Principles of fMRI

Part I

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@fMRIstats

Model Building III:
Filtering and nuisance covariates

GLM

A standard GLM can be written:

$$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon} \qquad \boldsymbol{\varepsilon} \sim N(\mathbf{0}, \mathbf{V})$$

where

$$\begin{bmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_n \end{bmatrix} = \begin{bmatrix} 1 & X_{11} & \cdots & X_{1p} \\ 1 & X_{21} & \cdots & X_{2p} \\ \vdots & \vdots & & \vdots \\ 1 & X_{n1} & \cdots & X_{np} \end{bmatrix} \times \begin{bmatrix} \beta_0 \\ \beta_1 \\ \vdots \\ \beta_p \end{bmatrix} + \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{bmatrix}$$

fMRI Data

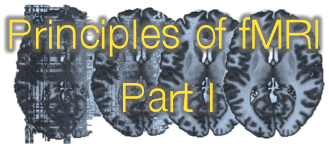
Design matrix

Regression coefficients

Noise

V is the covariance matrix whose format depends on the noise model.

Nuisance Covariates

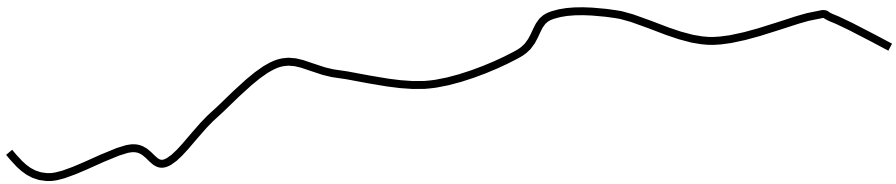


- Often model factors associated with known sources of variability, but that are not related to the experimental hypothesis, need to be included in the GLM.

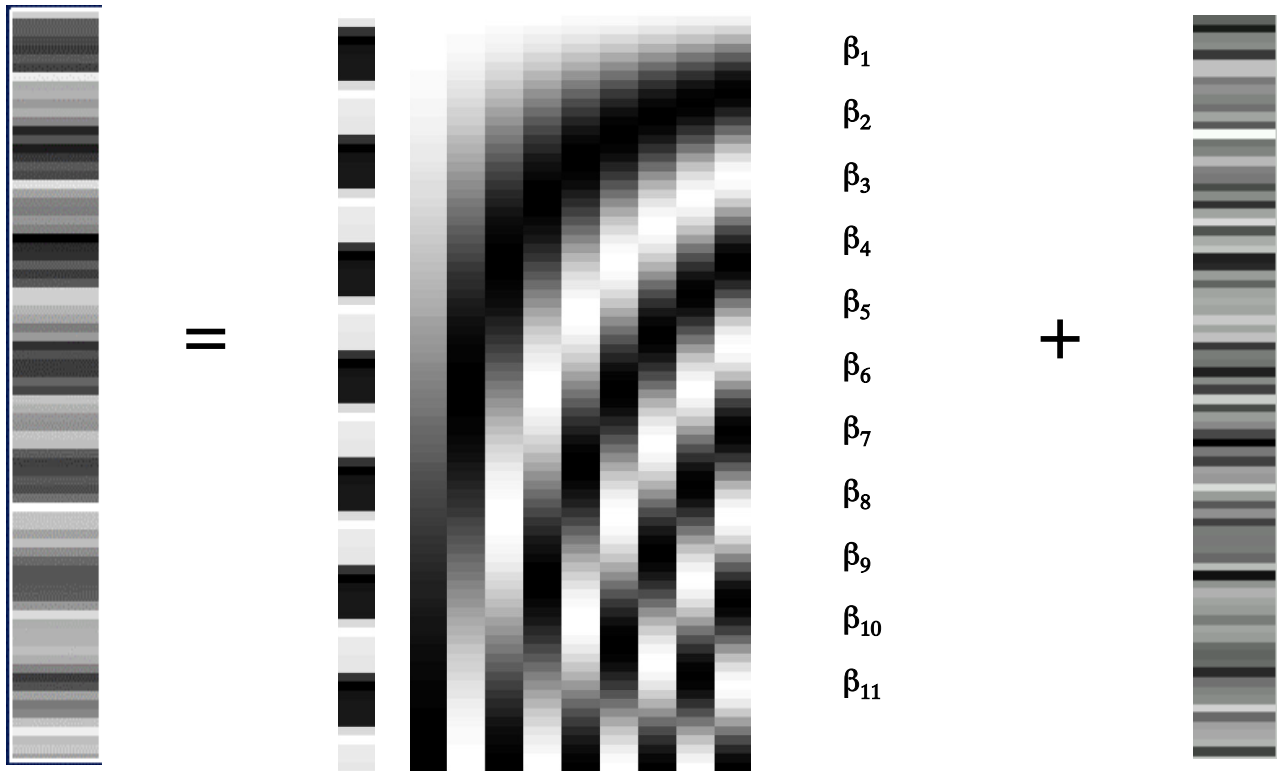
- Examples of possible 'nuisance regressors':
  - Signal drift
  - Physiological (e.g., respiration) artifacts
  - Head motion, e.g. six regressors comprising of three translations and three rotations.
    - Sometimes transformations of the six regressors also included.

Drift

- Slow changes in voxel intensity over time (low-frequency noise) is present in the fMRI signal.
- Scanner instabilities and not motion or physiological noise may be the main cause of the drift, as drift has been seen in cadavers.
- Need to include drift parameters in our models.
  - Use splines, polynomial basis or discrete cosine basis

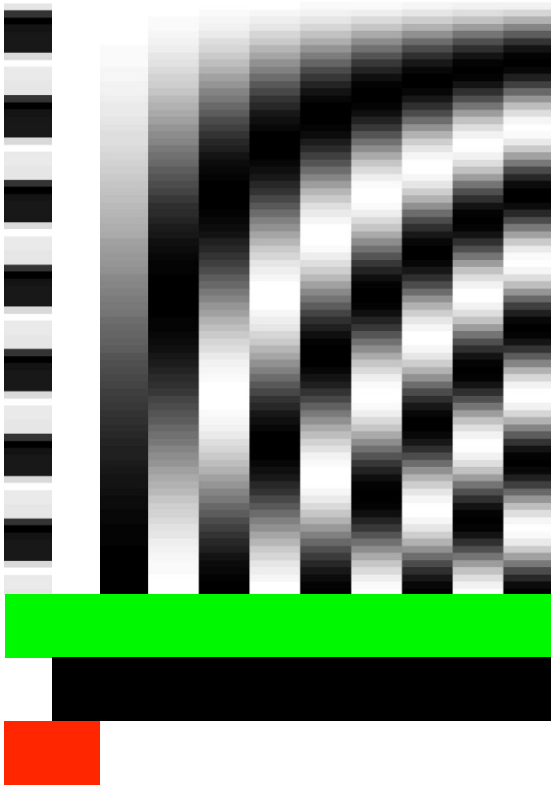


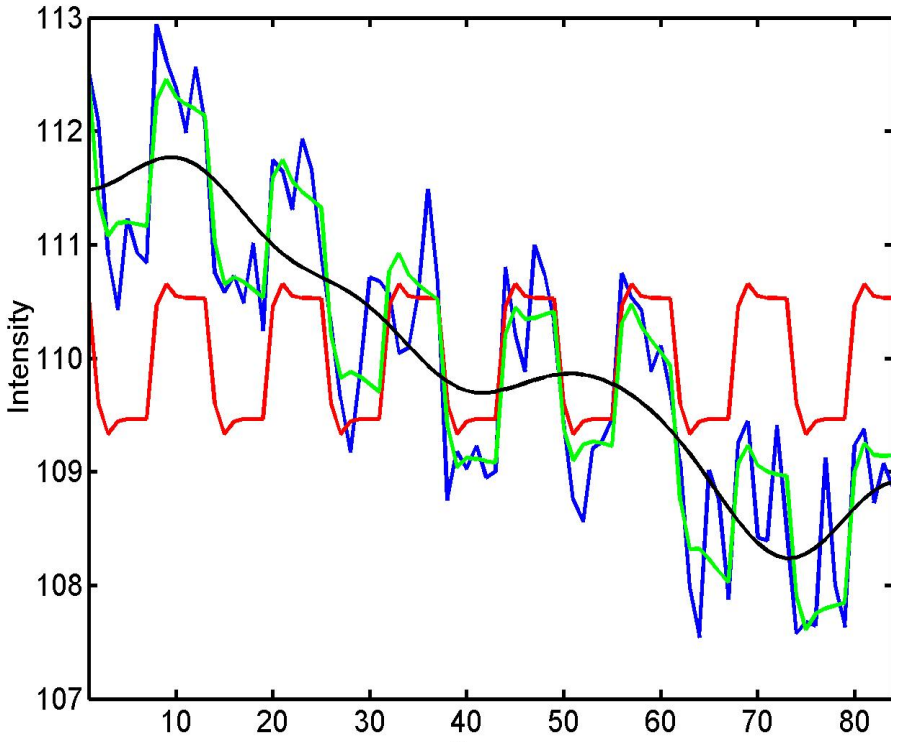
Model with Drift



$$Y = X \times \beta + \varepsilon$$

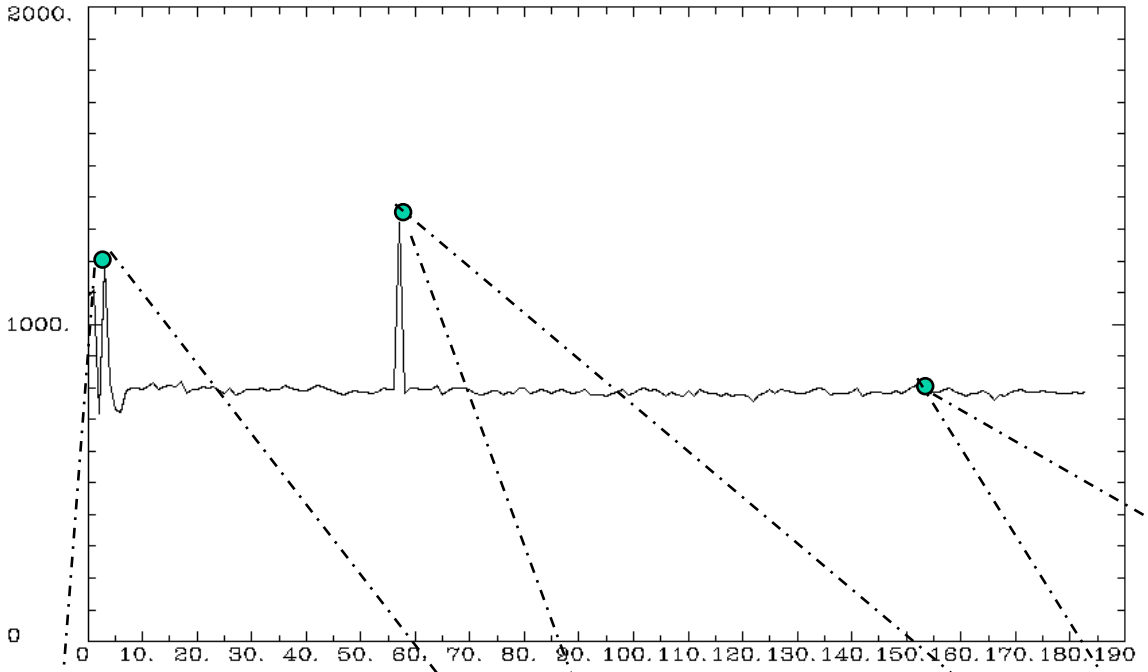
High Pass Filtering



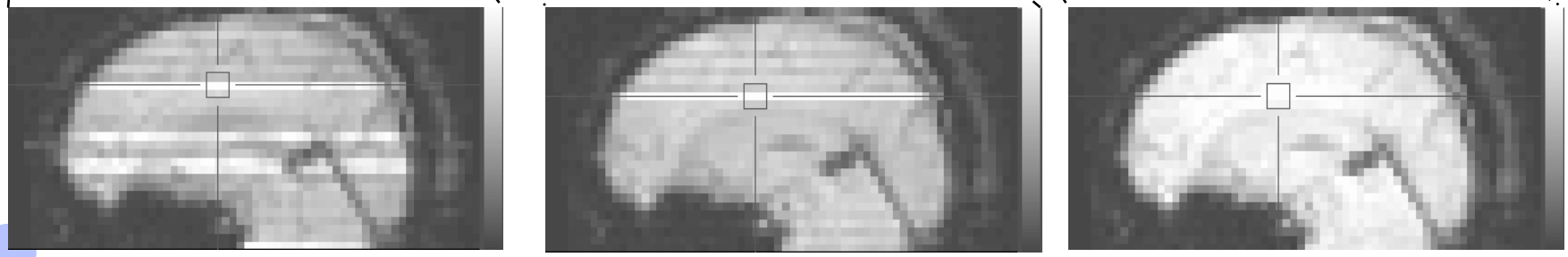


blue =	data
black =	mean + low-frequency drift
green =	predicted response, taking into account low-frequency drift
red =	predicted response (with low-frequency drift explained away)

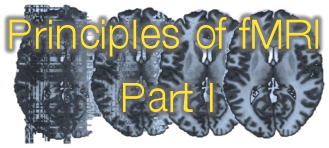
Transient gradient artifacts

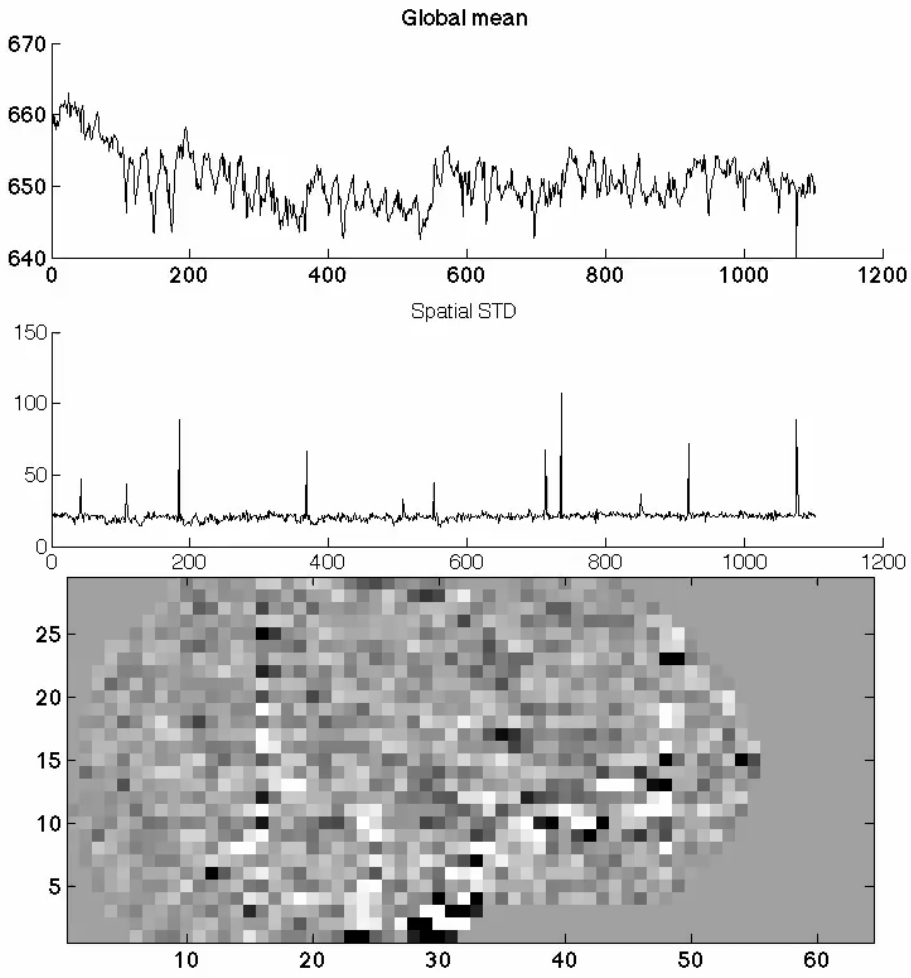


Transient spike artifacts in the data during isolated volume acquisitions are apparent in certain slices, as shown by the bright bands in the saggital slices (bottom). This suggests that gradient performance was affected during acquisition of some echo-planar images, which were acquired slice-by-slice in interleaved order in this experiment.



Modeling transient gradient artifacts





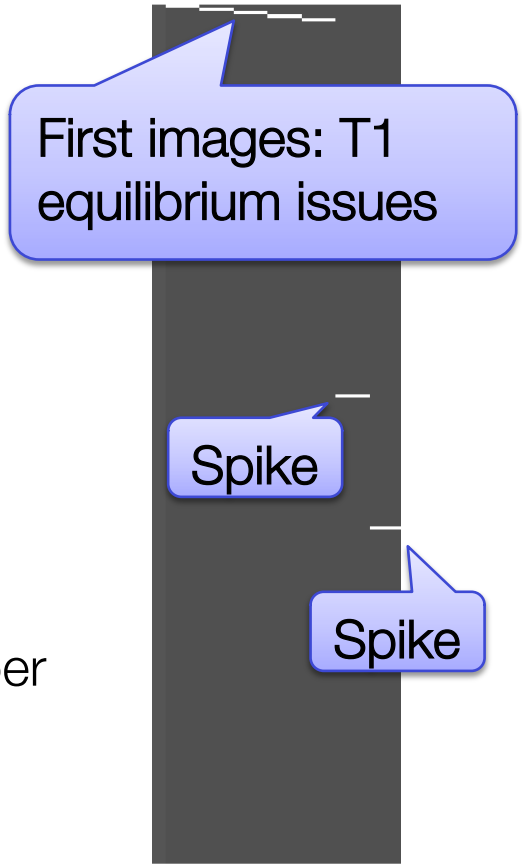
Outlier detection

- Global mean
- Successive differences (RMSSD)

- Include as covariates in design matrix

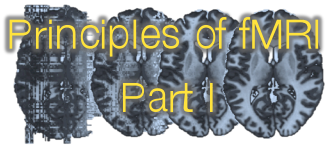
- One regressor per “bad” image

Example nuisance regressors in X



http://wagerlab.colorado.edu/wiki/doku.php/help/fmri_help/preprocessing/a_start_here

Physiological Noise

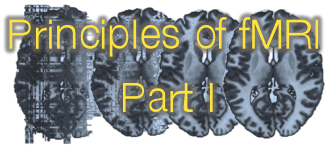


- Respiration and heart beat give rise to periodic noise, often aliased into task frequencies.

- It can potentially be modeled, but if the TR is too low there will be problems with aliasing.
  - Sampling rate must be at least twice as big as the frequency of the curve you seek to model.

- Hence, this type of noise is difficult to remove and is often left in the data giving rise to temporal autocorrelations.

Physio noise reduction



- Neuronal activation
- Respiration cycle
- Cardiac cycle
- Respiration volume (≈CO_2)
- Heart rate

RETROICOR

RVHRCOR

Courtesy Gary Glover

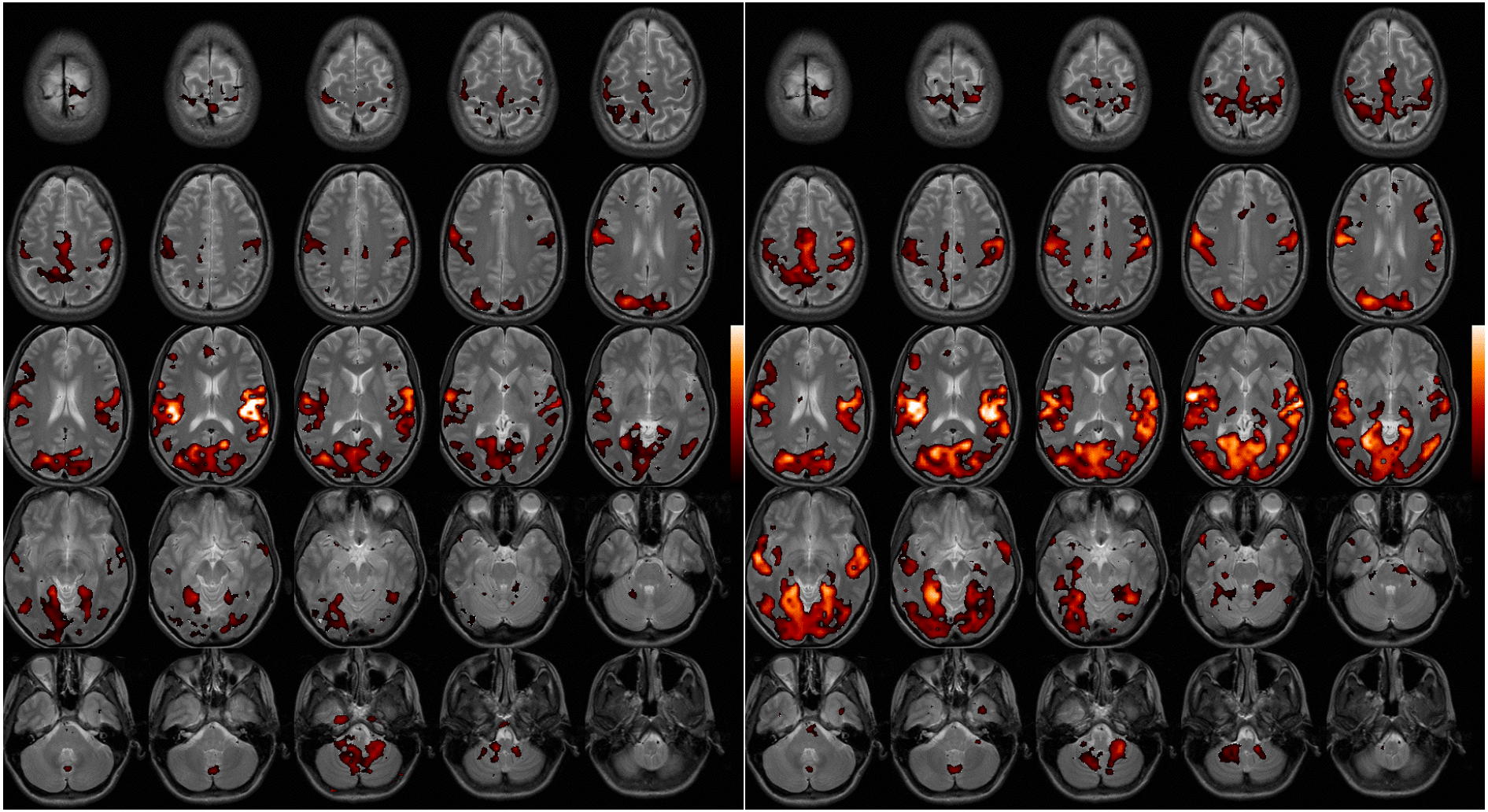
Glover MRM 2000; Chang and Glover 2009a, b

Courtesy Gary Glover

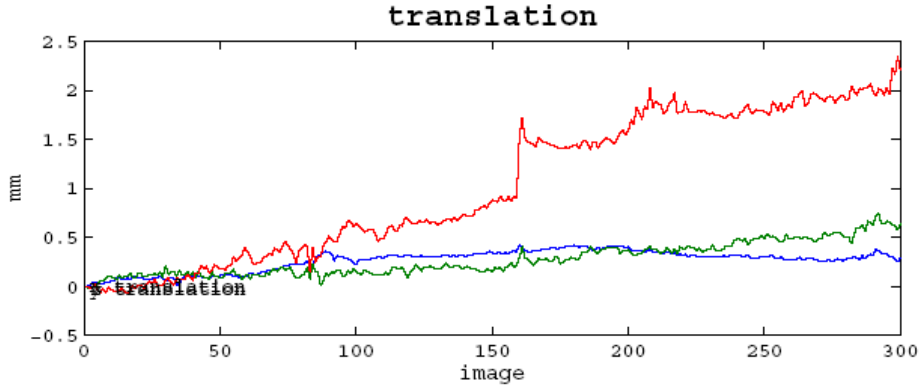
RETROICOR

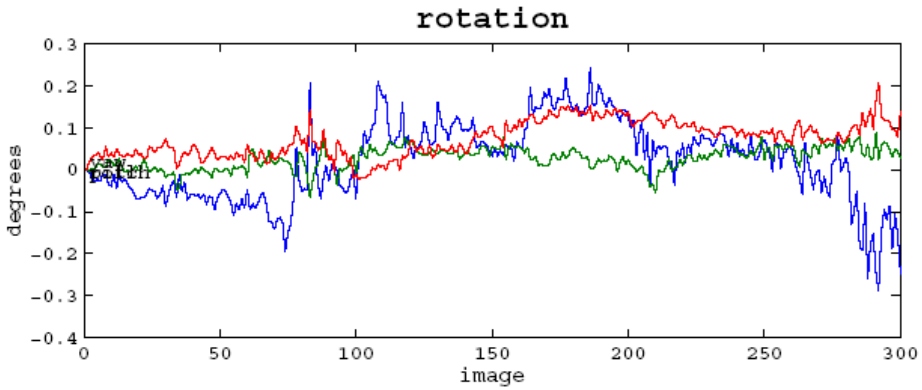
No retroicor

With retroicor

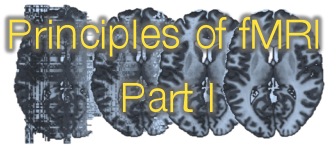


Head Motion


translation
2.5
2
1.5
1
0.5
0
-0.5
mm
x translation
0
50
100
150
200
250
300
image


rotation
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
degrees
pitch
0
50
100
150
200
250
300
image

Motion

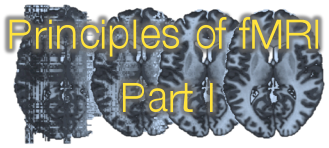


- Subject motion during the experiment can also give rise to serious problems.

- Basic motion correction (image realignment) is performed in the pre-processing stages of the analysis.

- However, motion induces complex changes in the magnetic field and ‘spin-history’ artifacts that cannot be removed.

Head movement-related artifacts



The influence of head motion on intrinsic functional connectivity MRI

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[b] Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Charlestown, MA, USA
[c] Computer Science and Artificial Intelligence Lab, Massachusetts Institute of Technology, Cambridge, MA, USA
[d] Department of Psychiatry, Massachusetts General Hospital, Boston, MA, USA
[e] Howard Hughes Medical Institute, Cambridge, MA, USA

Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion

Jonathan D. Power [a,*], Kelly A. Barnes [a], Abraham Z. Snyder [a,b], Bradley L. Schlaggar [a,b,c,d], Steven E. Petersen [a,b,d,e]

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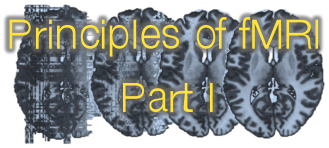
Head movement-related artifacts: Solutions



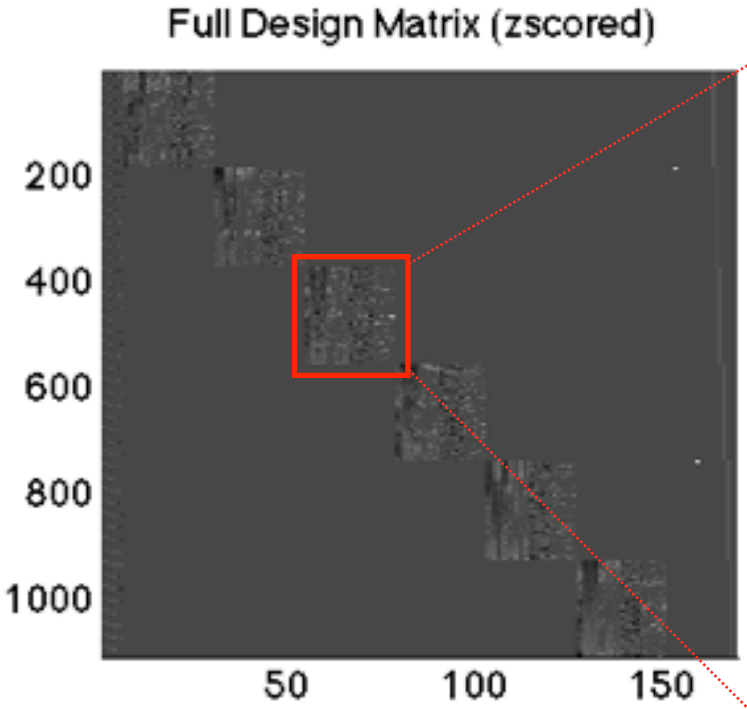
- **Nuisance regressors**: Movement- and global CSF-related covariates

- **'Scrubbing'**: Drop images with high movement estimates (treat as missing data)

Modeling movement

Nuisance regressors, one run

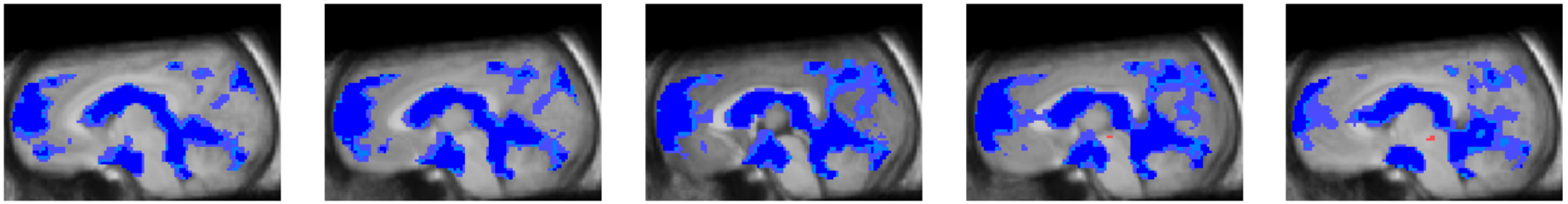
Mvmt (centered), squares, successive differences, squared diffs [24 covs]



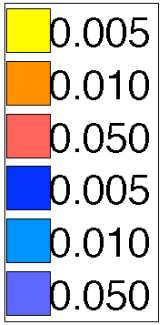
Lund et al. 2006

Trouble in paradise: Task-correlated movement and spike artifacts

- CS+ vs. CS- during Shock Conditioning
- Group analysis, N = 25. Problems should "average out"…right?

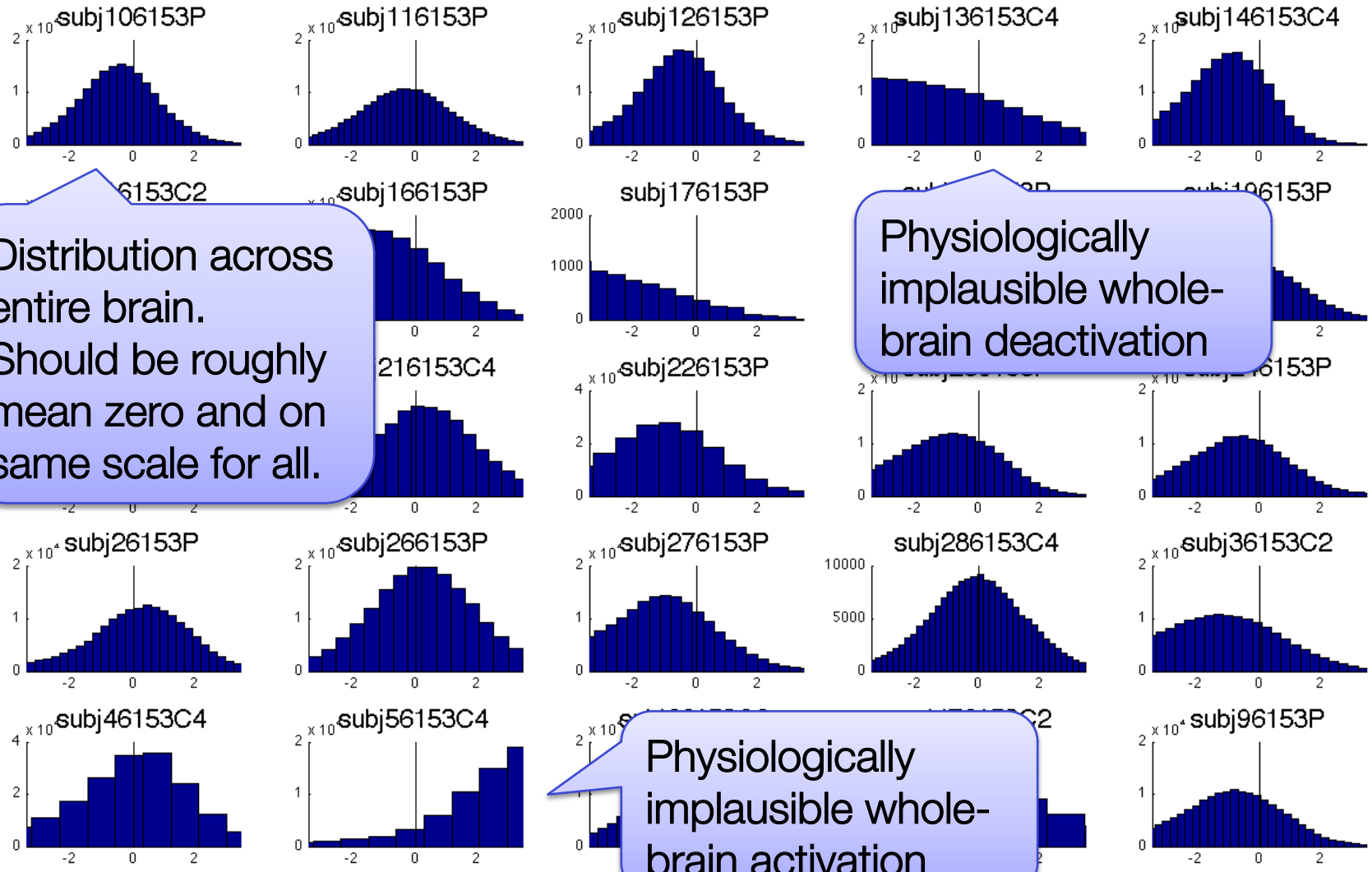


x = -6 x = -3 x = 0 x = 3 x = 6



Detecting problems

Histograms of contrast values across the brain for each subject

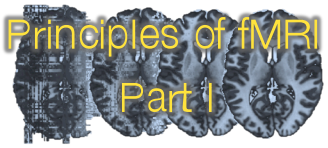


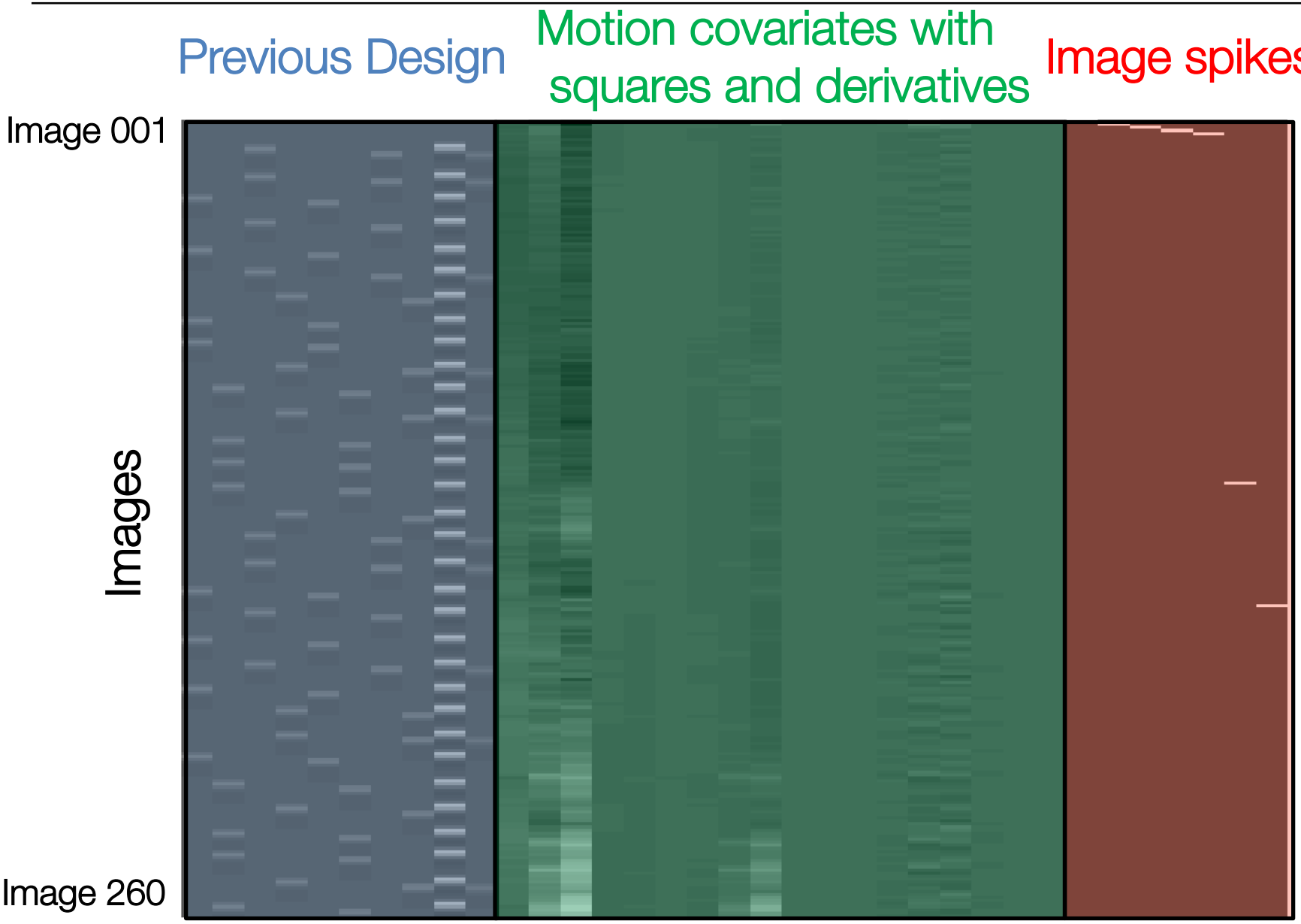
Distribution across entire brain. Should be roughly mean zero and on same scale for all.

Physiologically implausible whole-brain deactivation

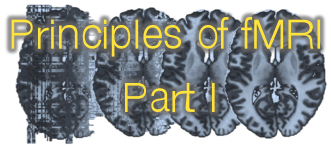
Physiologically implausible whole-brain activation

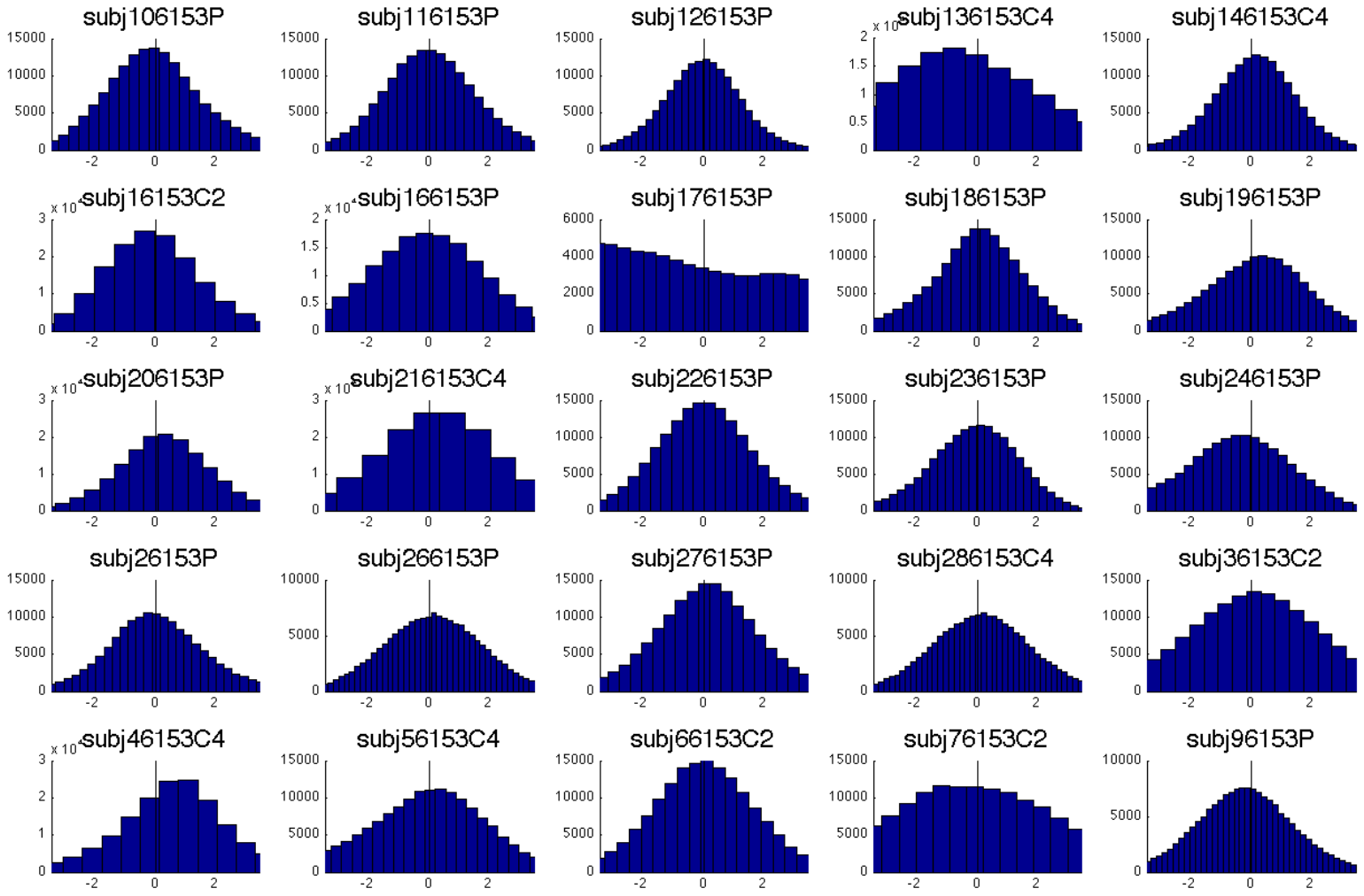
Additional nuisance covariates





After nuisance regressors included: Much better!

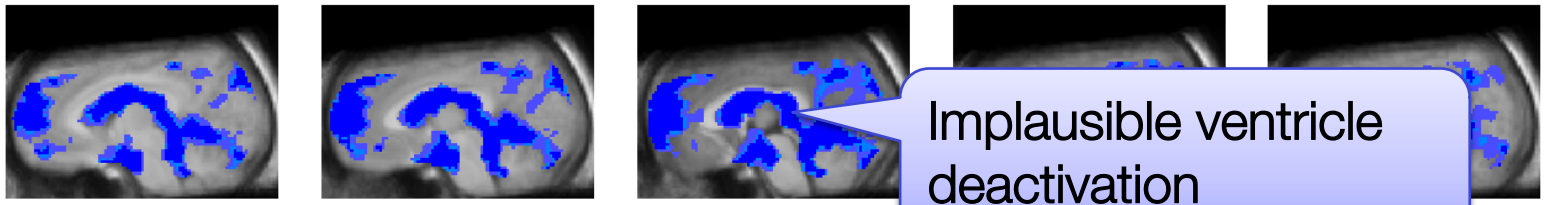




Before vs. after nuisance covariates

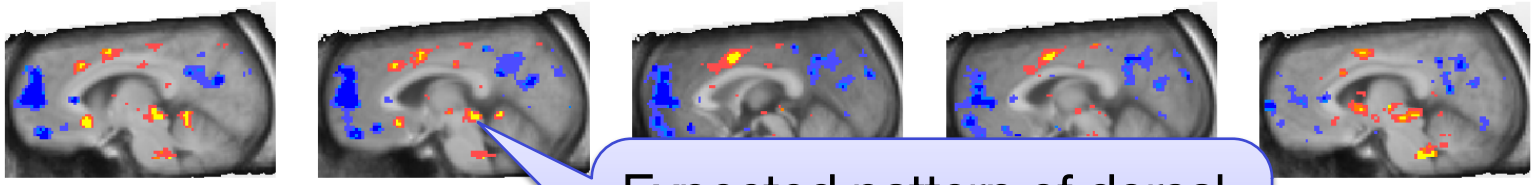
Contrast: CS+ vs. CS- during Shock Conditioning
Group analysis

Uncorrected



Implausible ventricle deactivation

Corrected



Expected pattern of dorsal cingulate increases and “default-mode” decreases

End of Module

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To scrub or not to scrub?

Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion

Jonathan D. Power [a,*], Kelly A. Barnes [a], Abraham Z. Snyder [a,b], Bradley L. Schlaggar [a,b,c,d], Steven E. Petersen [a,b,d,e]

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1. Missing not at random
- Movement scans are not independent of "treatment assignment:" experimental conditions and subject characteristics.

2. Artificially alters error distribution and autocorrelation

3. interpolation not accounted for in stats, degrees of freedom, p-values

4. what is the ground truth for validating the scrubbing?

5. Ad hoc user decisions - hard to replicate choices, arbitrary threshold

* A matter of degree