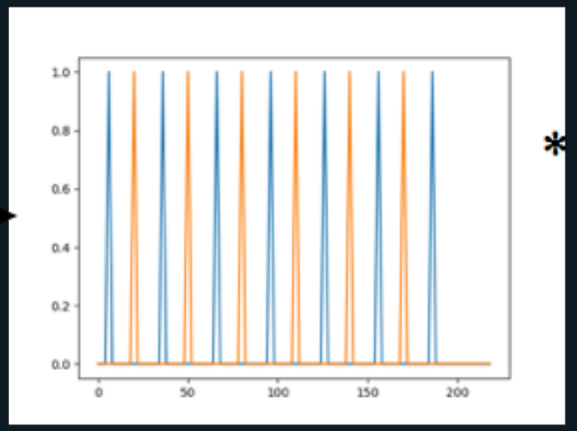
Statistics

— BOLD response is modeled in a GLM
— Stimulus onsets * HRF or basis
— GLM includes motion regressors and other confounds

Deconvolution

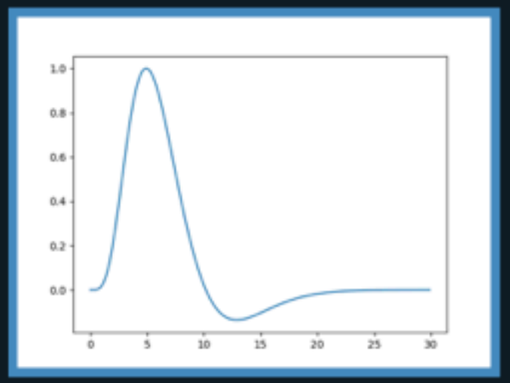


Observed



Known

*



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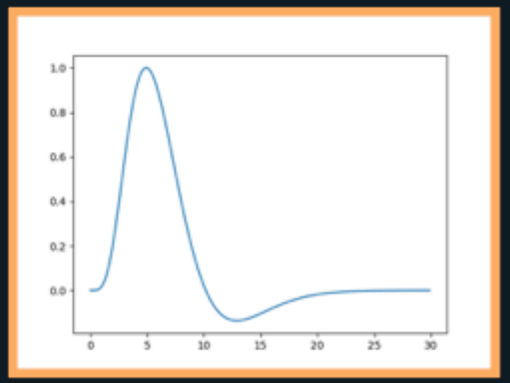

Unknown shape

Or assumed shaped with unknown amplitude

Basis Functions

- 'Canonical HRF': a double gamma response
  - Assumes the HRF has a particular shape
- FIR, tent, sine, spline
  - Estimates HRF

Stimulus Functions

- Delta function
  - Each event is instantaneous
- Block function
  - Events extend in time
  - HRF reaches a set maximum after time

Design Matrix

— Specify a basis and stimulus function for each condition

— Convolve the basis and stimulus functions

— Add motion and other non-task regressors

Statistics

— GLM (OLS or REML)
— Linear constrasts between conditions
— and/or F tests
— Result: t/z/F values and beta values

Multiple Comparisons

— Mass univariate statistics are over 10-100s of thousands of tests

— Statistics need to be corrected for number of comparisons

— Corrections should account for spatial structure

Correction Options

- Familywise Error (FWE)
- False Discovery Rate (FDR)
- Random field cluster-based correction
- Threshold based statistics (TBSS)
- Permutation cluster-based correction
- Permutation