Motion in resting-state fMRI analysis: Comparing different preprocessing strategies

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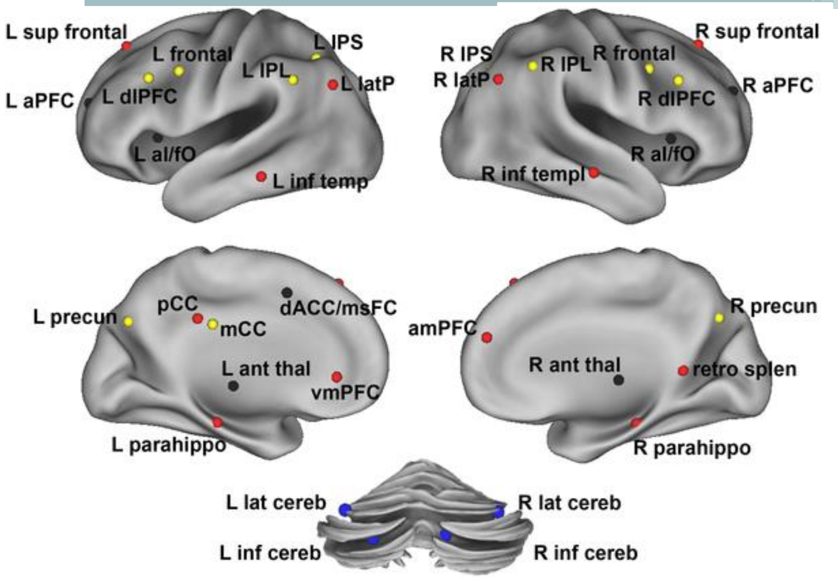
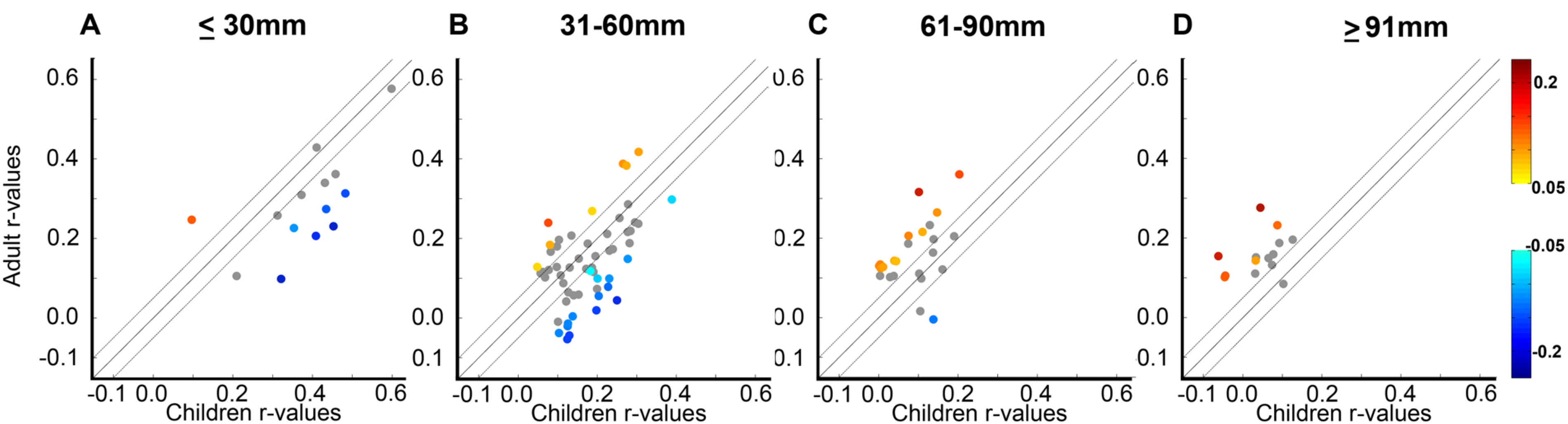
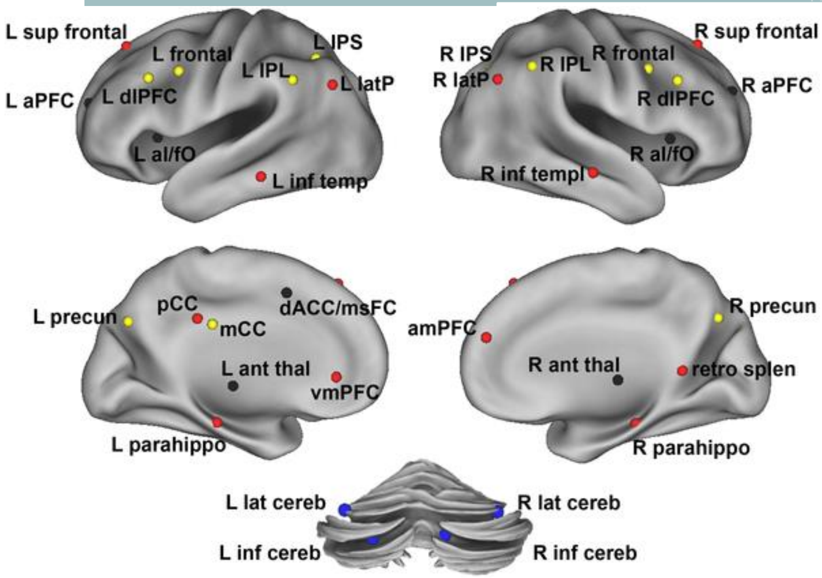
Functional Brain Networks Develop from a "Local to Distributed" Organization

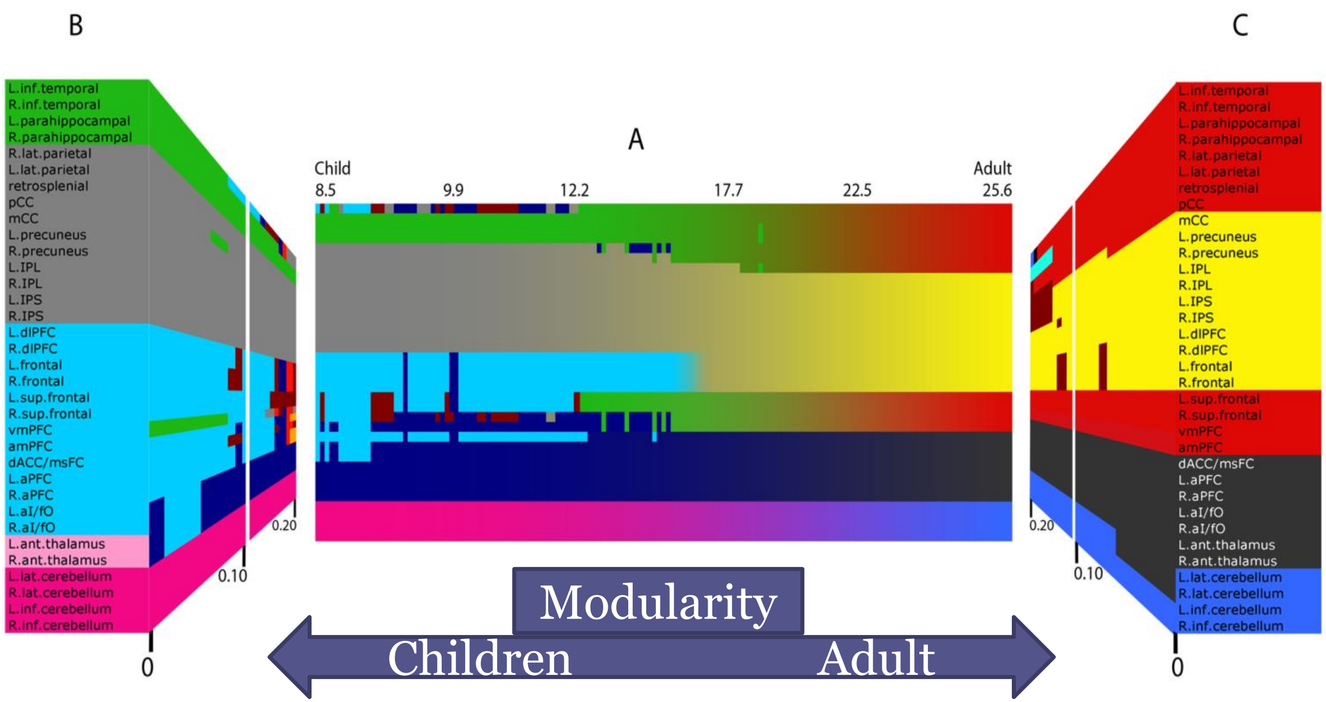




Fair DA, Cohen AL, Power JD, Dosenbach NUF, et al. (2009) PLoS Comput Biol 5(5): e1000381.

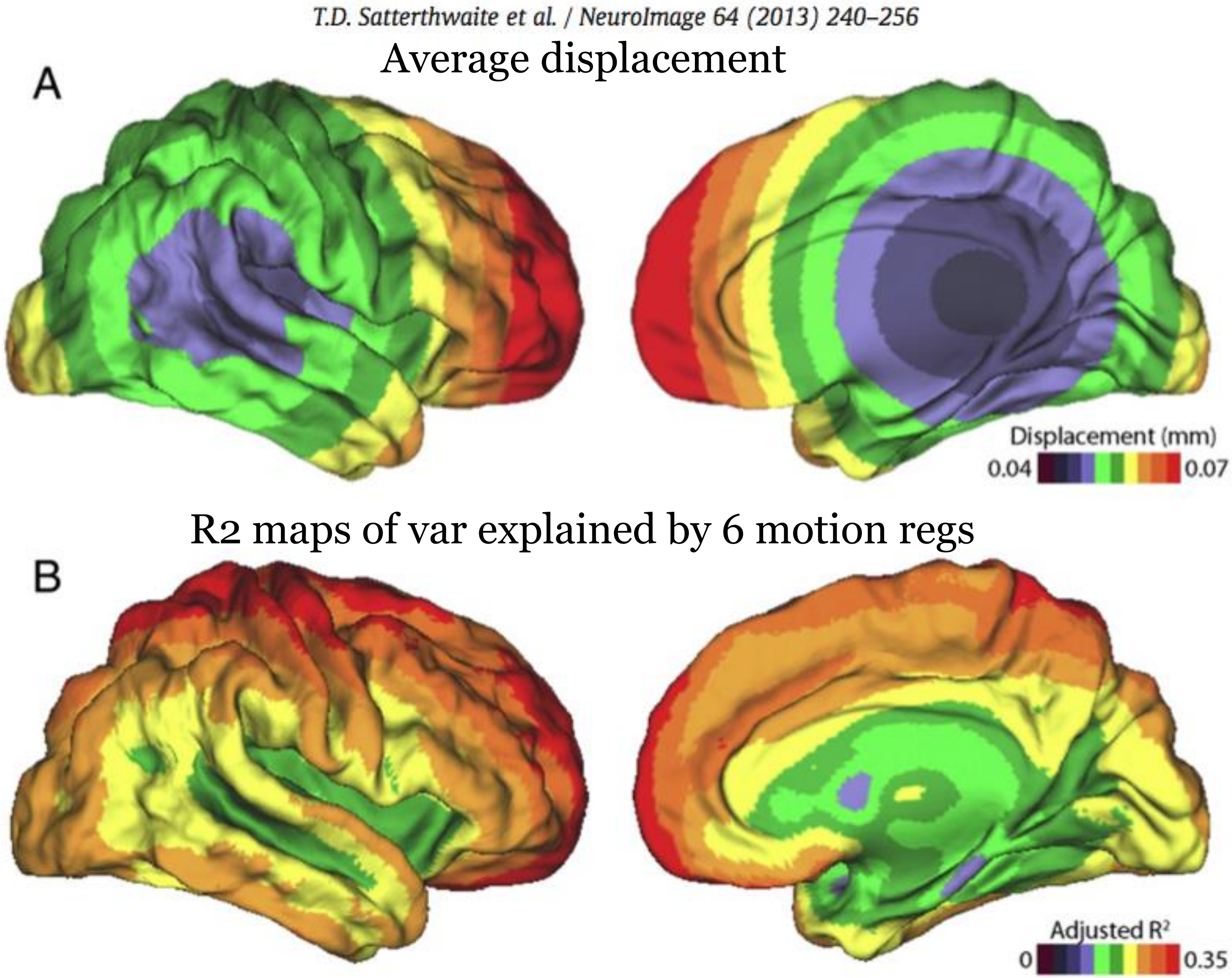
Functional Brain Networks Develop from a “Local to Distributed” Organization



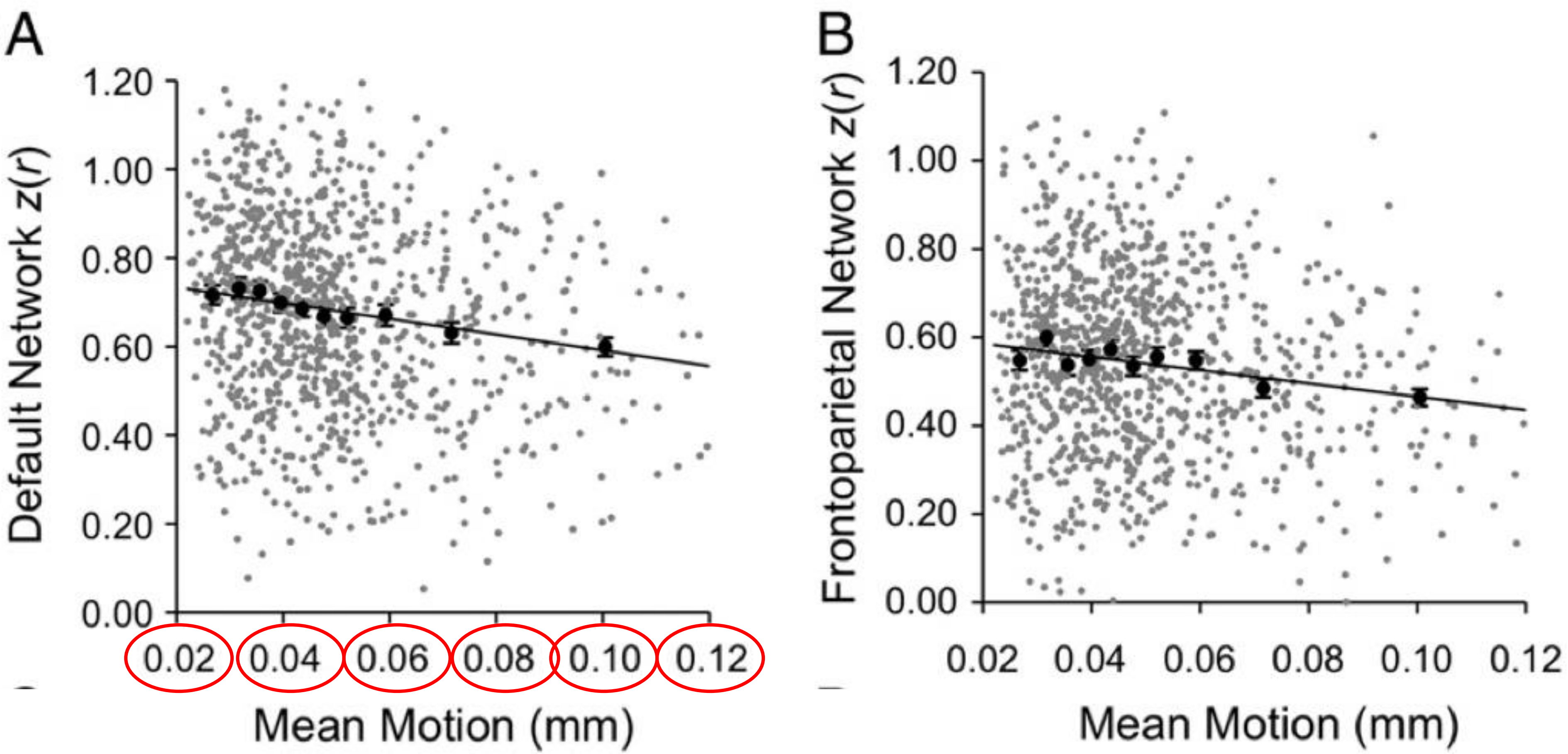


Fair DA, Cohen AL, Power JD, Dosenbach NUF, et al. (2009) PLoS Comput Biol 5(5): e1000381.

Not all motion is created equal

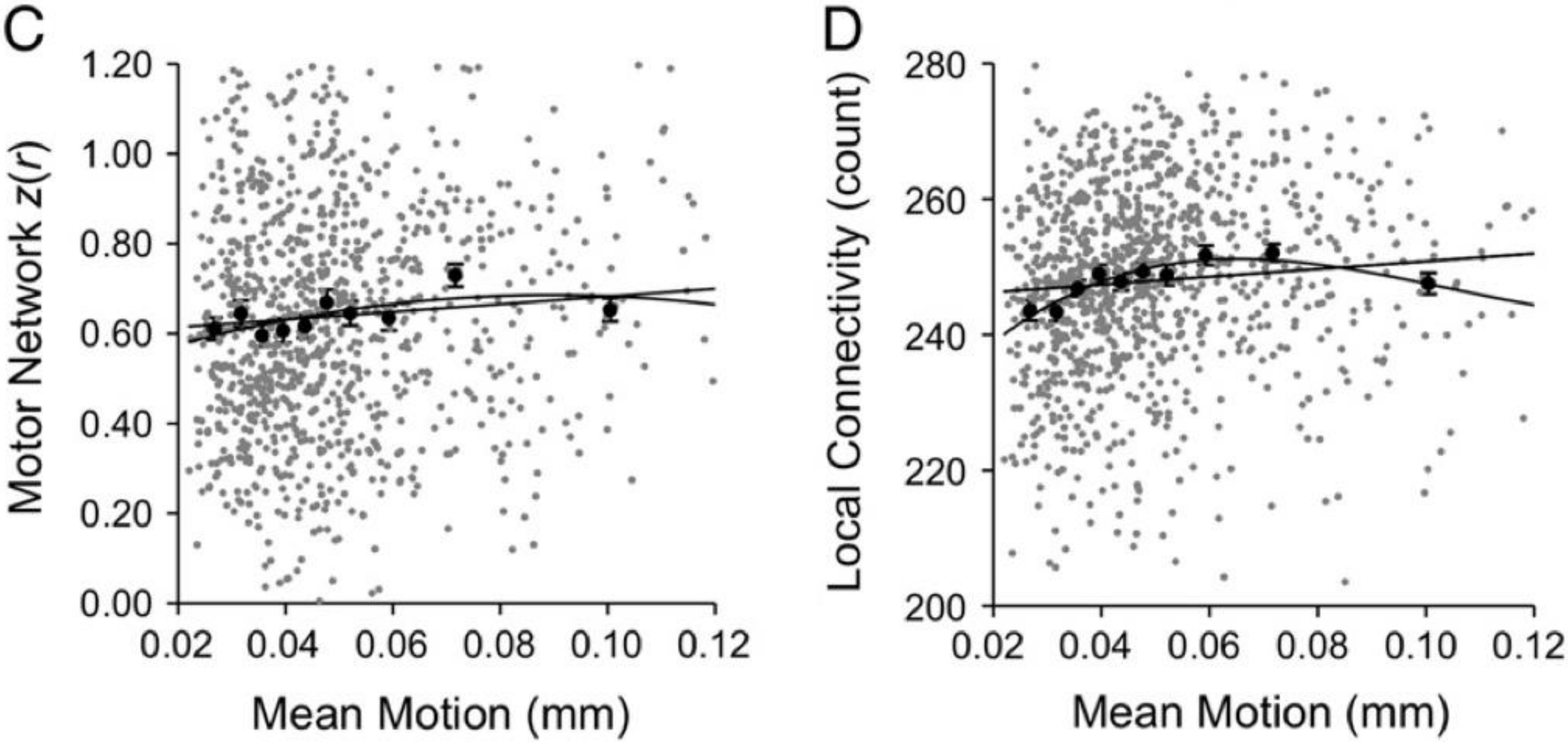


Long-range functional connectivity is diminished in wiggly subjects



Van Dijk, Sabuncu, & Buckner (2012) *NeuroImage*

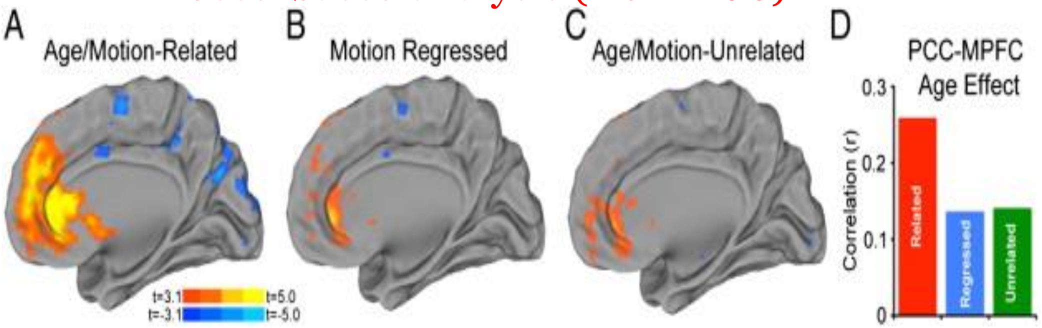
And short-range functional connectivity can be augmented in wiggly subjects



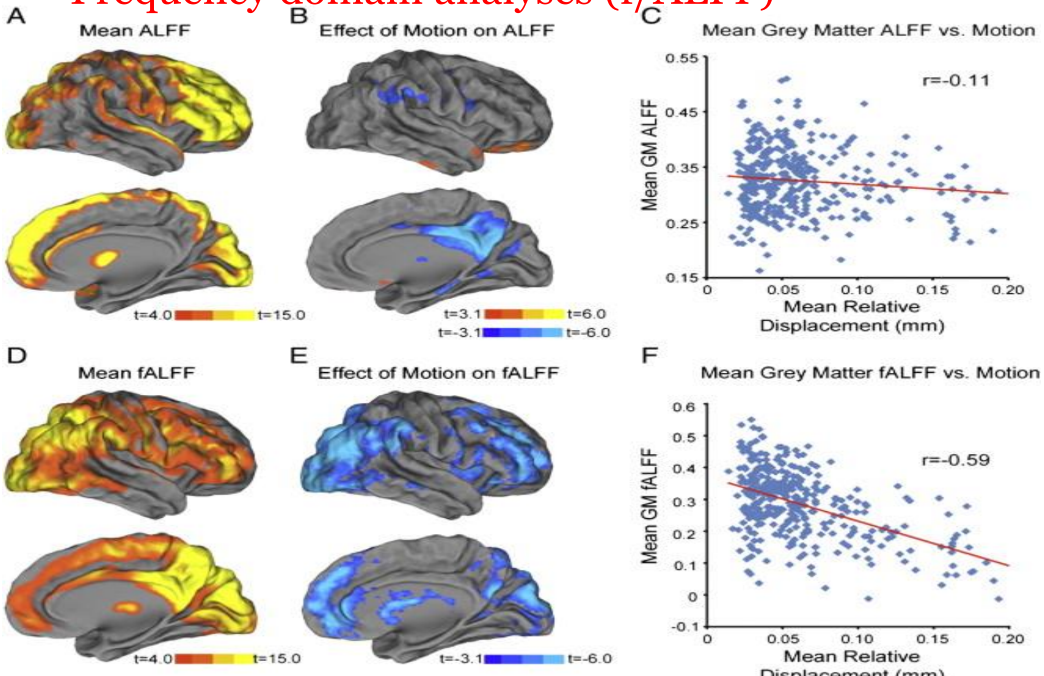
Van Dijk, Sabuncu, & Buckner (2012) *NeuroImage*

This problem affects all techniques

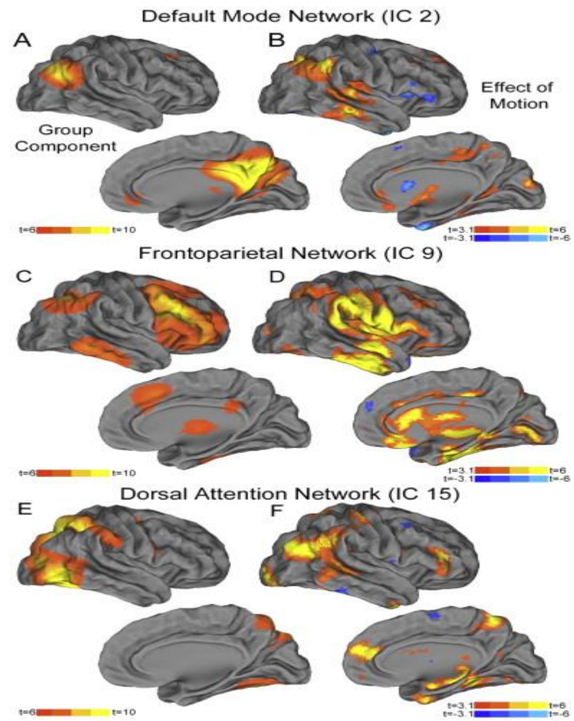
Seed-based analysis (from PCC)



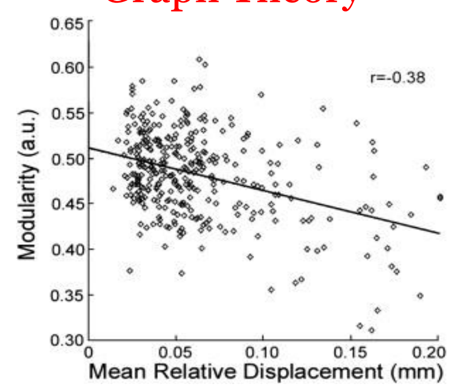
Frequency domain analyses (f/ALFF)



ICA



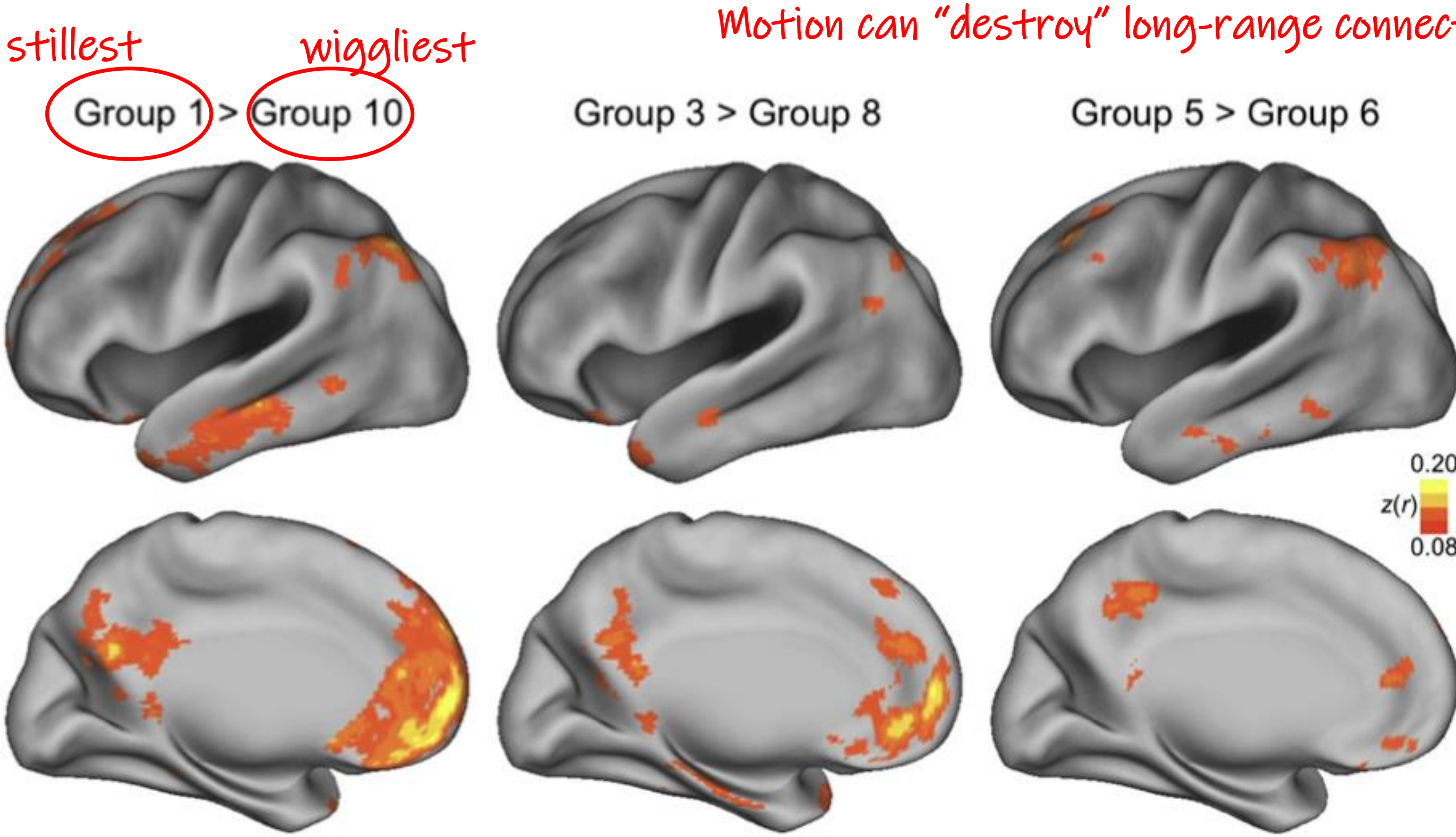
Graph Theory



Sattertwhaite et al, 2012

PCC connectivity X motion interaction

Motion can "destroy" long-range connectivity



- Default Mode Network connectivity (PCC seed) is reduced in subject groups with more motion, even when differences are miniscule (0.044mm vs. 0.048mm mean motion)

Van Dijk, Sabuncu, & Buckner (2012) *NeuroImage*

Framewise displacement (FD)

- $FD_i = |\Delta d_{ix}| + |\Delta d_{iy}| + |\Delta d_{iz}| + |\Delta\alpha_i| + |\Delta\beta_i| + |\Delta\gamma_i|$
  - Where $\Delta d_{ix} = d_{(i-1)x} - d_{ix}$
- This variable measures movement of any given frame relative to the previous frame (as opposed to relative to the reference frame of motion parameter estimation & regression).

Power et al. (2012) *NeuroImage*

DVARS

- **D** referring to temporal derivative of timecourses
- **VARS** referring to RMS variance over voxels
- Indexes the rate of change of BOLD signal across the entire brain at each frame of data.
- DVARS is a measure of how much the intensity of a brain image changes in comparison to the previous timepoint (as opposed to the global signal, which is the average value of a brain image at a timepoint).

$$\mathrm{DVARS}(\Delta I)_i = \sqrt{\left\langle \left[\Delta I_i\left(\vec{x}\right)\right]^2 \right\rangle} = \sqrt{\left\langle \left[I_i\left(\vec{x}\right) - I_{i-1}\left(\vec{x}\right)\right]^2 \right\rangle}$$

Power et al. (2012) *NeuroImage*

DVARS

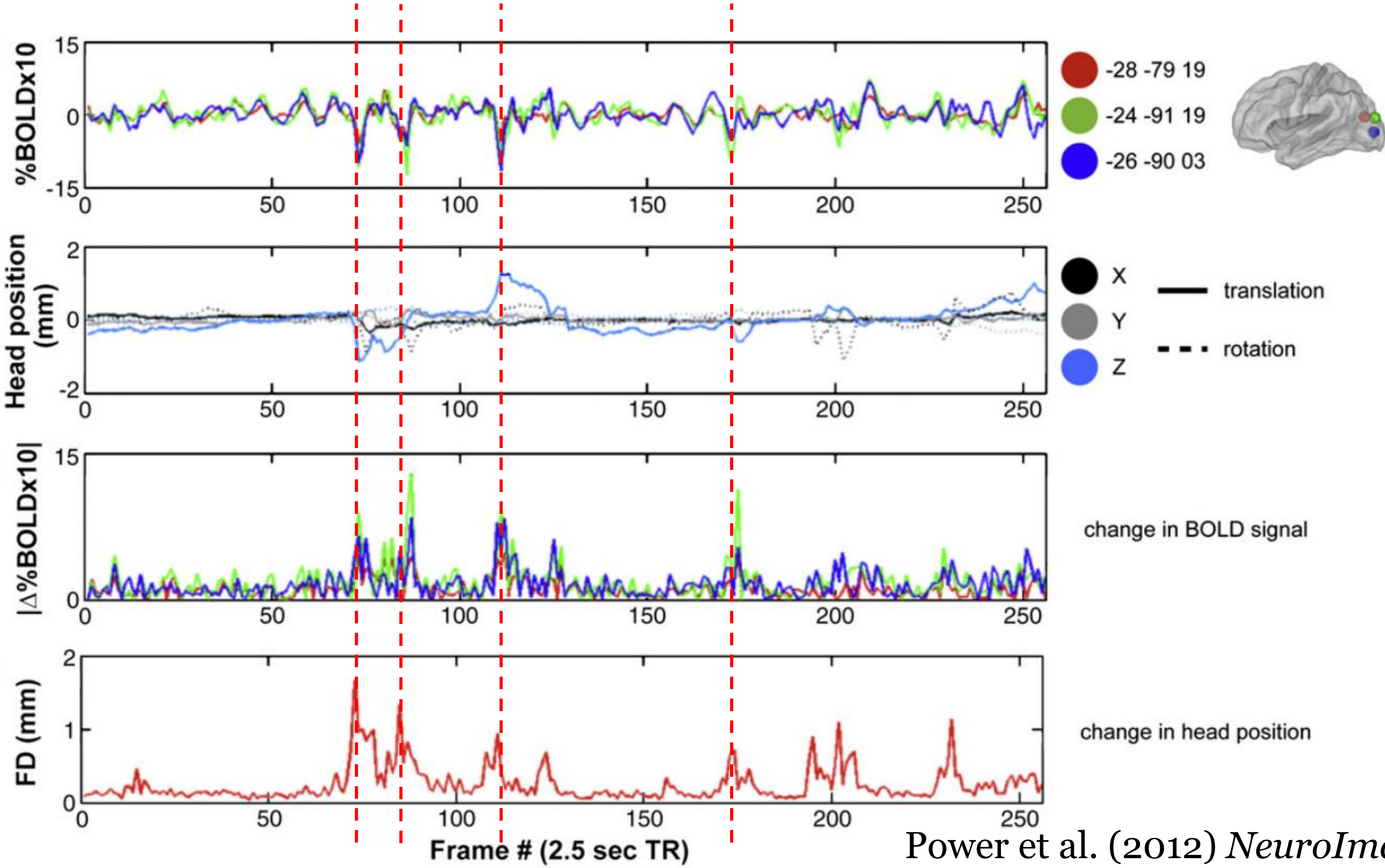
- Because frame-to-frame changes in signal intensity related to movement are significantly greater than those caused by neurophysiologic changes in the BOLD signal, this measure provides a natural parameter with which to directly examine the relationship of movement measurements and the BOLD response (Fair et al 2013)

$$\mathrm{DVARS}(\Delta I)_i = \sqrt{\left\langle \left[\Delta I_i\left(\vec{x}\right)\right]^2 \right\rangle} = \sqrt{\left\langle \left[I_i\left(\vec{x}\right) - I_{i-1}\left(\vec{x}\right)\right]^2 \right\rangle}$$

Power et al. (2012) *NeuroImage*

Single subject motion RMS = 0.55mm

A “traditionally” high quality dataset



Power et al. (2012) *NeuroImage*

Head motion & BOLD relationship

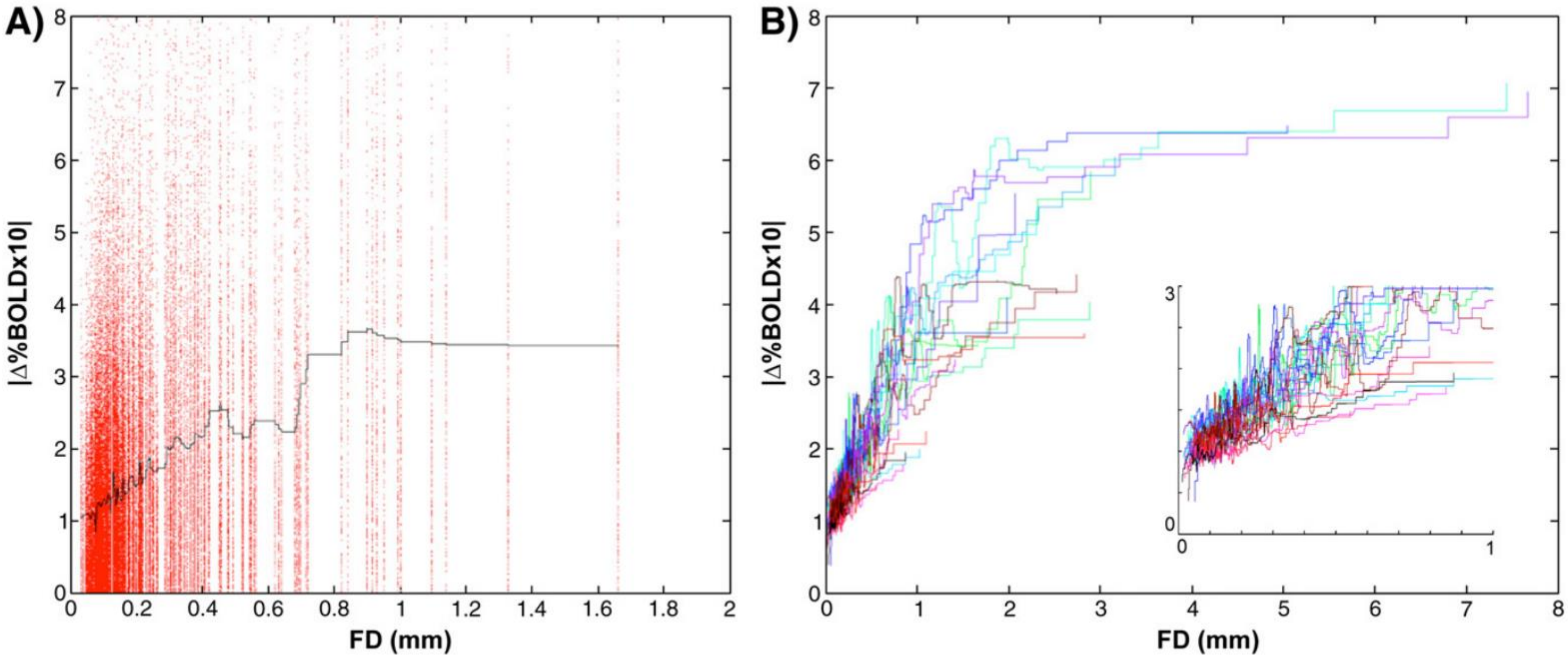
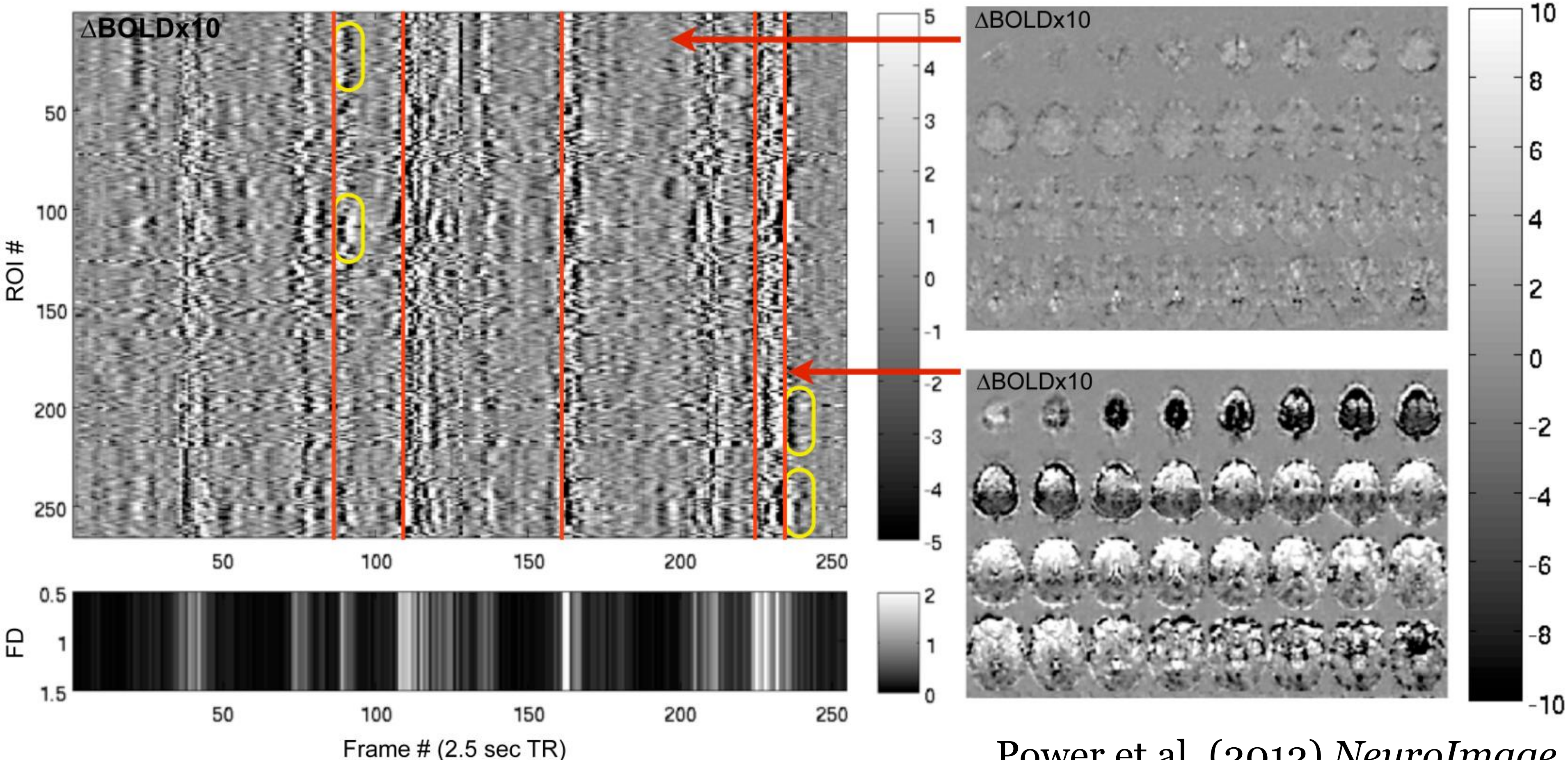


Fig. 2. Frame-by-frame head displacement is related to frame-by-frame changes in rs-fcMRI signal throughout the brain and across subjects. (A) For each frame of data in the same subject used in Fig. 1, the framewise displacement (FD) of a frame of data is plotted against the absolute values of the differentials of rs-fcMRI timecourses of 264 ROIs (locations listed and shown in Table S1 and Figure S3). These data are fitted with a loess curve (black line) sampling the nearest 5000 data points. (B) Identically produced loess curves from all 22 subjects in Cohort 1 are plotted against framewise displacement. There is a clear trend for larger frame-by-frame head displacement to co-occur with larger changes in rs-fcMRI signal. The inset magnifies the plot between framewise displacements of 0 and 1, demonstrating that this relationship exists even for very small movements.

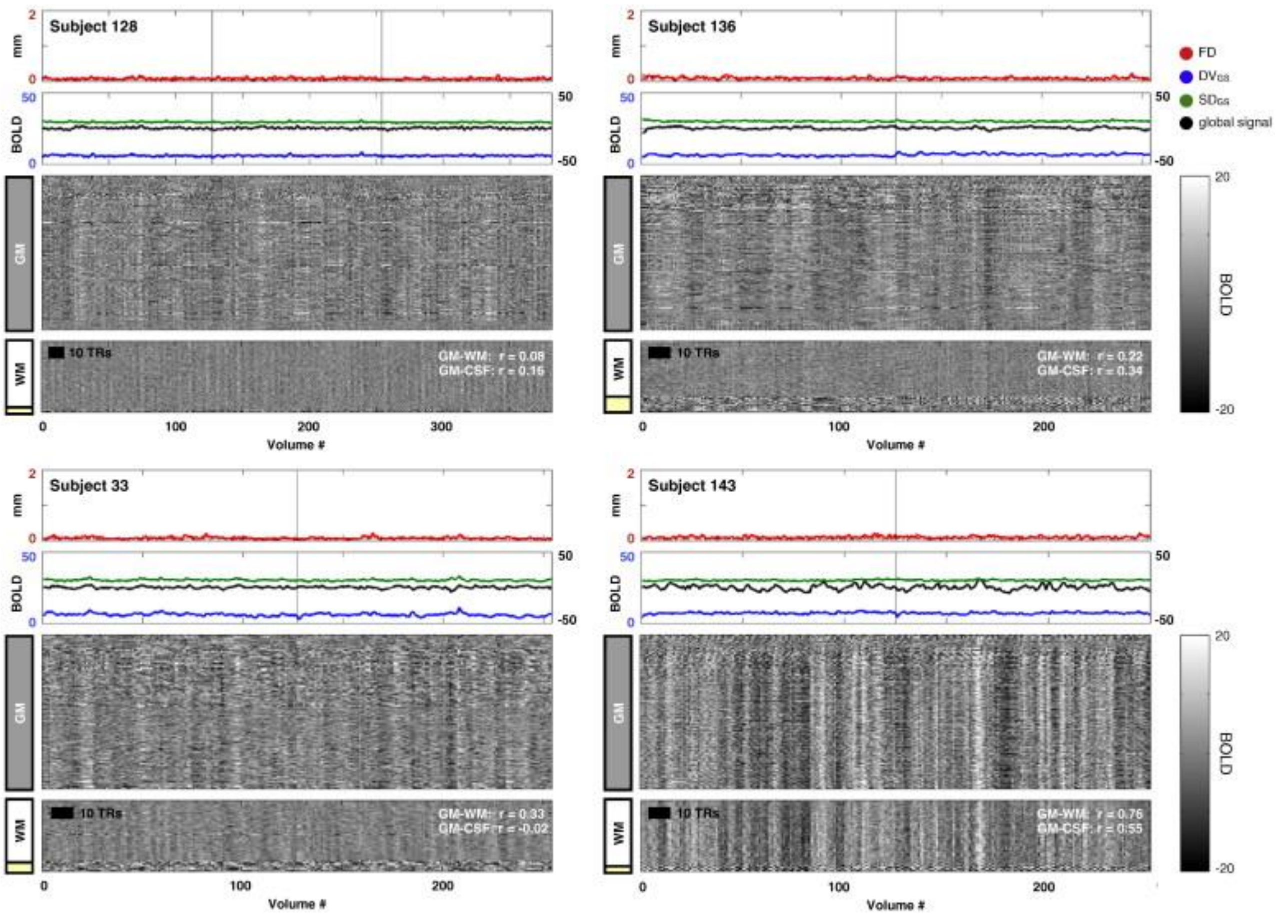
Why does traditional motion correction not work?



Power et al. (2012) *NeuroImage*

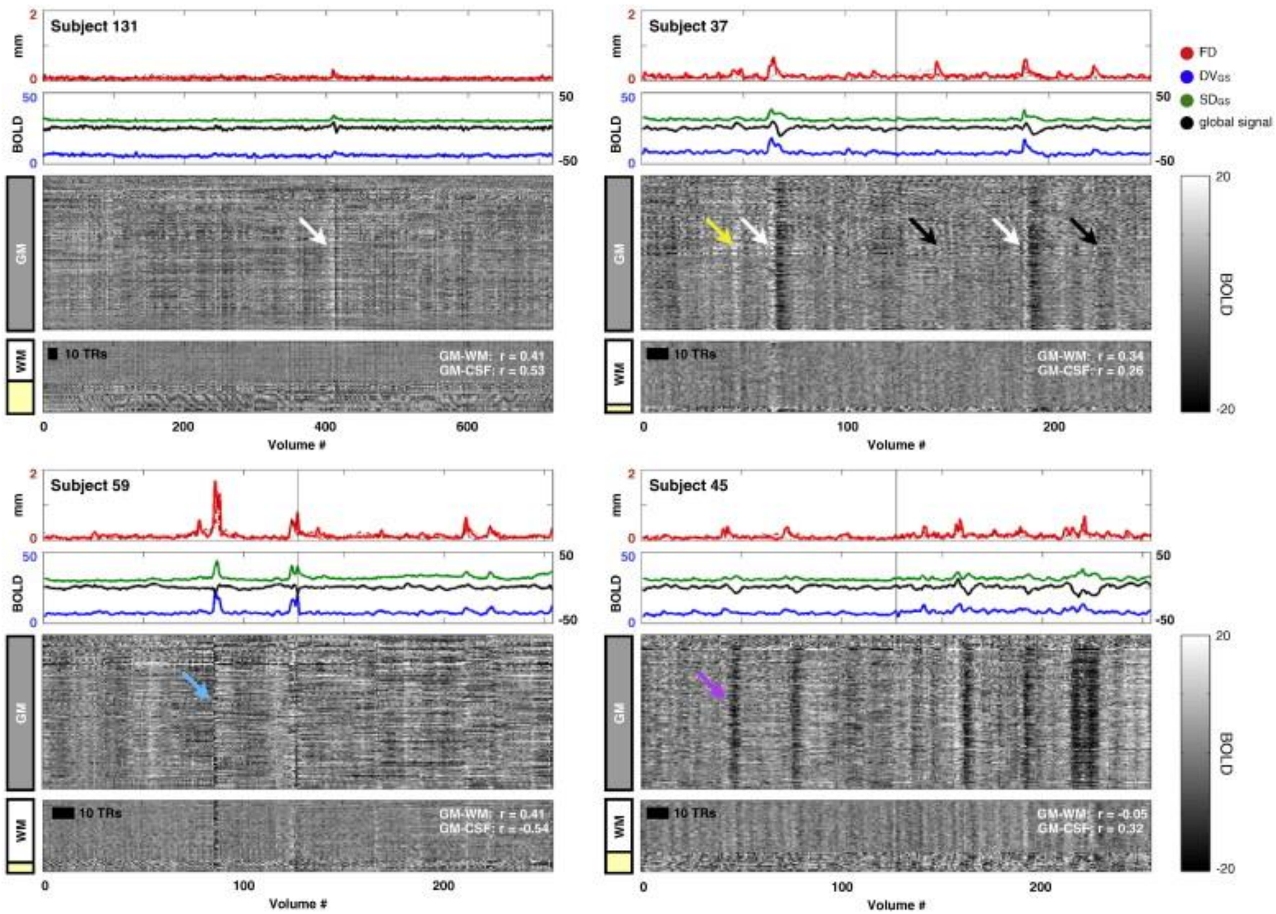
Figure S4: **Head motion simultaneously induces changes in BOLD signal in opposite directions in various parts of the brain.** In a single subject, the derivatives of 264 timecourses are plotted in grayscale, with time on the x-axis. Here, white indicates positive displacements of BOLD signal, and black indicates negative displacements of BOLD signal. Below this plot the framewise displacement (FD) is plotted in grayscale. Several periods of movement are indicated by the red lines in the upper plot. Looking directly to the right of the lines (using the red lines as a reference point), note that at identical time points, that BOLD signal is dramatically increased in some ROIs, and simultaneously dramatically decreased at other ROIs. Some examples are circled in yellow. At right, whole-brain images of the derivative of the BOLD signal are plotted for a low-motion frame (top) and a high-motion frame (bottom). Note the ringing artifact, as well as dorsal-ventral and anterior-posterior orientations of artifactual signal change. Plots in other subjects have similar characteristics.

Low-motion subjects



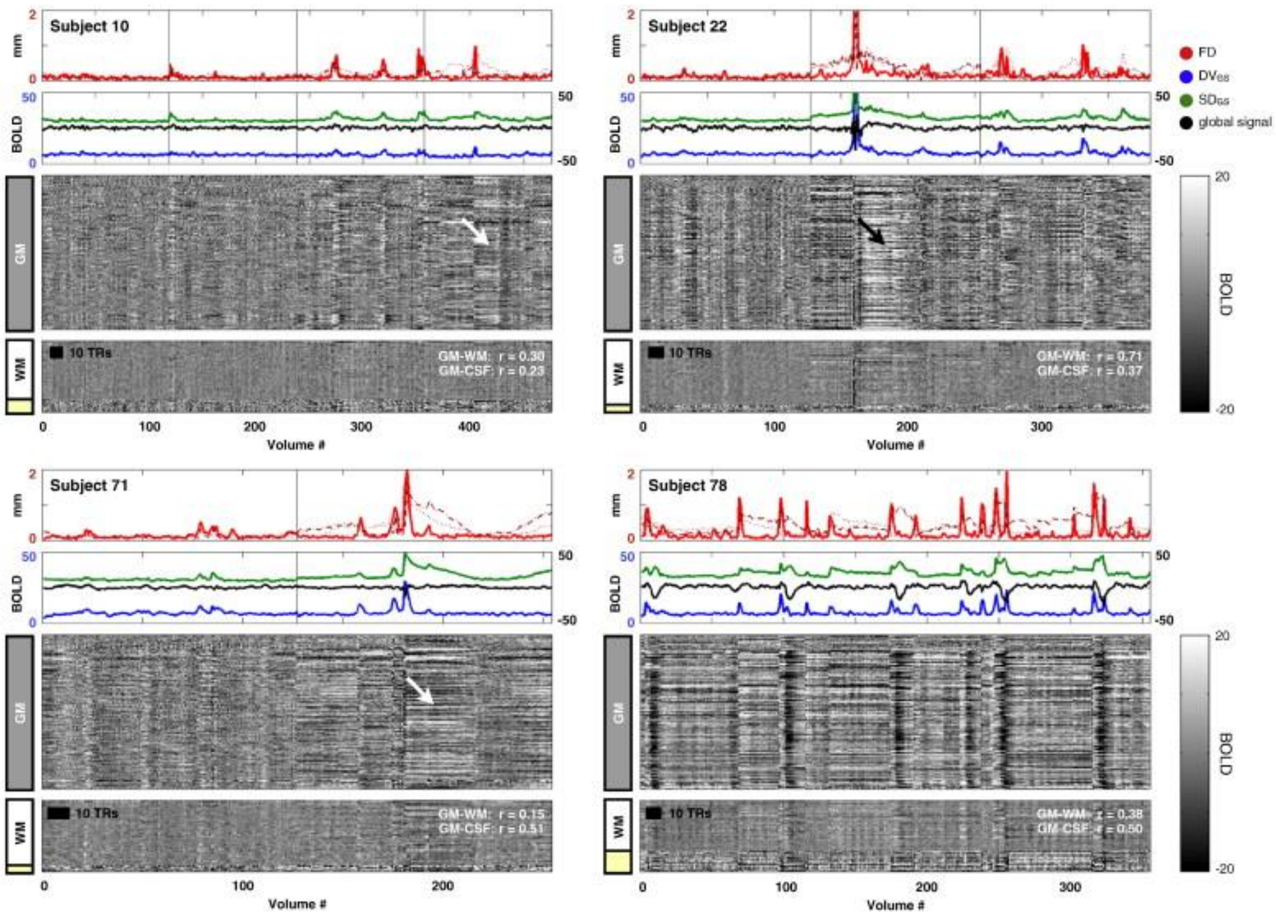
Power et al 2014, Neuroimage

Intermittent-motion subjects



Power et al 2014, Neuroimage

Head shift-motion subjects

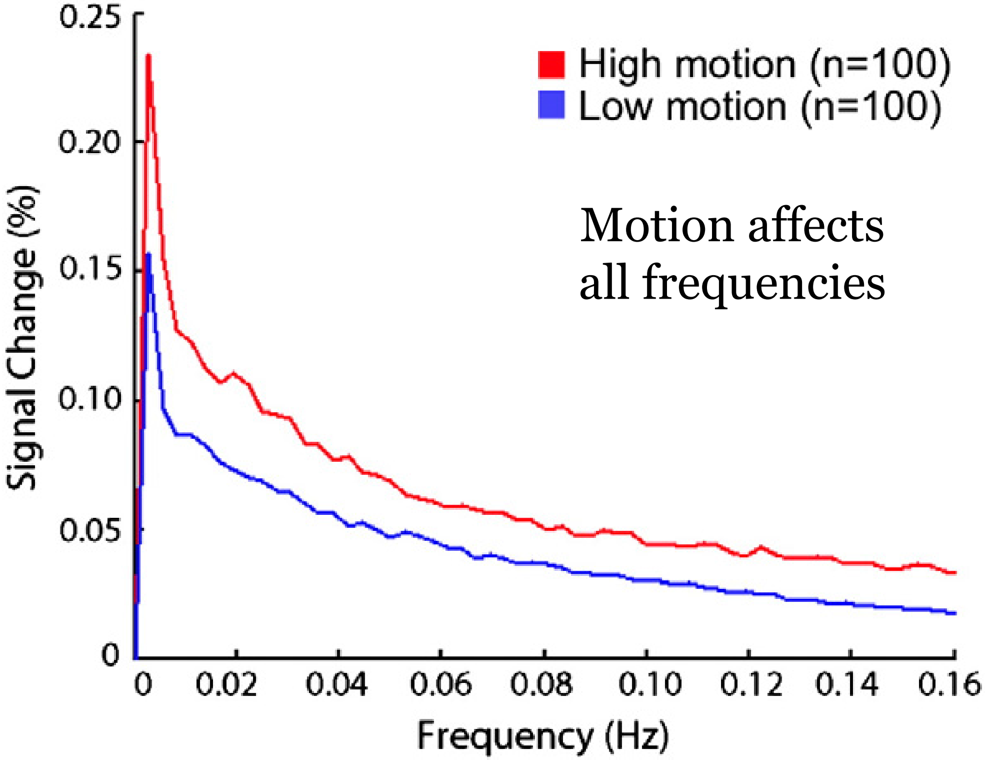


Power et al 2014, Neuroimage

Expand motion parameters (+Spikes)

- 3 par: GMS, WM, CSF
- 9 par: 3par + 6Motion (tra,rot)
- 18 par: 9par + f'(t)
- 36 par: 18 par + f''(t)

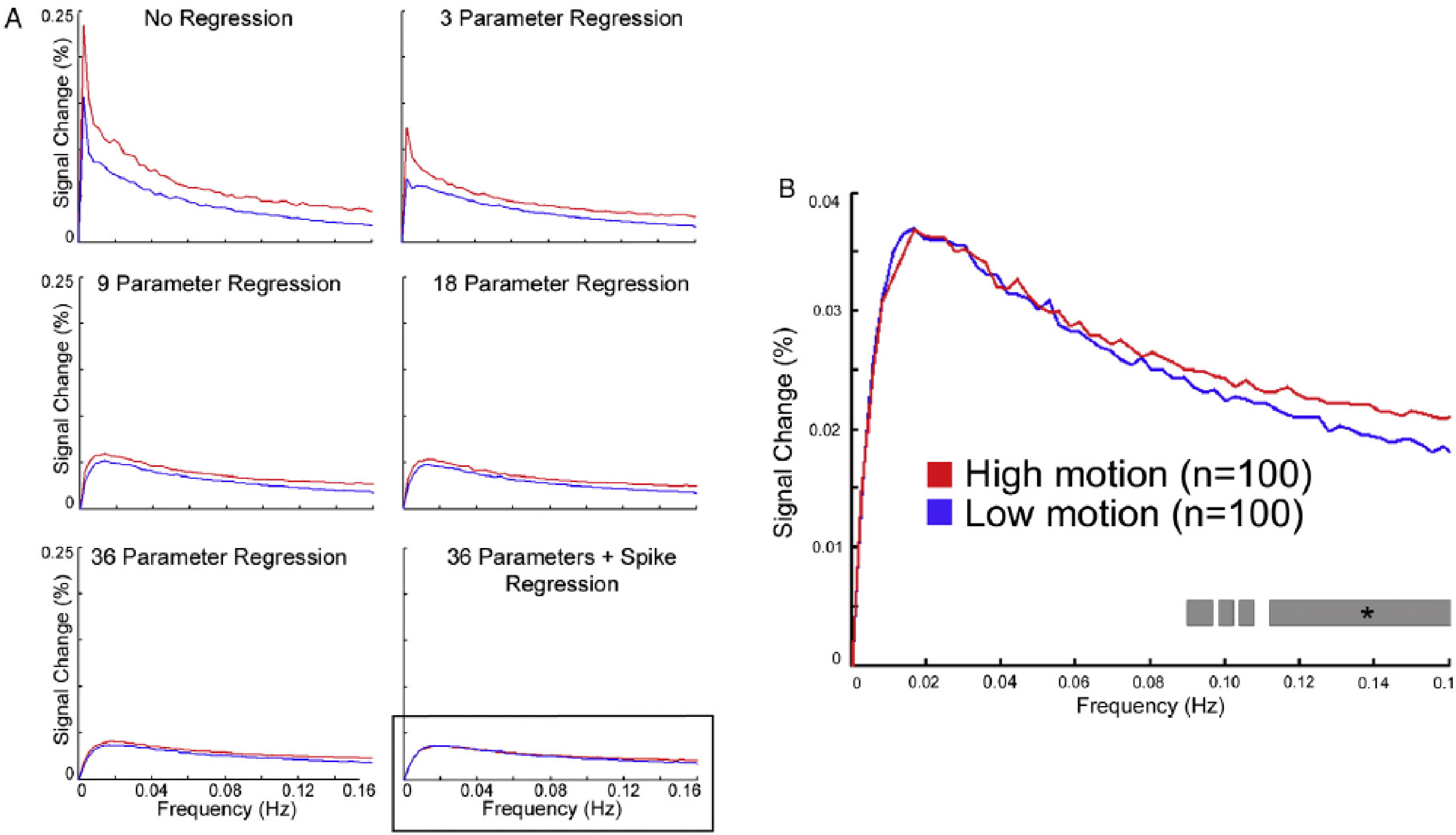
Including the temporal derivatives and quadratic terms of the realignment estimates in the confound model to account for delayed and non-linear motion-induced spin history effects.



Motion affects all frequencies

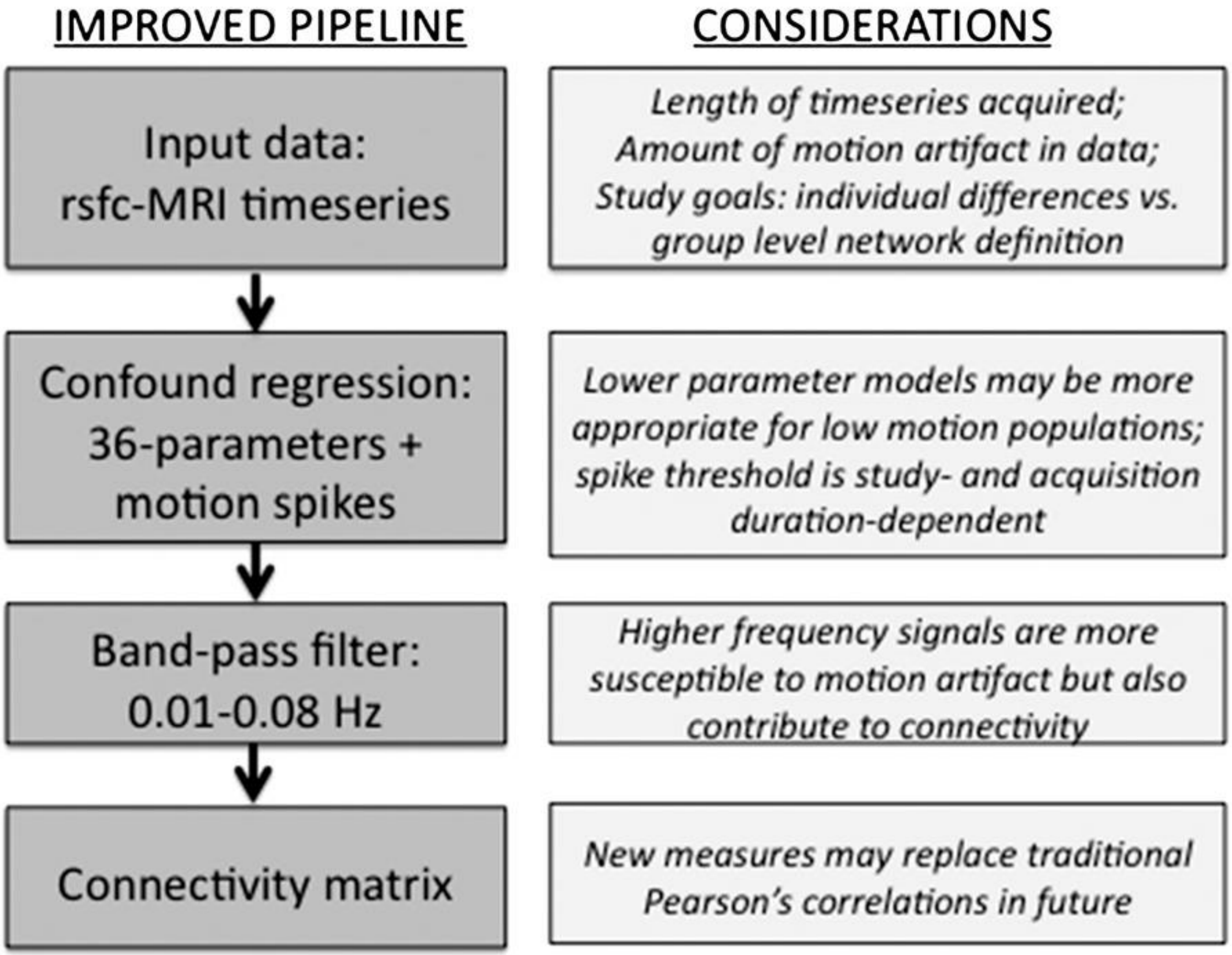
Satterthwaite et al. (2013)

Expand motion parameters (+Spikes)



Satterthwaite et al. (2013)

Expand motion parameters (+Spikes)



Satterthwaite et al. (2013)

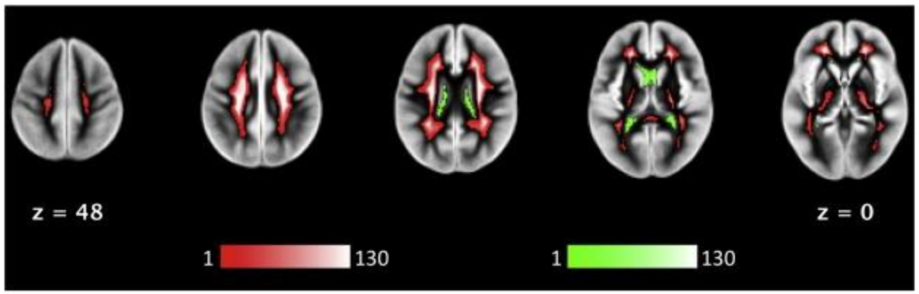
Power et al 2014, Neuroimage

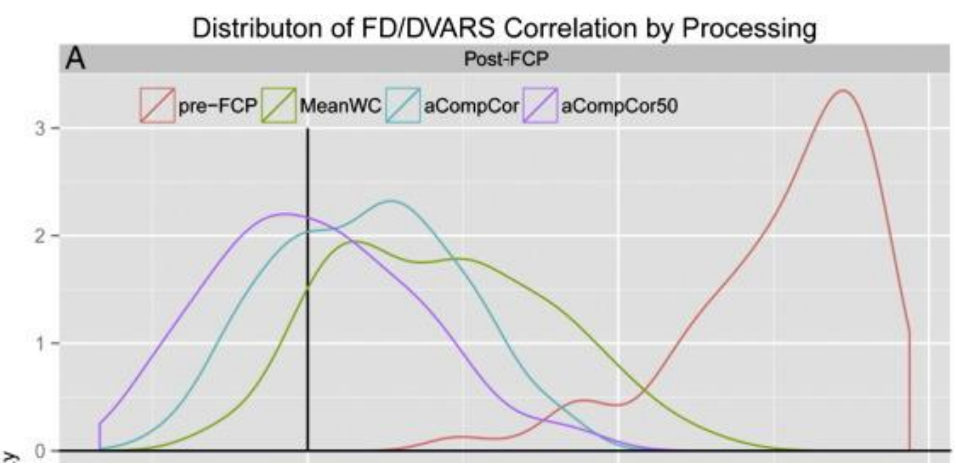
Include global signal regression

From a perspective of eliminating artifactual variance, especially motion-related variance, GSR is unquestionably powerful. However, GSR is a contentious step in processing [e.g., mean centering of correlations will induce false anticorrelations and potentially remove signal]

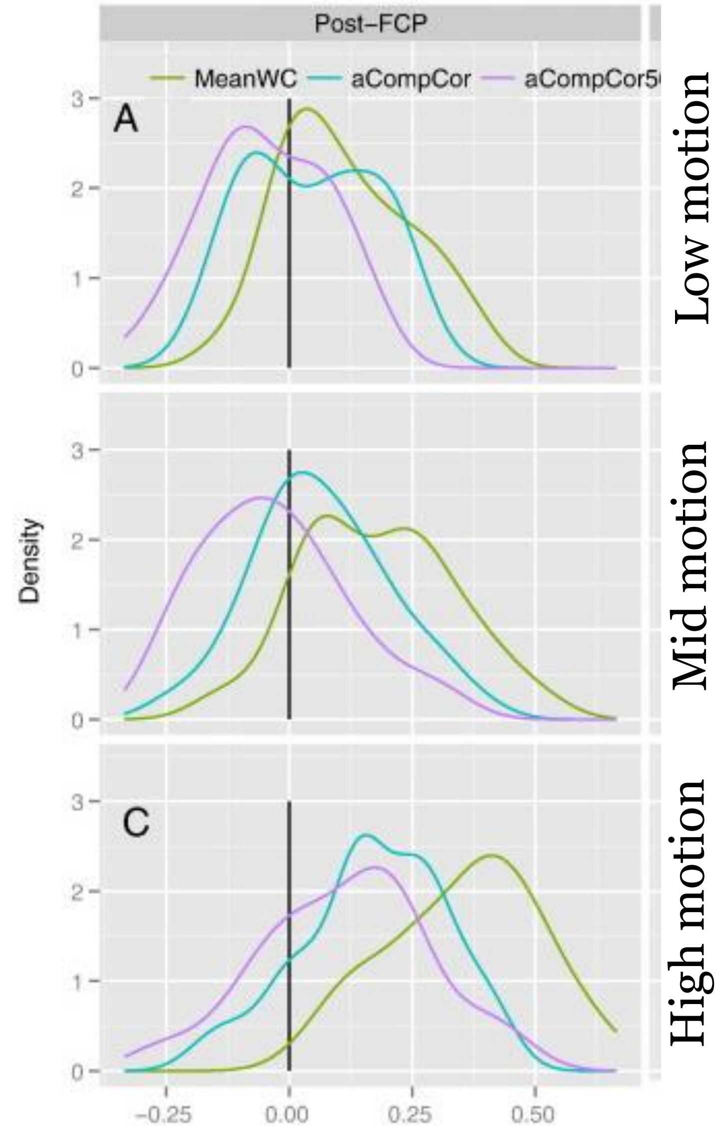
CompCor: component based noise correction method

aCompCor50



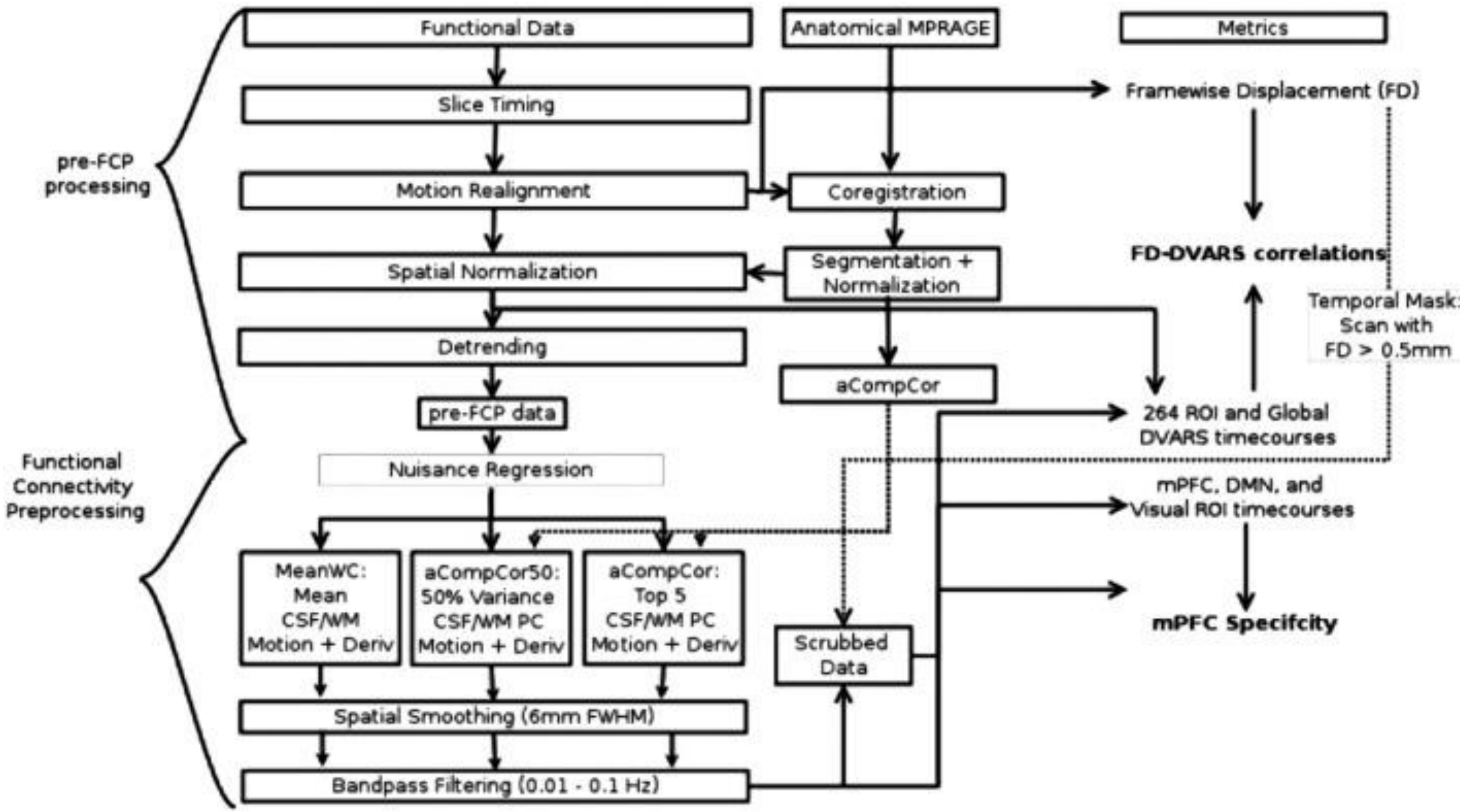


FD/DVARS correlation



Behzadi et al., 2007; Muscheli et al 2014

aCompCor50

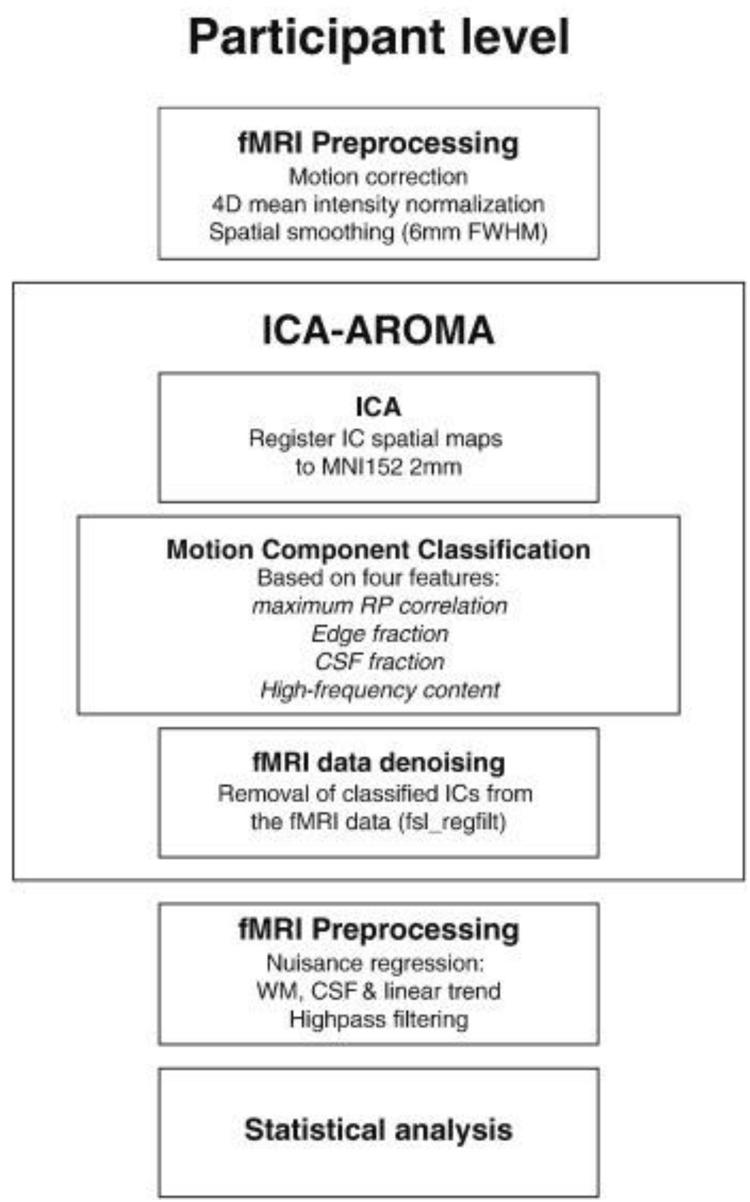


Functional Data
Anatomical MPRAGE
Metrics
Slice Timing
Framewise Displacement (FD)
pre-FCP processing
Motion Realignment
Coregistration
Spatial Normalization
Segmentation + Normalization
FD-DVARS correlations
Temporal Mask: Scan with FD > 0.5mm
Detrending
aCompCor
pre-FCP data
264 ROI and Global DVARS timecourses
Functional Connectivity Preprocessing
Nuisance Regression
mPFC, DMN, and Visual ROI timecourses
MeanWC: Mean CSF/WM Motion + Deriv
aCompCor50: 50% Variance CSF/WM PC Motion + Deriv
aCompCor: Top 5 CSF/WM PC Motion + Deriv
Scrubbed Data
mPFC Specifcity
Spatial Smoothing (6mm FWHM)
Bandpass Filtering (0.01 - 0.1 Hz)

ICA-AROMA

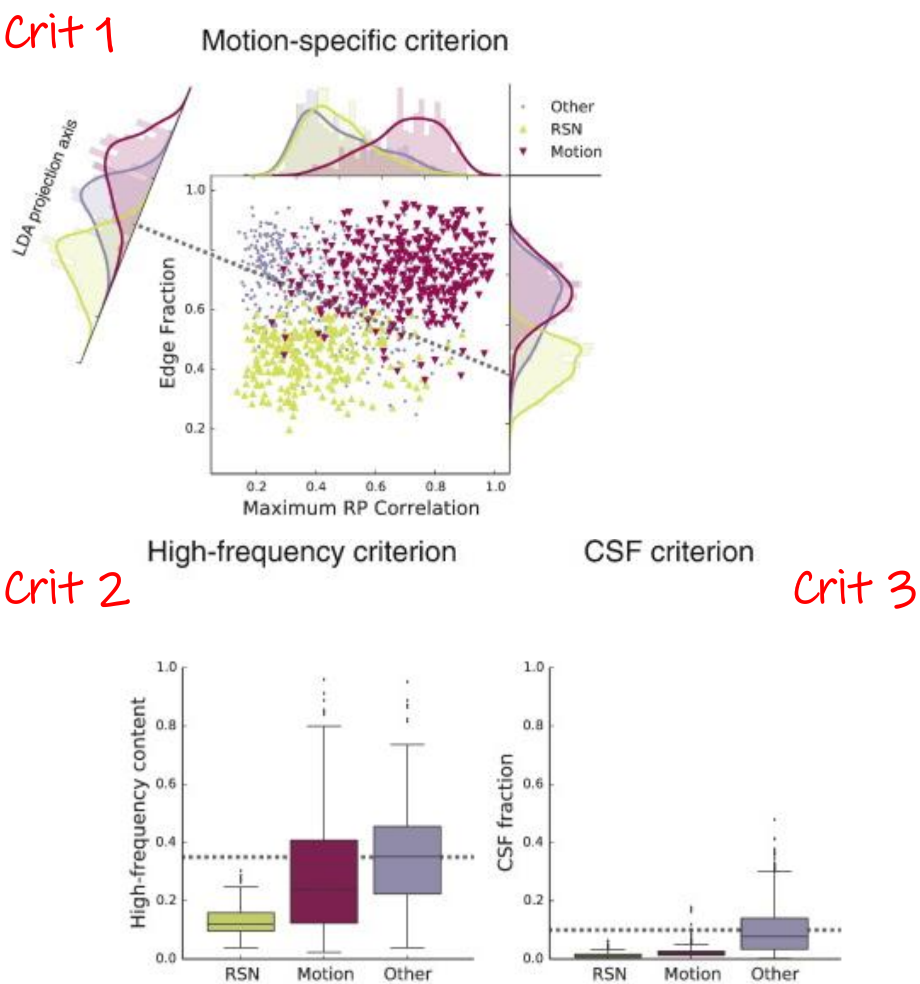
- ICA strategy focused on removing motion artifacts.
- Uses small set of spatial and temporal rules (4) to define motion components:

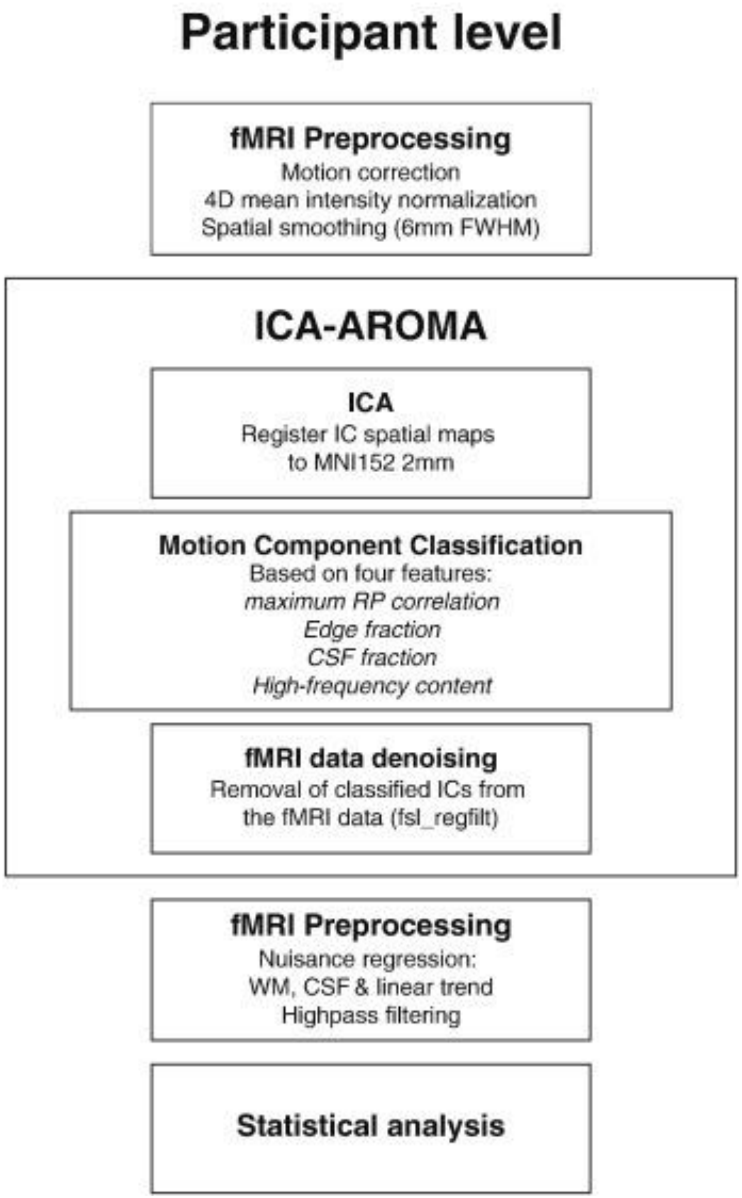
1. High frequency
2. Correlated with Motion Parameters
3. Fraction near borders
4. Fraction in CSF



Pruim et al 2015 Neuroimage

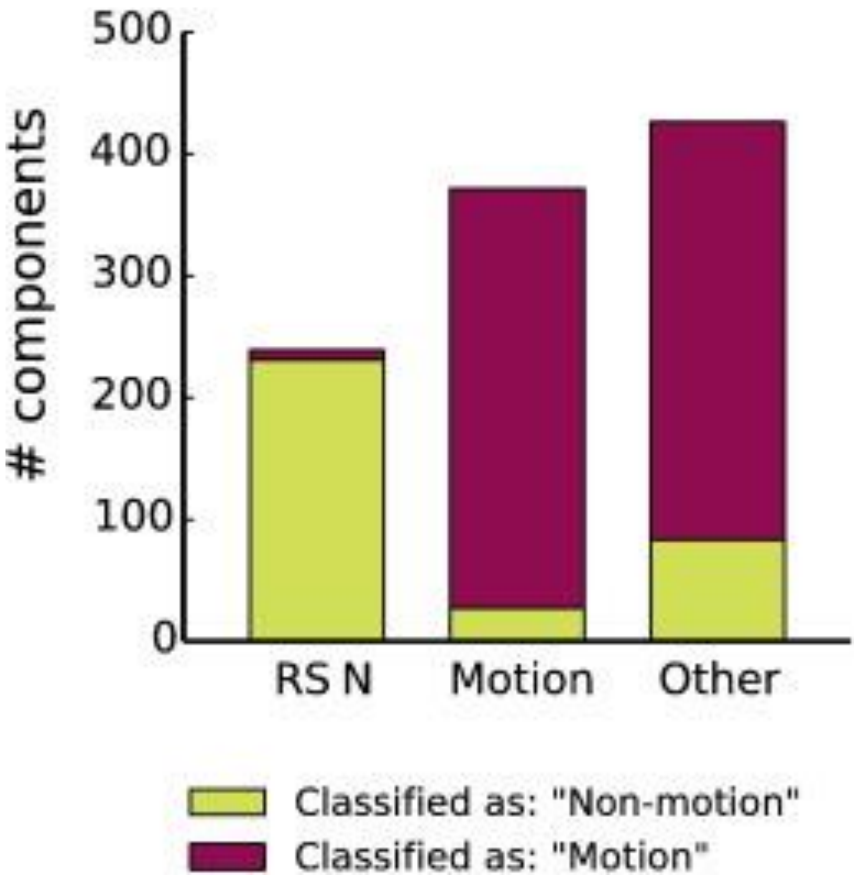
ICA-AROMA

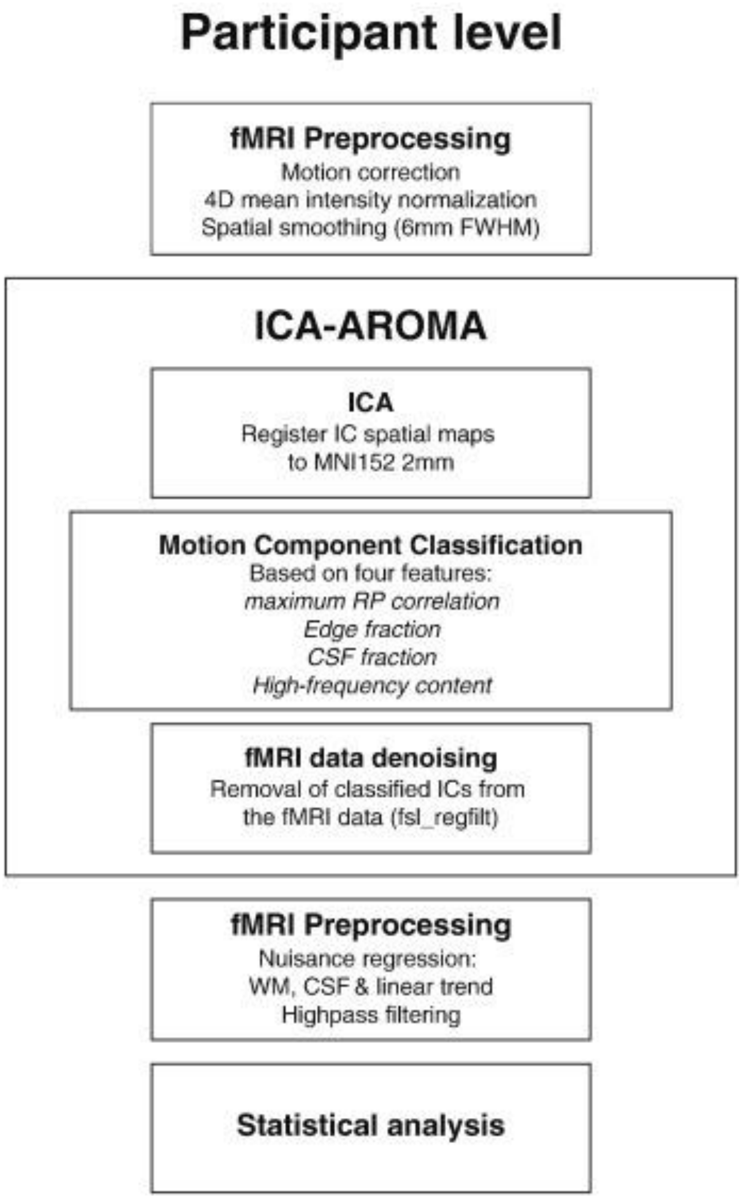




Pruim et al 2015 Neuroimage

ICA-AROMA

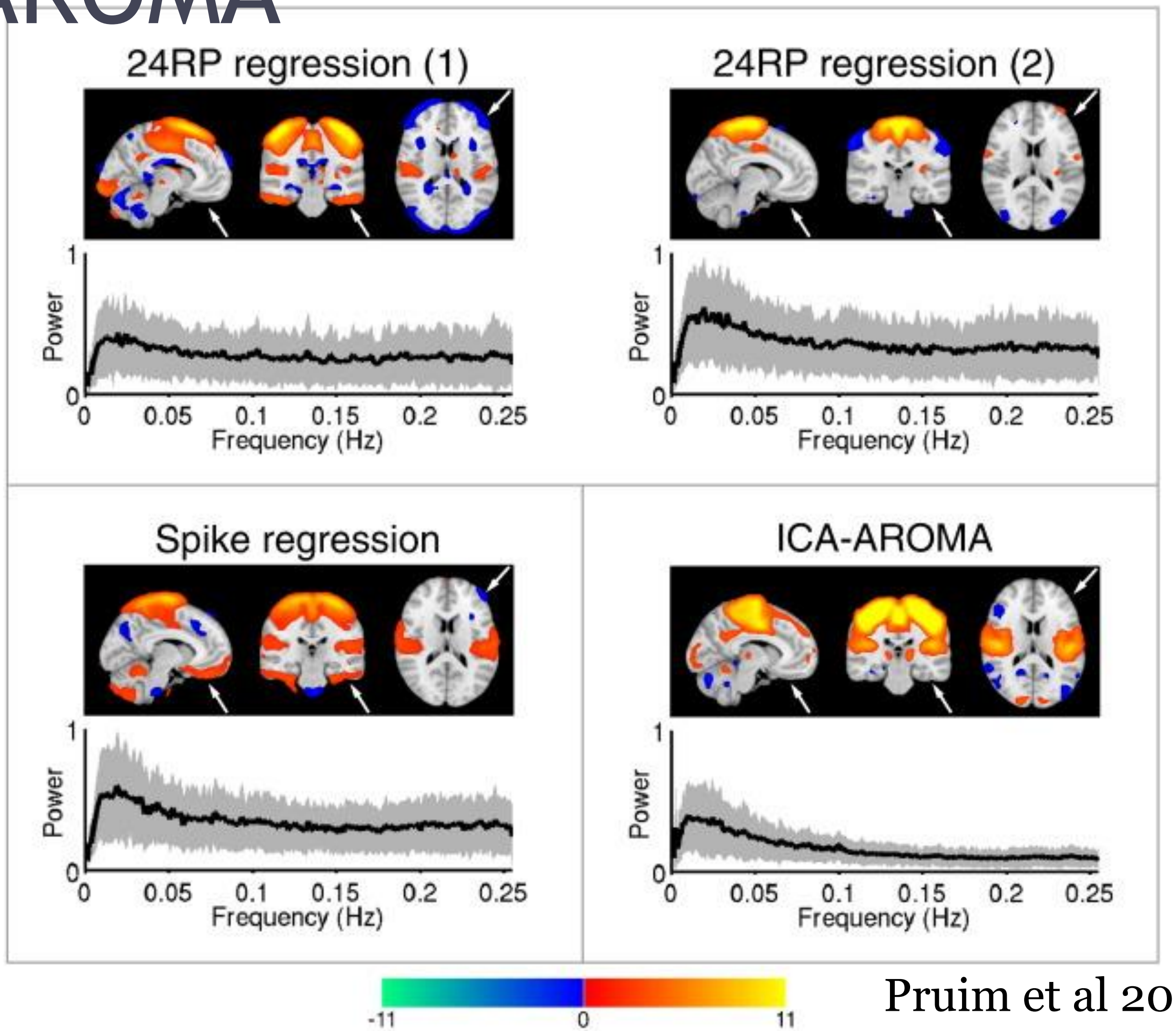




Pruim et al 2015 Neuroimage

Ex. Sensory-motor component

ICA-AROMA



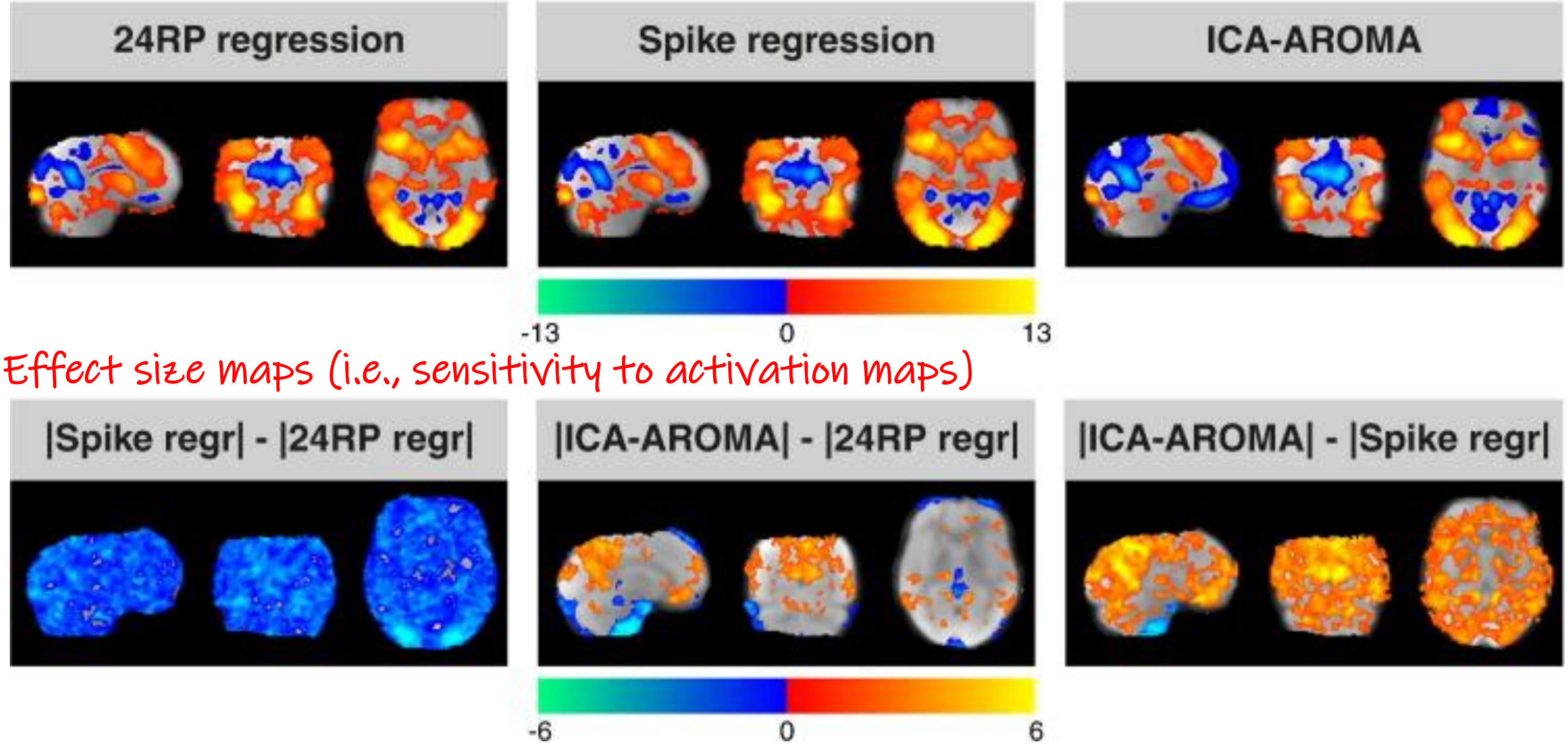
Pruim et al 2015 Neuroimage

Ex. Task data

ICA-AROMA

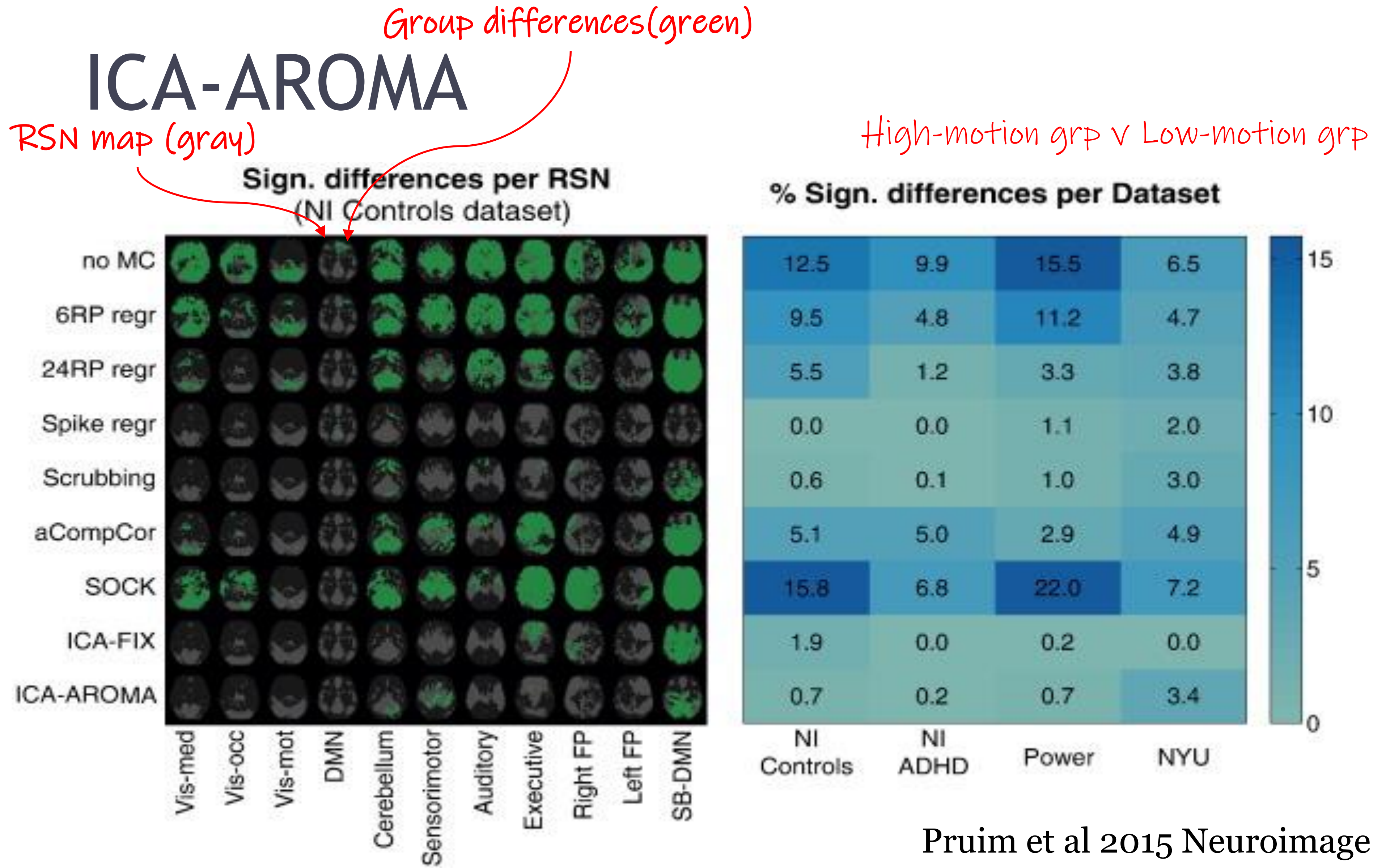
Group effects

Effect size maps (i.e., sensitivity to activation maps)



Pruim et al 2015 Neuroimage

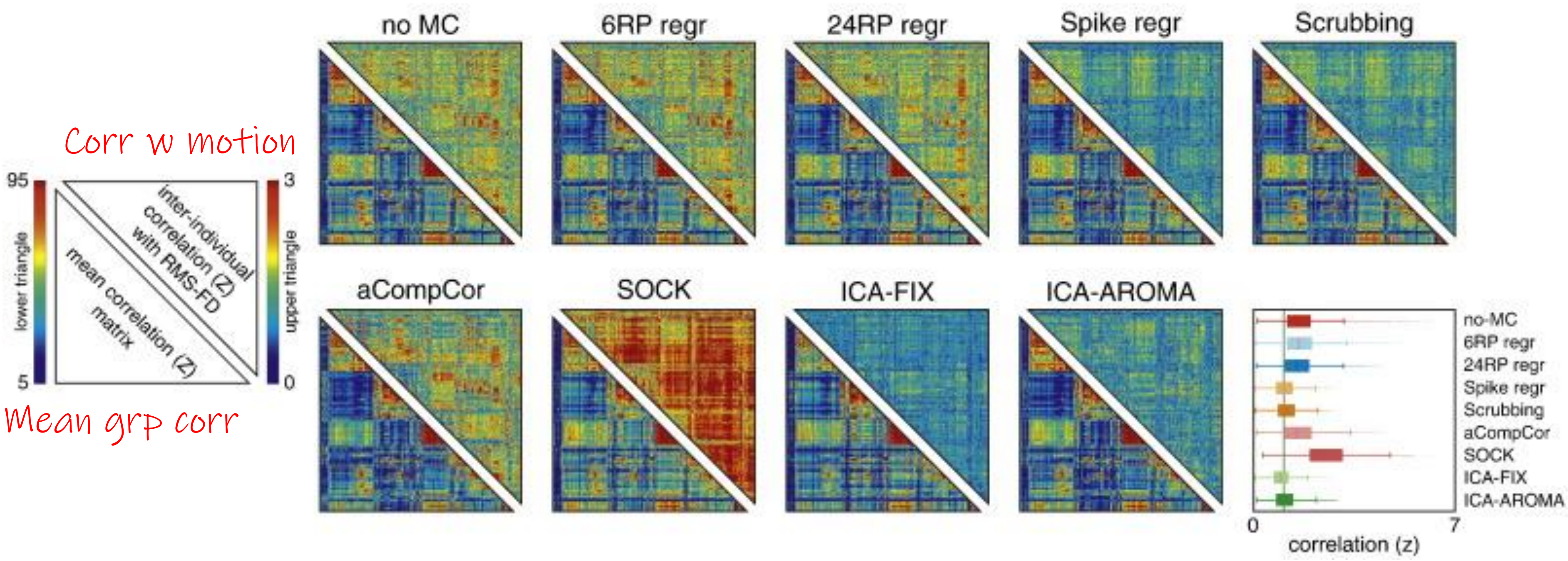
ICA-AROMA



	NI Controls	NI ADHD	Power	NYU
no MC	12.5	9.9	15.5	6.5
6RP regr	9.5	4.8	11.2	4.7
24RP regr	5.5	1.2	3.3	3.8
Spike regr	0.0	0.0	1.1	2.0
Scrubbing	0.6	0.1	1.0	3.0
aCompCor	5.1	5.0	2.9	4.9
SOCK	15.8	6.8	22.0	7.2
ICA-FIX	1.9	0.0	0.2	0.0
ICA-AROMA	0.7	0.2	0.7	3.4

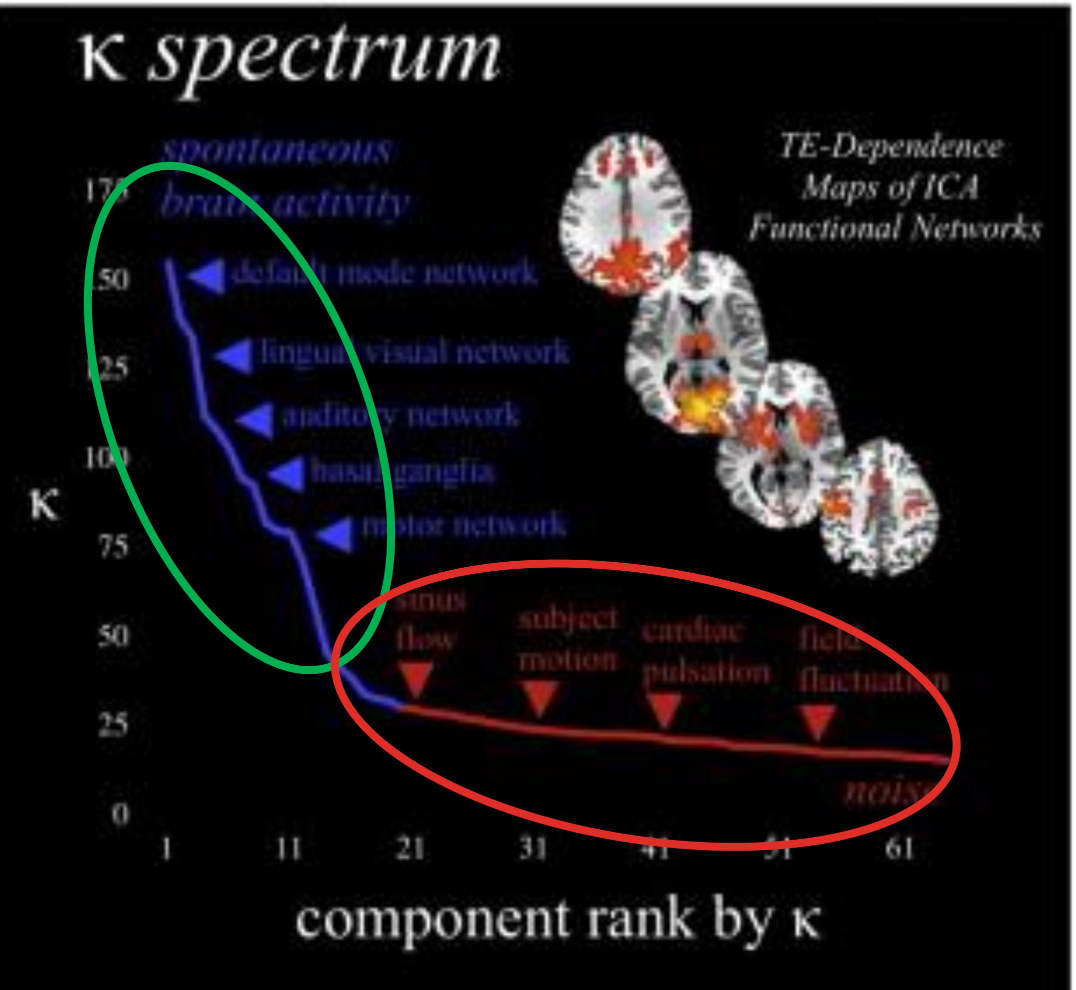
Pruim et al 2015 Neuroimage

ICA-AROMA



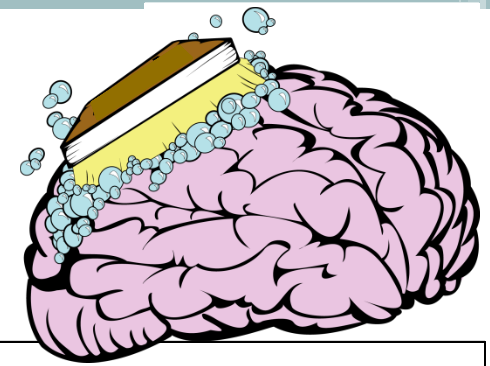
Pruim et al 2015 Neuroimage

Multi-echo fMRI (remember?)



- Use multi-echo data and discard any component which does not exhibit the expected T2 decay

"Scrubbing"



NeuroImage 59 (2012) 2142–2154

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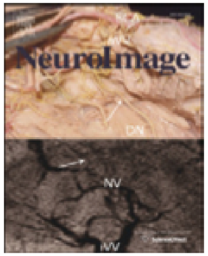

ELSEVIER

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

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Choice of a cut-off threshold

- From Power et al. (2012): "After studying the plots of dozens of healthy adults, values of **0.5 mm for framewise displacement** and **0.5% ΔBOLD for DVARS** were chosen to represent values well above the norm found in still subjects."
  - Also removed *1 TR before* and *2 TRs after* bad frame
- Fair et al. (2013) used an even more stringent FD cut-off of 0.2 mm and DVARS cut-off of 0.4%
- Power et al. (2013) FD 0.2 mm or DVARS 0.3%
- Power et al. (2014) iterative procedure and DVARS 0.2%

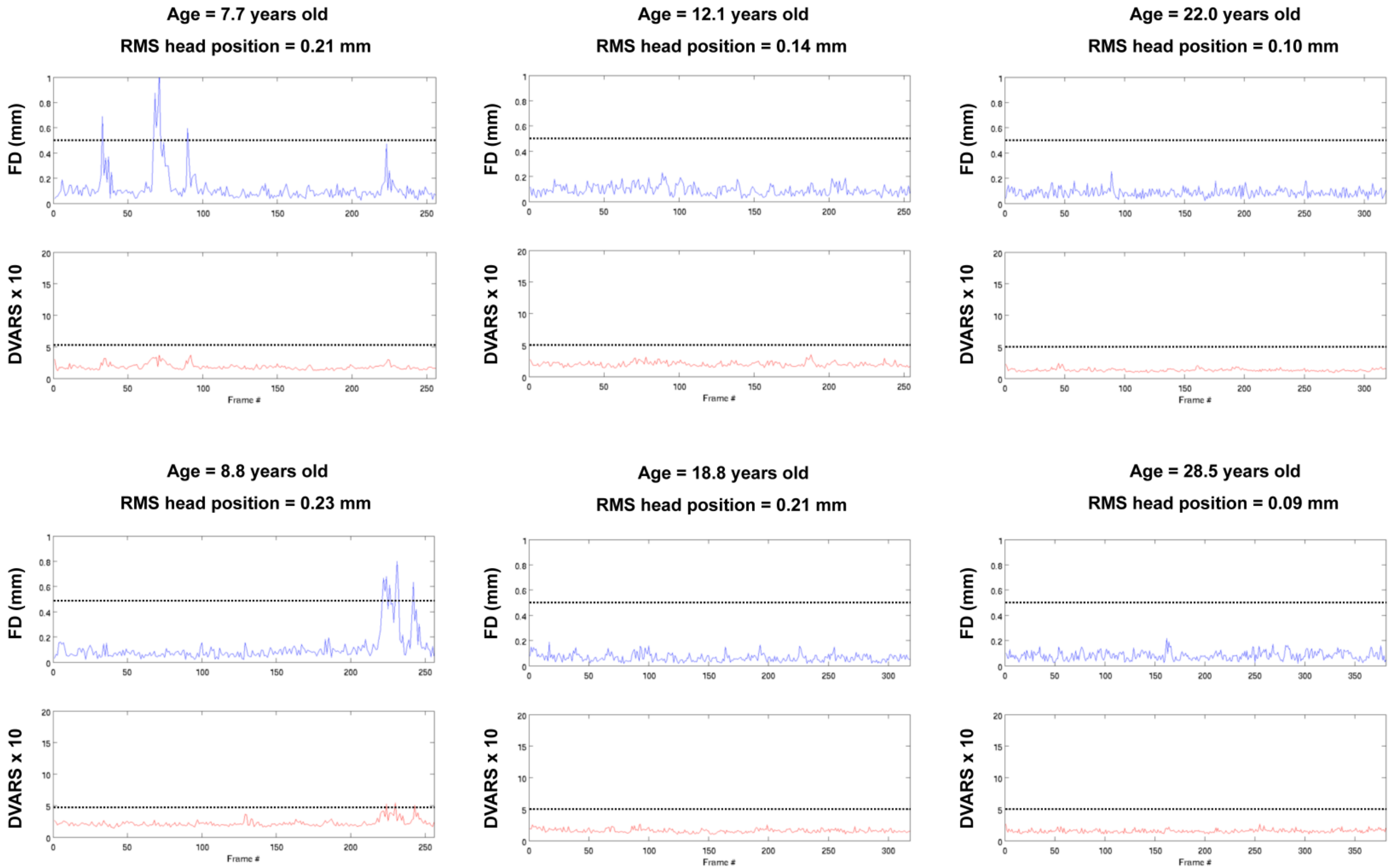
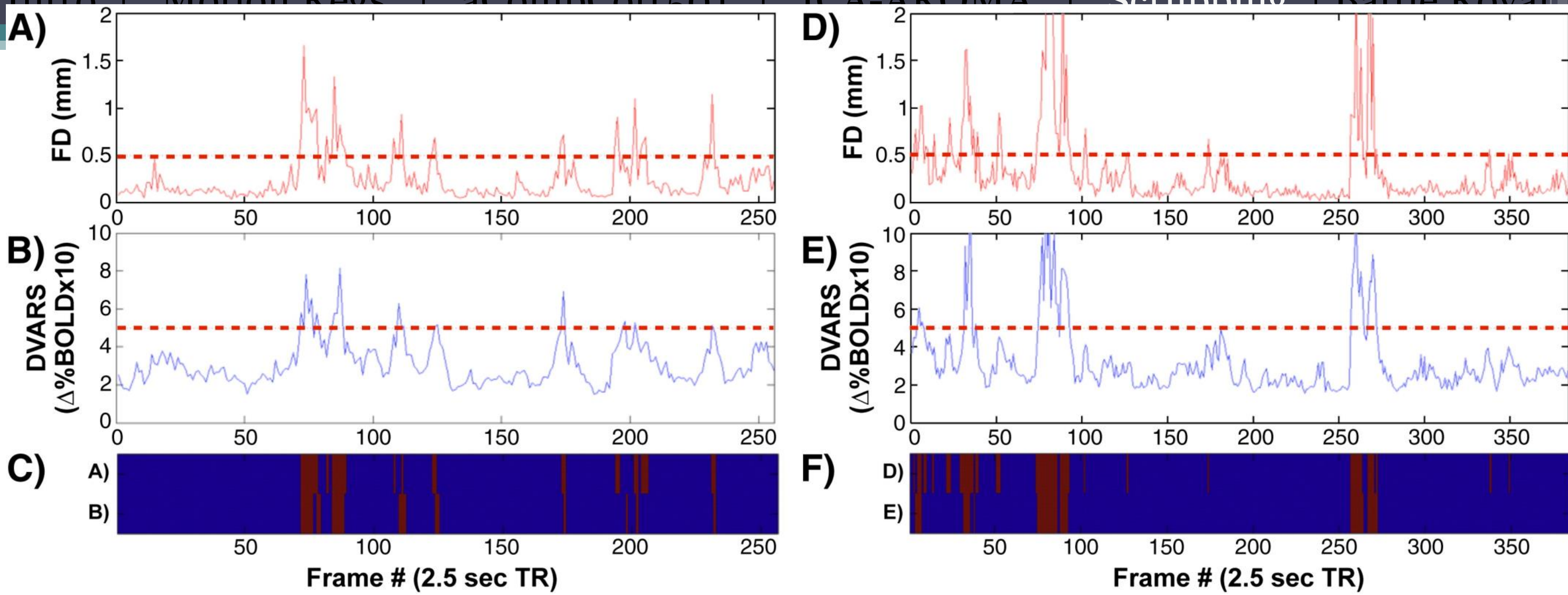


Figure S5: **Floors in DVARS and framewise displacement values exist at all age ranges.** Data from six relatively still subjects are shown, including the age, RMS head position, the framewise displacement (FD), and the DVARS calculations on the functional connectivity image. A floor in FD and DVARS values exists across all ages. Examination of these plots in hundreds of subjects gave rise to the standard thresholds used in this study to identify periods of movement, indicated by the horizontal black lines in the plots (0.5 mm framewise displacement and 0.5% ΔBOLD DVARS (5 on the scales of this figure)).

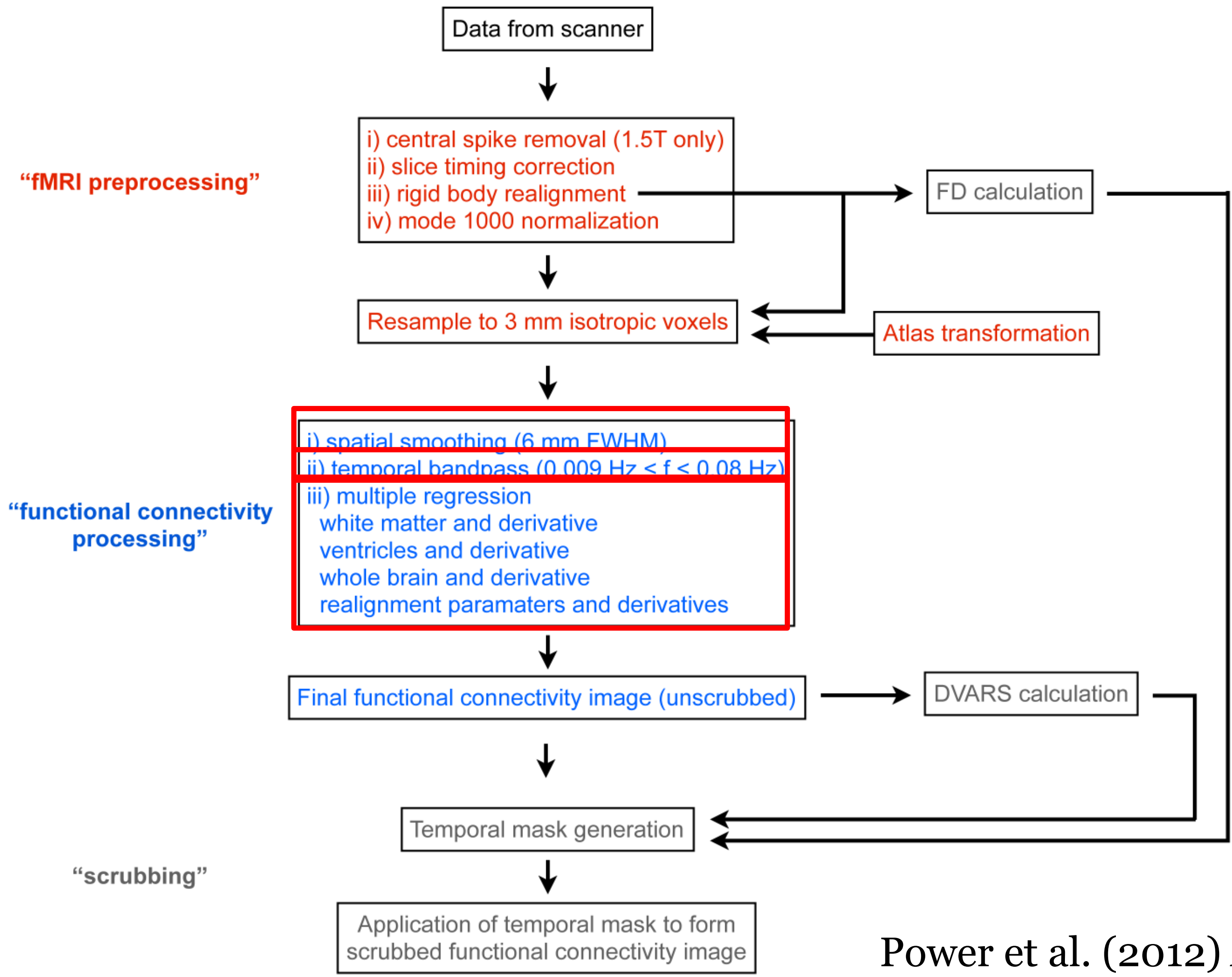
Power et al. (2012) *NeuroImage*



- Temporal masks (red bars) were augmented by also marking the frames 1 back and 2 forward
- All removed frames must *both*:
  1) be high-motion frames (based on FD)
  2) display evidence of widespread and/ or large amplitude changes in BOLD signal (based on DVARS)

Power et al. (2012) *NeuroImage*

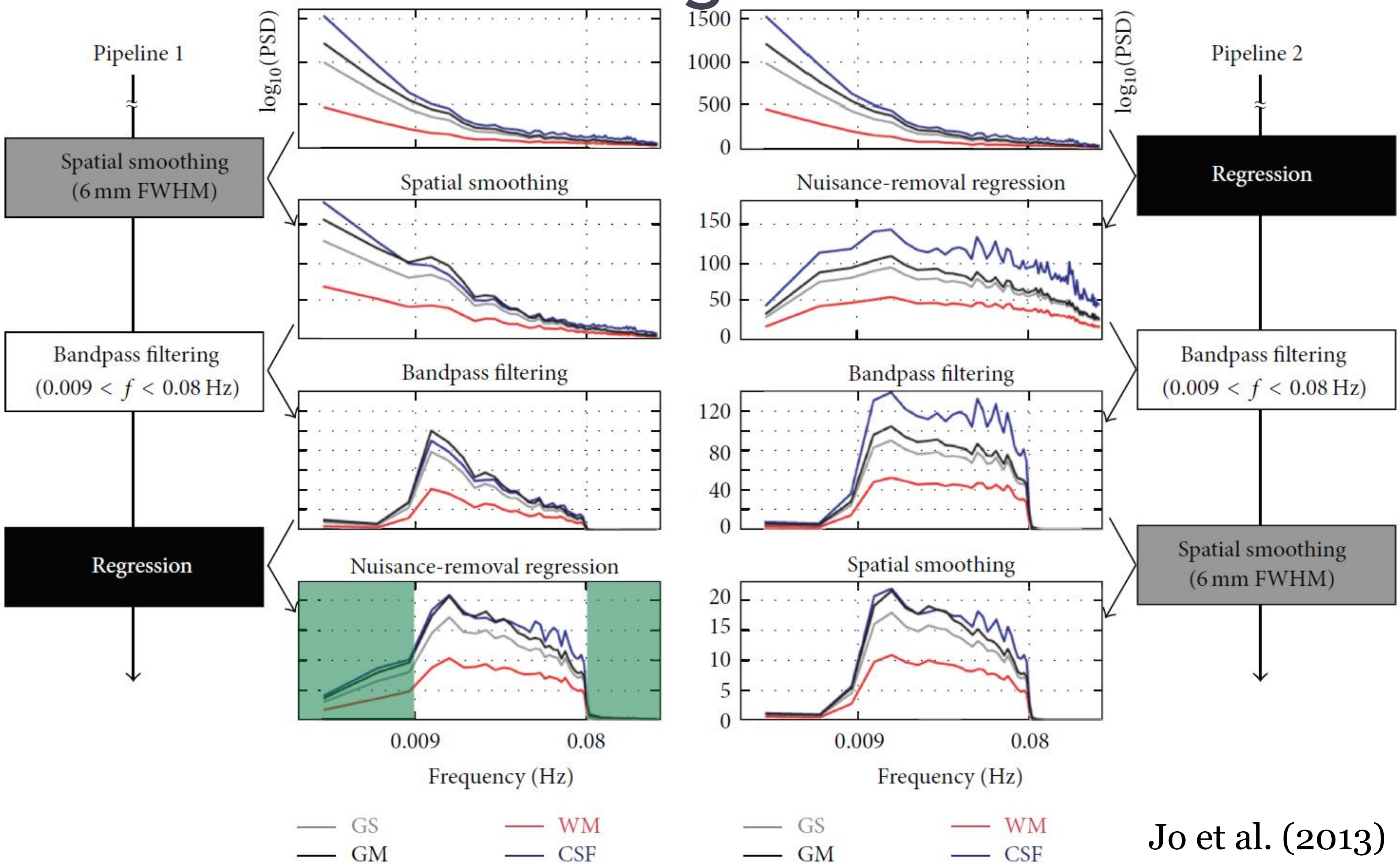
Example data processing workflow



Power et al. (2012) *NeuroImag*

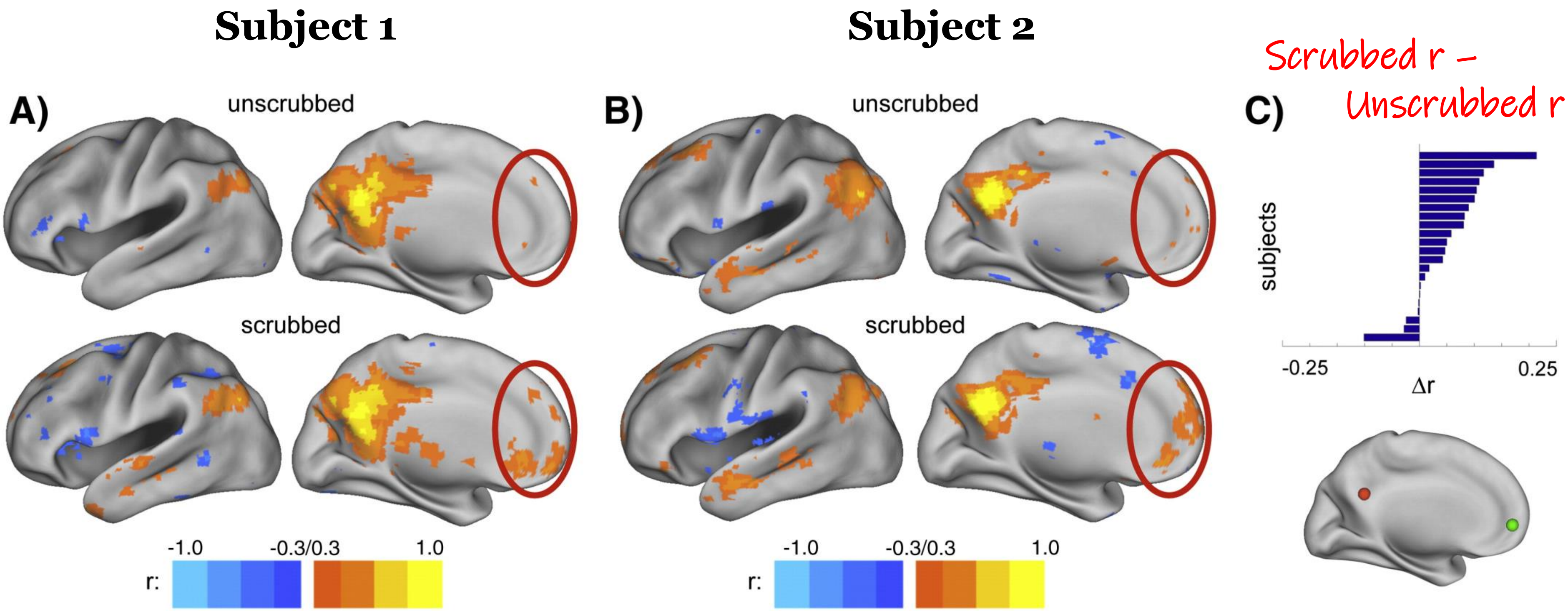
Power spectra analysis

The order of things matters!



Jo et al. (2013)

Impact of scrubbing on rs-fMRI data

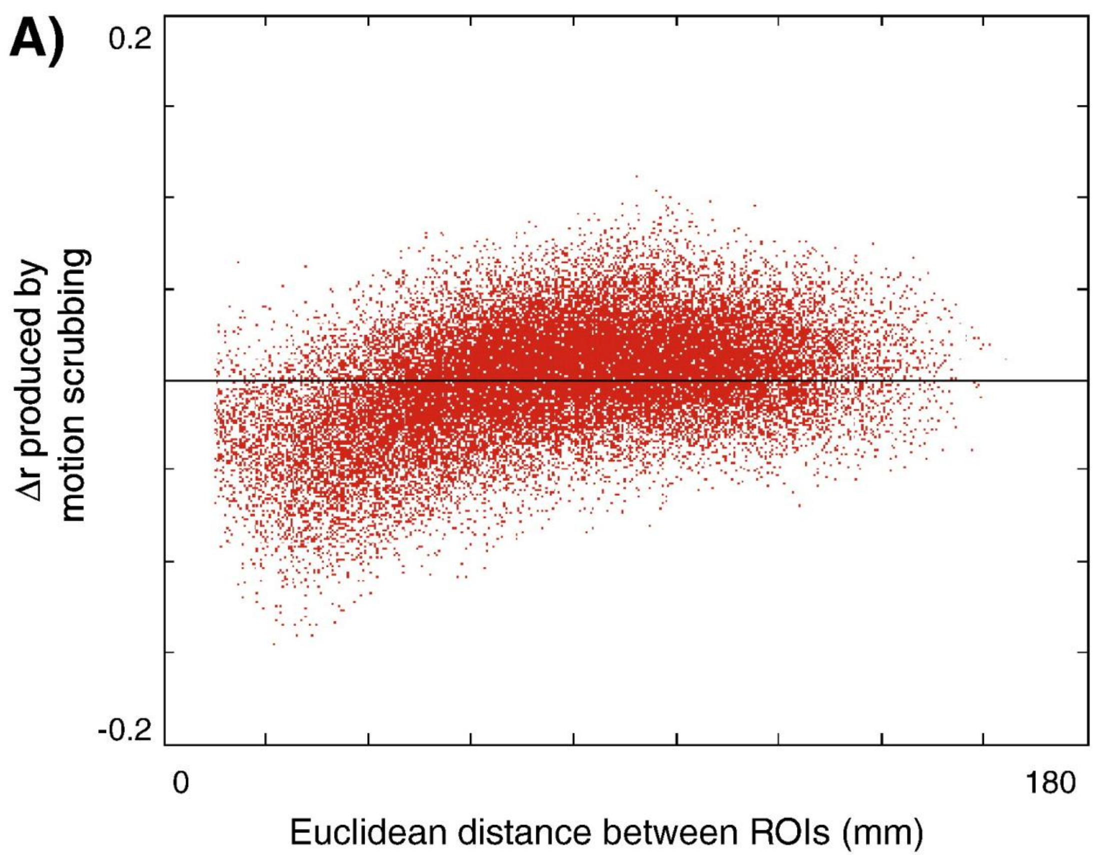


35% of data scrubbed out **39% of data scrubbed out**

- Scrubbing increases this long-distance correlation in most subjects, does not substantially alter it in others, and reduces it in a small number of subjects.

Power et al. (2012) *NeuroImage*

Impact of scrubbing on rs-fMRI data

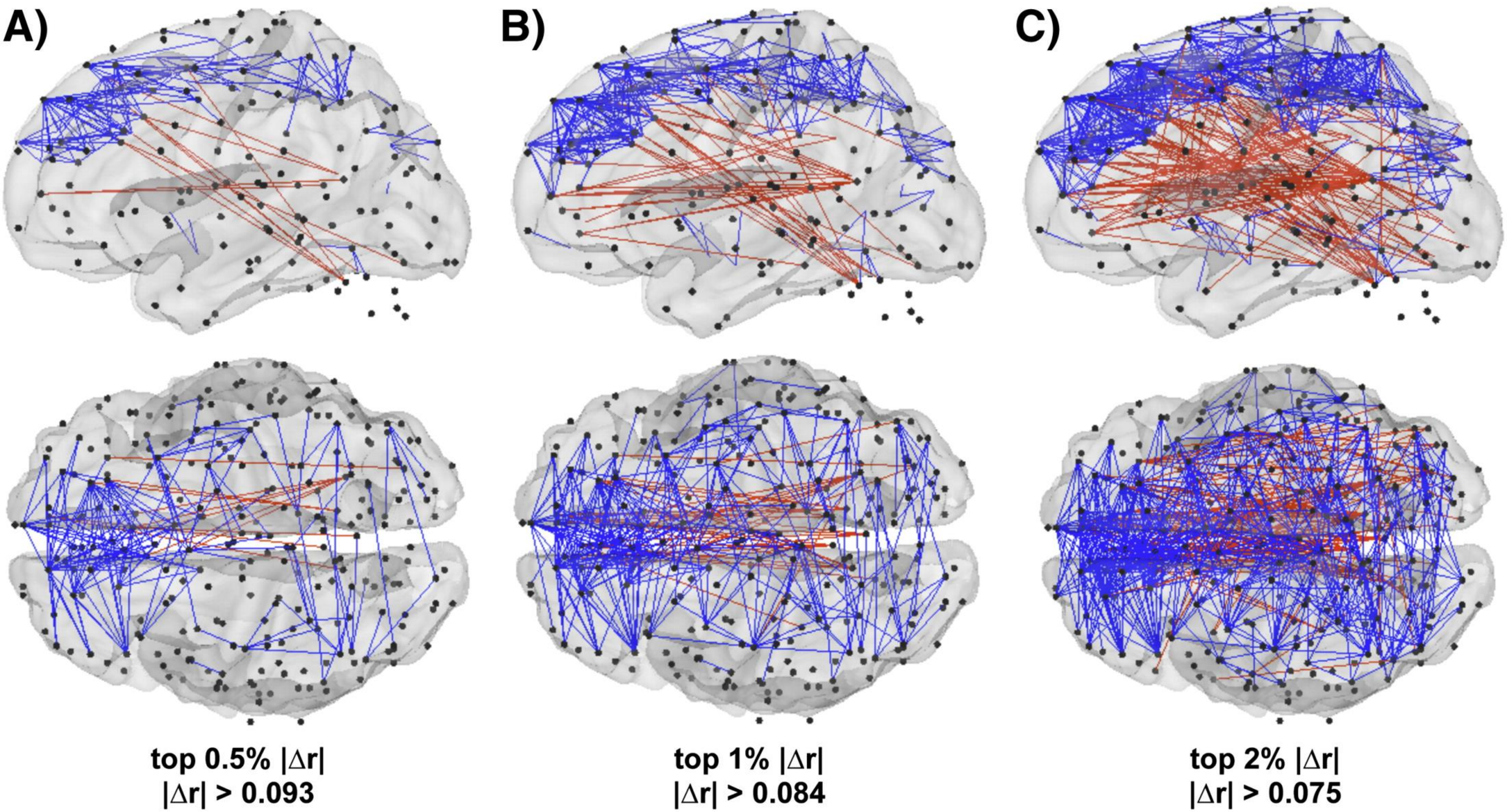


- Scrubbing high-motion frames decreases short-distance correlations and augments long-distance correlations

Power et al. (2012) *NeuroImage*

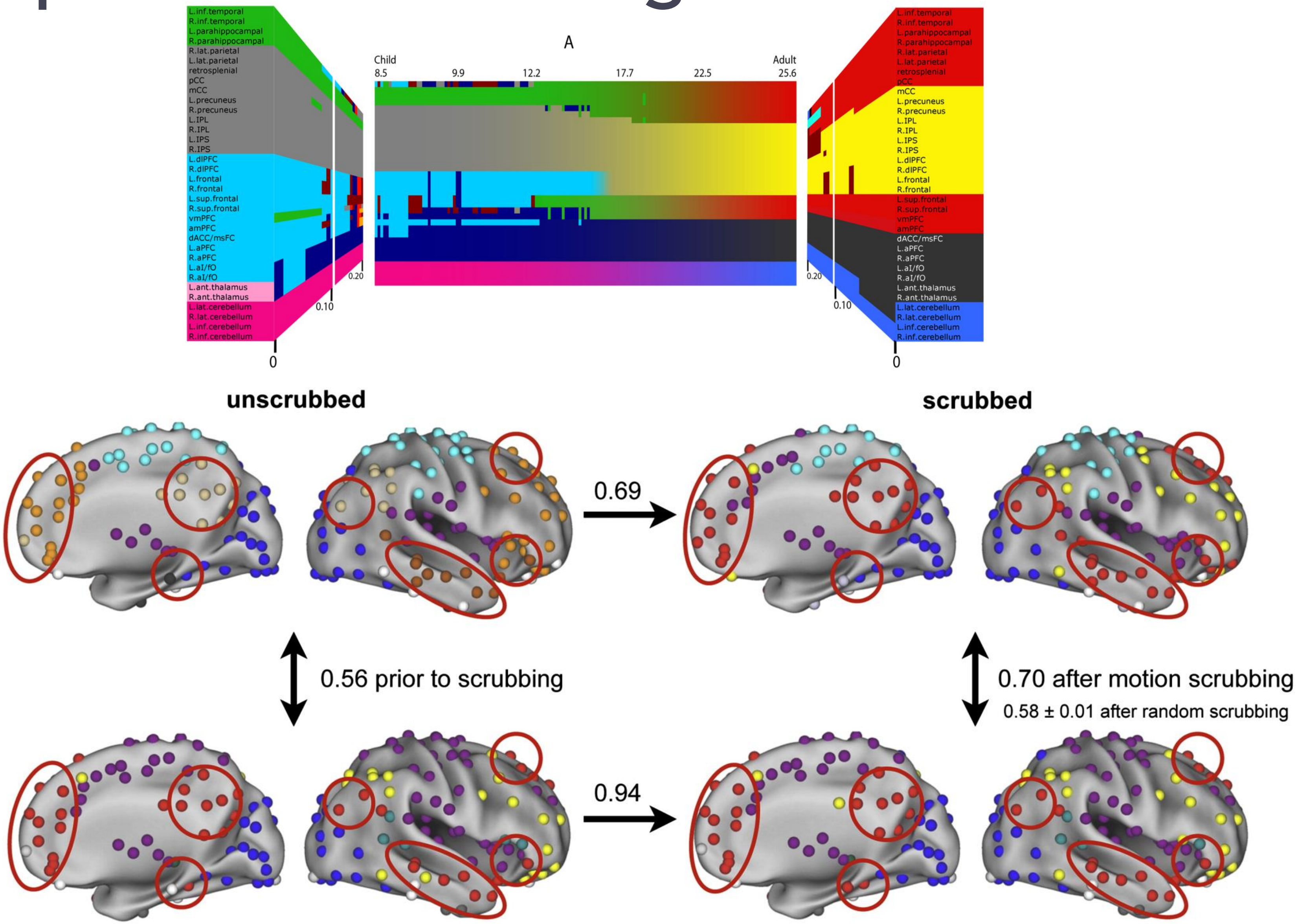
Spatial distribution of scrubbing on rsfc

Most **blue vectors** are short/medium range; most **red vectors** are medium/long range.



Power et al. (2012) *NeuroImage*

Impact of scrubbing on rs-fMRI data



Power et al. (2012) *NeuroImage*

So is scrubbing *the* thing?

- Exclusion of TRs might have unwanted effects:
  1. Loss of dfs (might/might not be a big deal at 1st lvl)

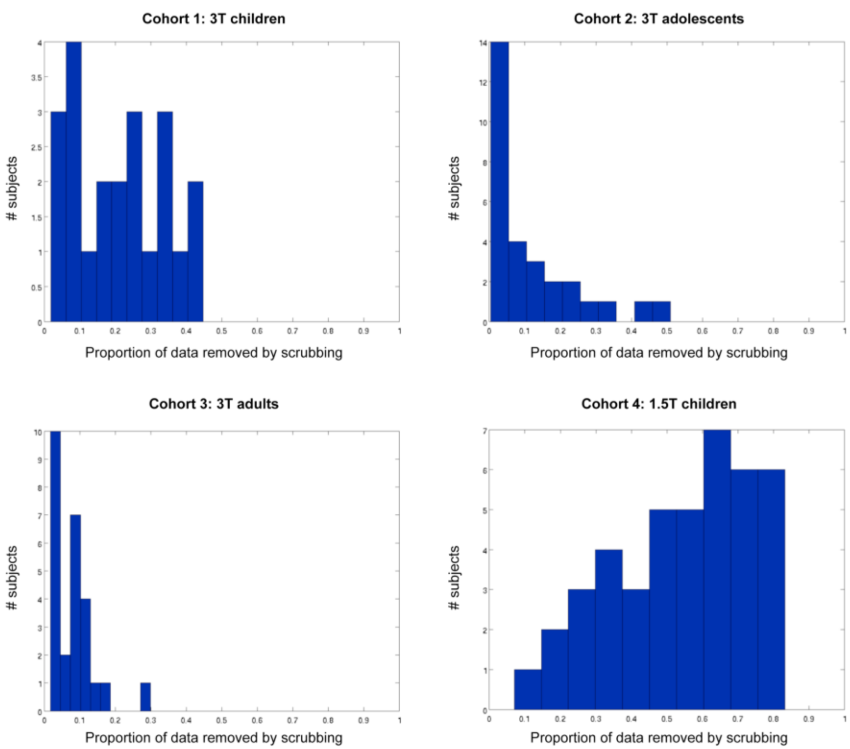
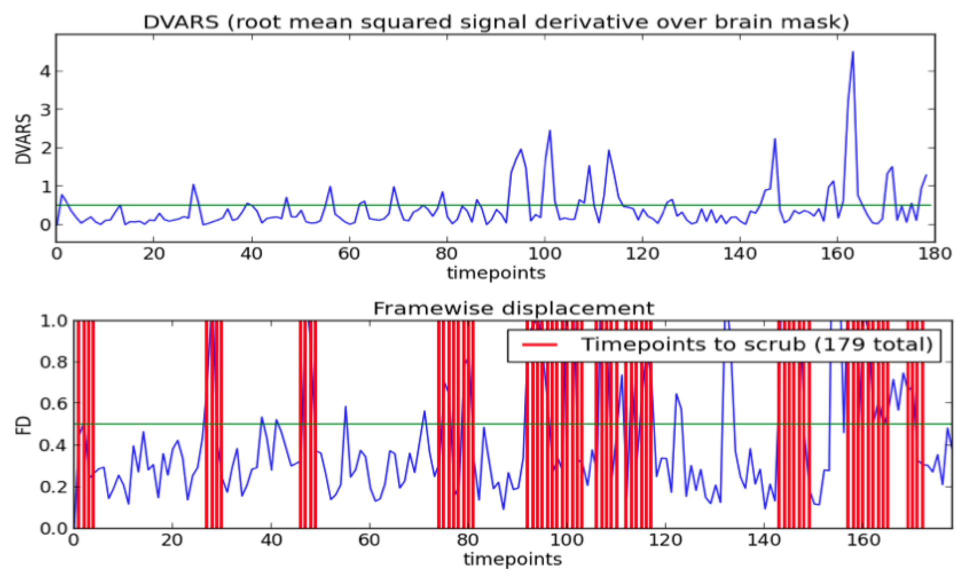


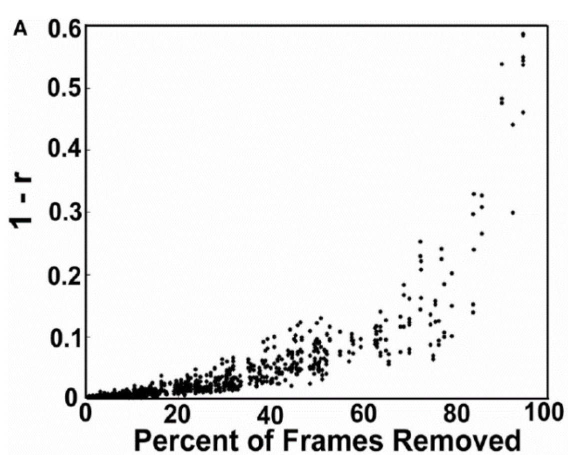
Figure S7: **The impact of scrubbing on data retention.** For each cohort analyzed in this report, the proportion of data removed within each subject is plotted as a histogram. More data was removed in younger subjects, who tended to move more than older subjects (see Table 1). All subjects had more than 125 frames (~5 min) of data remaining after scrubbing.

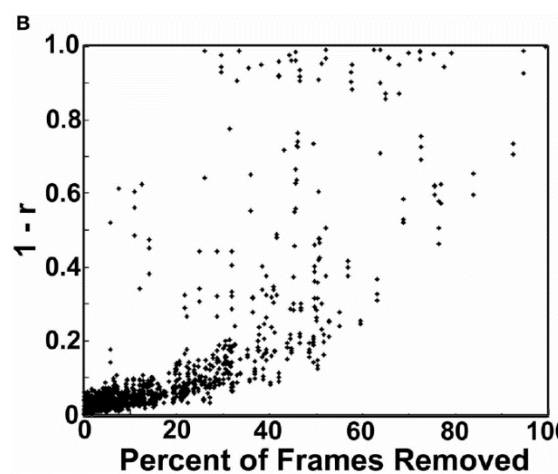


Power et al. (2012) *NeuroImage*

So is scrubbing *the* thing?

- Exclusion of TRs might have unwanted effects:
  1. Loss of dfs (might/might not be a big deal at 1st lvl)
  2. Uneven loss of dfs across groups/conditions
     - Randomly remove equal # of TRs from ‘good’ runs?
     - Turns out, that might be problematic too (A)
     - Using interpolations to “impute” excised data is also problematic (B)





Fair et al. (2012) *Frontiers*

So is scrubbing *the* thing?

- Exclusion of TRs might have unwanted effects:
  1. Loss of dfs (might/might not be a big deal at 1^{st} lvl)
  2. Uneven loss of dfs across groups/conditions
  3. Destroys autocorrelation structure (Lose the ability to perform any frequency-based analysis)

Parkes et al 2018 Neuroimage

So, which one should I use?

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An evaluation of the efficacy, reliability, and sensitivity of motion correction strategies for resting-state functional MRI

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A R T I C L E I N F O

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fMRI
Functional connectivity
Resting-state
Motion
Noise
Artefact

A B S T R A C T

Estimates of functional connectivity derived from resting-state functional magnetic resonance imaging (rs-fMRI) are sensitive to artefacts caused by in-scanner head motion. This susceptibility has motivated the development of numerous denoising methods designed to mitigate motion-related artefacts. Here, we compare popular retrospective rs-fMRI denoising methods, such as regression of head motion parameters and mean white matter (WM) and cerebrospinal fluid (CSF) (with and without expansion terms), aCompCor, volume censoring (e.g., scrubbing and spike regression), global signal regression and ICA-AROMA, combined into 19 different pipelines. These pipelines were evaluated across five different quality control benchmarks in four independent datasets associated with varying levels of motion. Pipelines were benchmarked by examining the residual relationship between in-

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So, which one shoul

Table 2
Characteristics of 19 denoising pipelines analysed here.

	Pipeline	Noise corrections methods	No. of regressors
	1	6HMP	6
MotReg	2	6HMP+2Phys	8
	3	6HMP+2Phys+GSR	9
Expand	4	24HMP	24
	5	24HMP+8Phys	32
MotReg	6	24HMP+8Phys+4GSR	36
	7	24HMP+aCompCor	34
	8	24HMP+aCompCor50	24+*k*
aCompCor	9	24HMP+aCompCor+4GSR	38
	10	24HMP+aCompCor50+4GSR	28+*k*
	11	12HMP+aCompCor (Muschelli et al., 2014)	22
	12	12HMP+aCompCor50 (Muschelli et al., 2014)	12+*k*
	13	ICA-AROMA+2Phys (Pruim et al., 2015b)	2+*k*
ICA-AROMA	14	ICA-AROMA+2P+GSR	3+*k*
	15	ICA-AROMA+8Phys	8+*k*
	16	ICA-AROMA+8P+4GSR	12+*k*
	17	24HMP+8Phys+4GSR+SpikeReg	36+*k*
Ceonsoring	18	24HMP+8Phys+4GSR+JP12Scrub	36+*k*
	19	24HMP+4Phys+2GSR+JP14Scrub	30+*k*

Notes. HMP, head motion parameters. Phys, average white matter (WM) and cerebrospinal fluid (CSF) signals. GSR, global signal regression. aCompCor, anatomical component correction using top the 5 components in each of WM and CSF compartments. aCompCor50, anatomical component correction using enough components to explain 50% of the variance in each of WM and CSF compartments. SpikeReg, spike regression. JP12Scrub, basic scrubbing. JP14Scrub, optimized scrubbing. *k* denotes an arbitrary number of additional regressors estimated automatically by the denoising method and which can vary from person to person.

Summary of quality control metrics.

Quality control benchmark	Summary	References
QC-FC correlations	The cross-subject correlation between framewise displacement (FD) and functional connectivity at each pair of regions after noise correction.	(Ciric et al., 2017; Power et al., 2015, 2012; Satterthwaite et al., 2013, 2012)
QC-FC distance-dependence	The dependence of QC-FC correlations on the distance between brain regions.	(Ciric et al., 2017; Power et al., 2012; Satterthwaite et al., 2012)
Motion-BOLD contrasts	Statistical parametric mapping of the association between FD and voxelwise BOLD time courses, to identify regions showing significant motion contamination.	(Yan et al., 2013a)
high-motion vs low-motion contrasts (HLM contrasts)	The mean difference in functional connectivity between healthy control participants split into high- and low-motion subgroups	(Pruim et al., 2015a; Satterthwaite et al., 2013; Van Dijk et al., 2012)
FD-DVARS correlations	The cross-subject correlation between motion and the temporal Derivative of root mean square VARiance over voxelS (DVARS), which indexes the rate of change of BOLD signal across the entire brain between consecutive time points.	(Muschelli et al., 2014)
tDOF-loss	The loss in temporal degrees of freedom (tDOF) sustained due to noise correction, calculated as the number of nuisance regressors input to the general linear model used to model noise in the BOLD data.	(Ciric et al., 2017; Yan et al., 2013a)
Test-retest reliability (TRT)	The test-retest reliability of functional connectivity, quantified using intra-class correlation coefficients in longitudinally acquired data.	(Birn et al., 2014; Van Dijk et al., 2012; Yan et al., 2013a)

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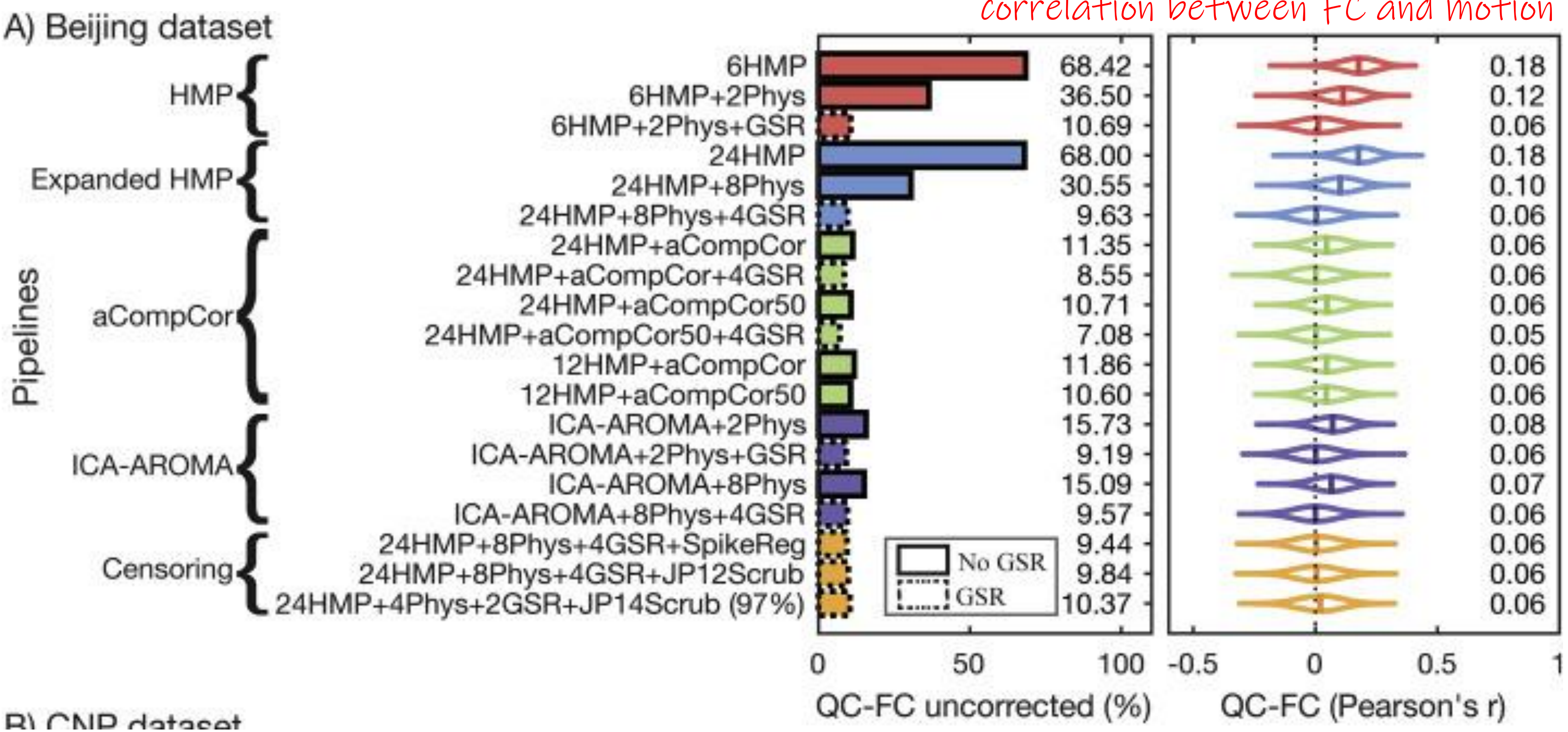
So, which one should I use?

% edges still correlated with motion & correlation between FC and motion



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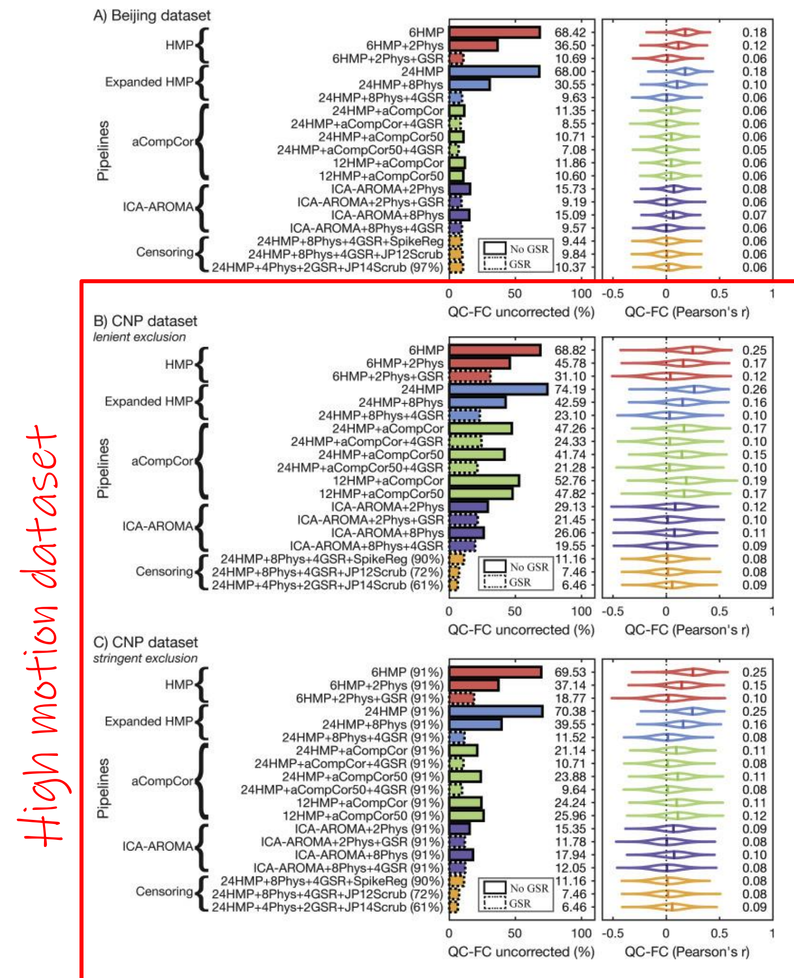
So, which one should I use?

- No pipeline reduces corrs to 0
- Head Motion Param approaches were the worst ones
- aCorrComp50 worked well with low motion, but not well with more motion
- Scrubbing worked typically the best
- ICA-AROMA second best



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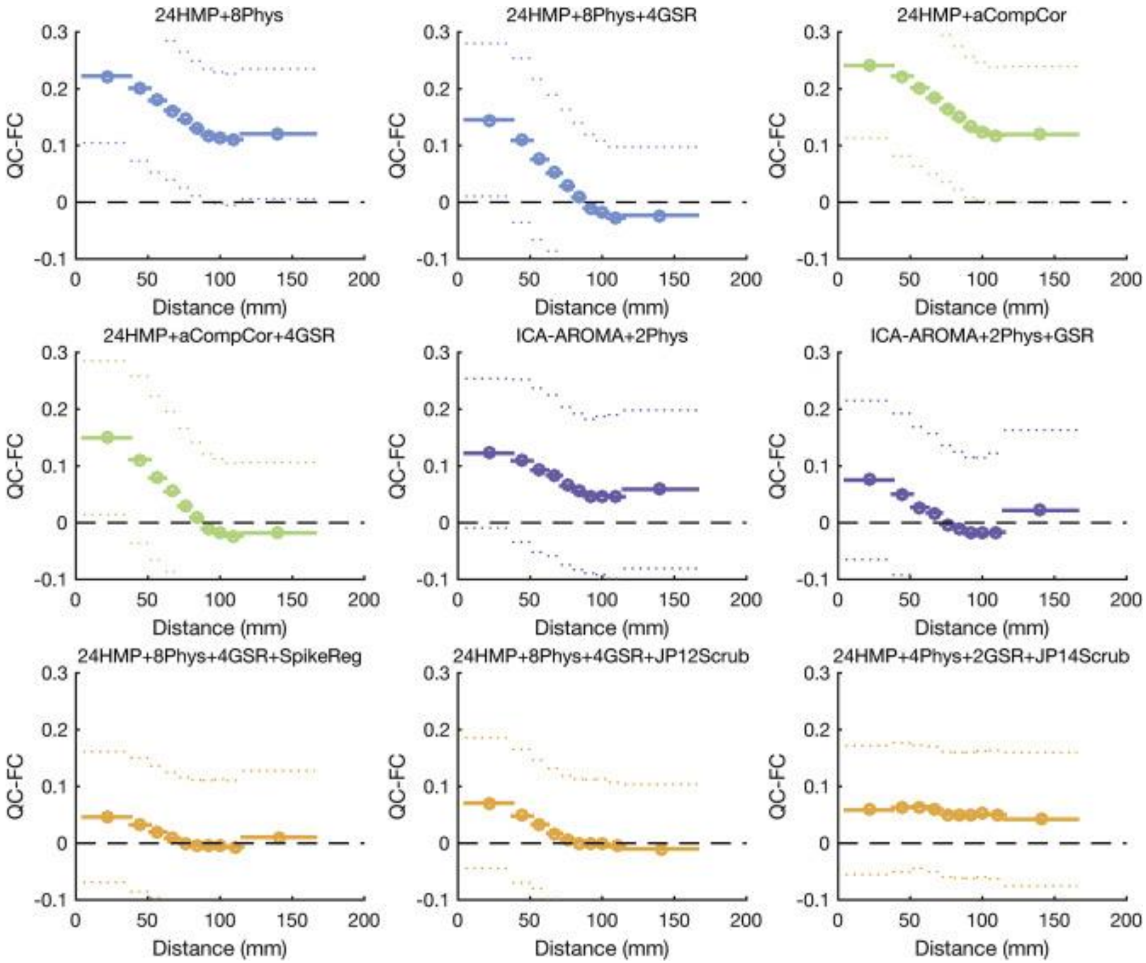
So, which one should I use?



Is the correlation between FC and motion spatial dependent?

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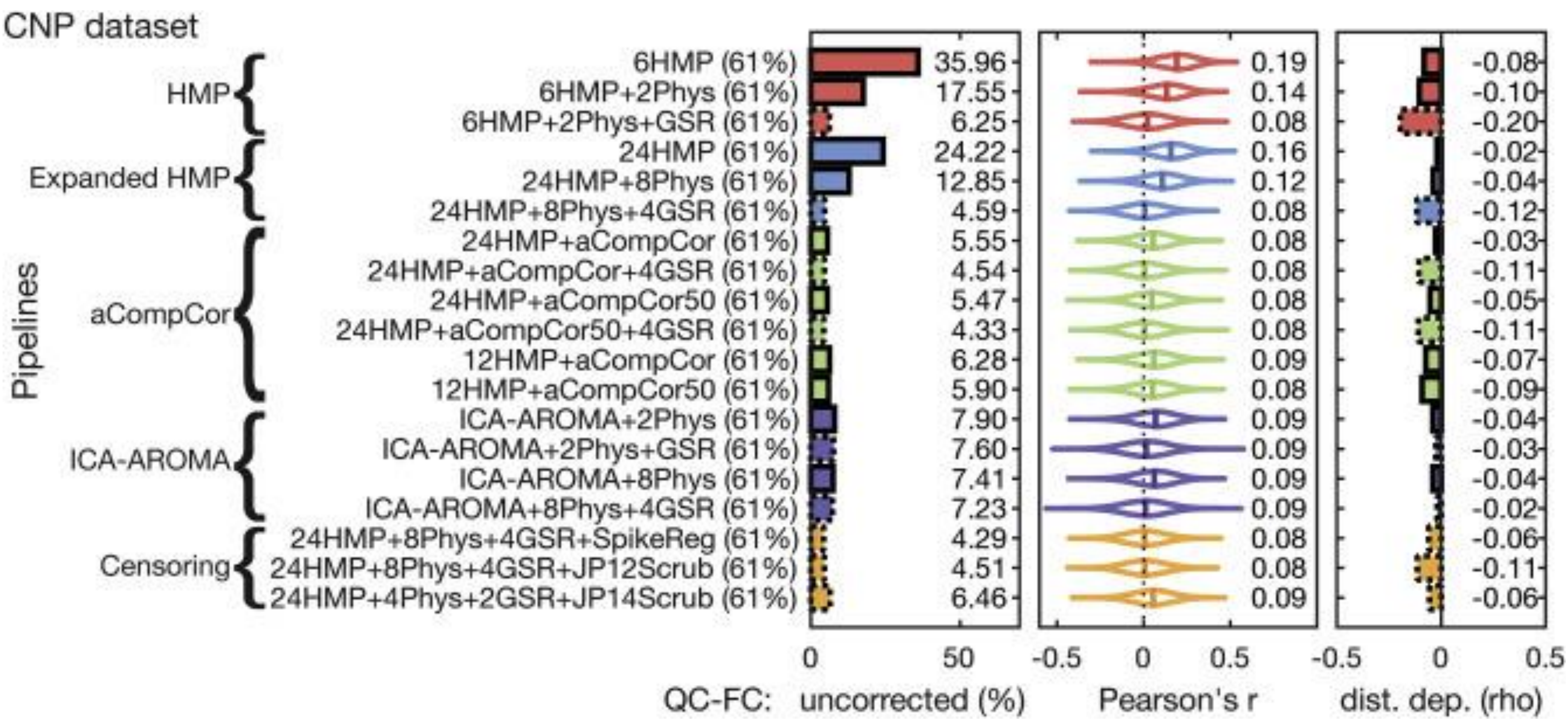
So, which one should I use?

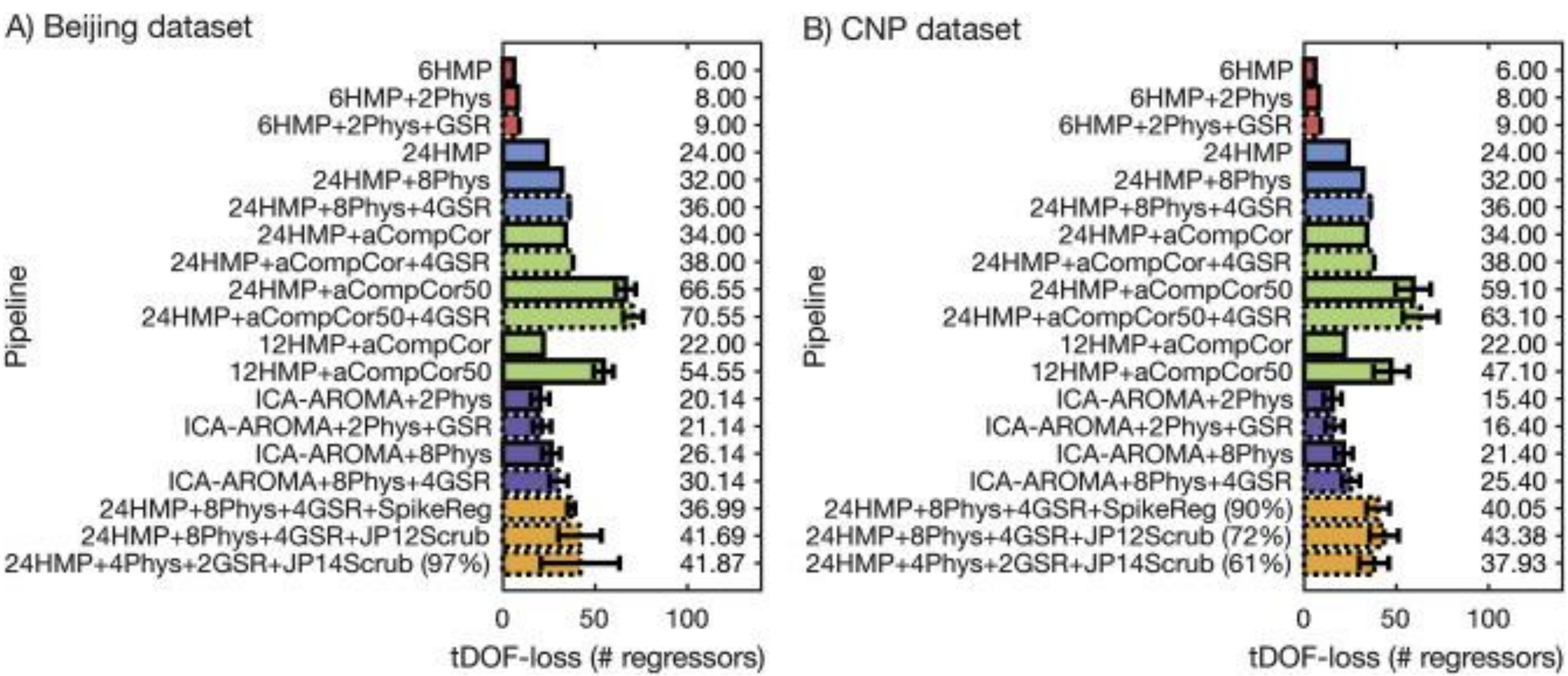
Stringent subject selection (subs with < 4 min of data after scrubbing) works best!!



Parkes et al 2018 Neuroimage

So, which one should I use?

Loss of degrees of freedom



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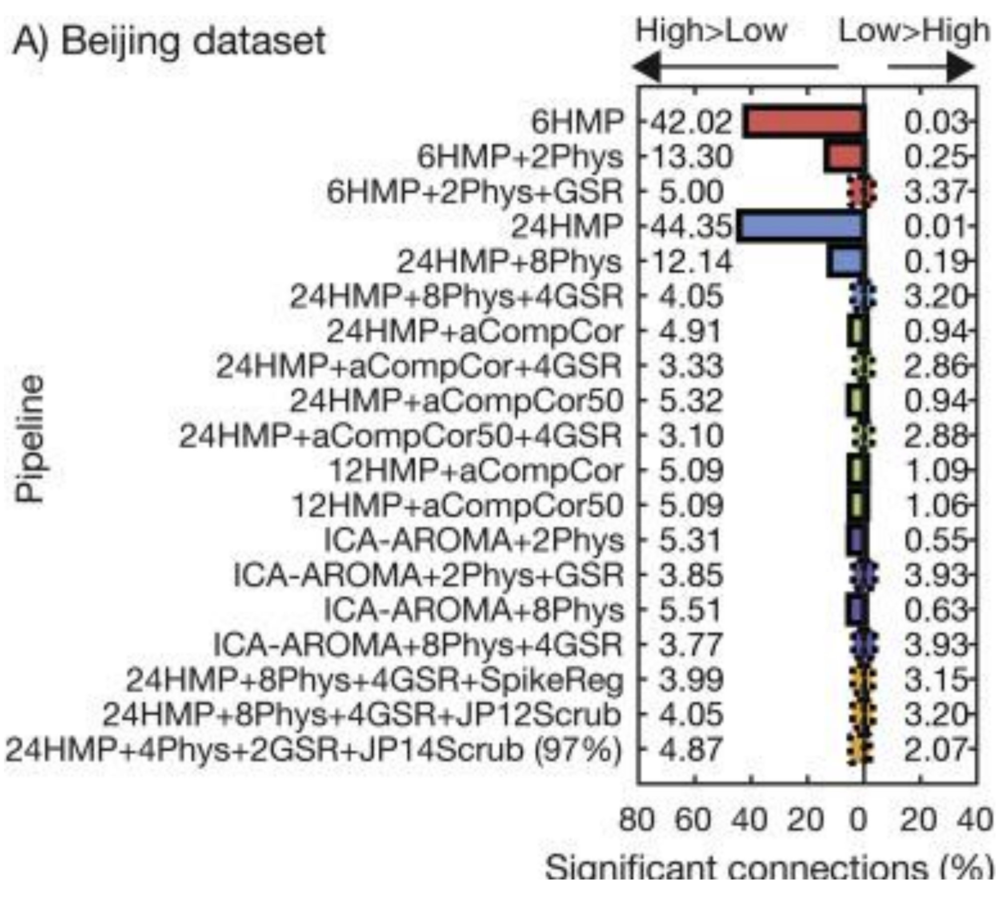
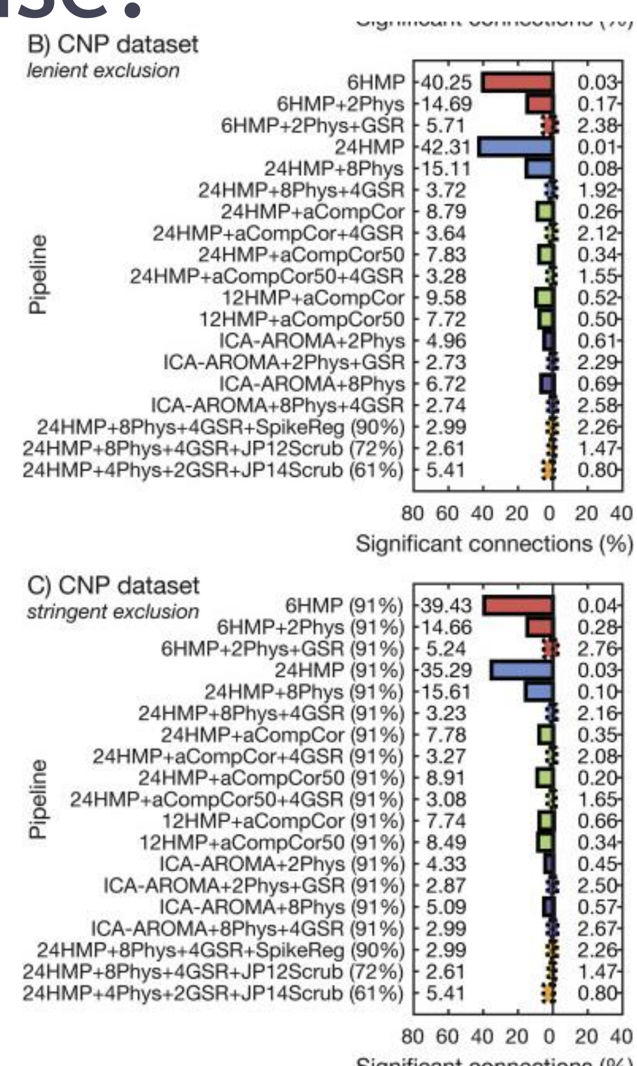
So, which one should I use?

% sign conn in High motion v Low Motion individuals





So, which one should I use?

- HMP + Phys models without GSR are ineffective at mitigating motion-related artefact regardless of the level of motion, exclusion criteria applied, or the use of expansion terms
- GSR dramatically improves the performance of the pipelines
- aCompCor pipelines may only be viable in low-motion datasets and perform poorly in high motion data
- ICA-AROMA & censoring pipelines are superior to other strategies, with the lowest QC-FC correlations, lowest QC-FC distance-dependence, & minimal differences between high- and low-motion healthy controls
- Censoring performs well because it excludes Ss with <4 min of uncensored data. When this criterion is applied to all pipelines, performance differences are marginal (except HMP pipel without GSR)
- aCompCor and censoring pipelines yield high tDOF-loss.
- Methods that were more effective at denoising were associated with reduced test-retest reliability, suggesting that noise signals in BOLD data are reproducible.

So, which one should I use?

- ***Head motion regression:*** this strategy is not effective even in low-motion datasets, unless GSR is also applied. "[A]*nalyses that rely on HMP models alone are likely to be heavily contaminated by motion.*"
- ***GSR:*** led to major improvements in QC-FC correlations for HMP & aCompCor, and (though little) for ICA-AROMA pipelines. However, controversial, leads to false anti-correlations. Need more work..
- ***aCompCor/aCompCor50:*** outperform HMP & Phys models (but best in low-motion data), not as effective in high-motion data, but as effective as ICA-ARMOA/Scrubbing if you drop high motion Ss. High loss of DOFs.
- ***ICA-AROMA:*** performed well across all datasets. Less in high-motion data but still more effective than HMP and aCompCor/aCompCor50. Robust/consistent results with slightly different pipelines.
- ***Censoring (i.e., scrubbing):*** the primary advantage of censoring is exclusion of Ss with high FDs. Applying same criterion increased dramatically all pipelines. However, distorts the temporal properties of the data, precluding analysis of time-resolved dynamics

Reading list (i)

- Description of the problem:
  - Power JD, Barnes KA, Snyder AZ, Schlaggar BL, Petersen SE. (2012) *Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion*. Neuroimage 59(3):2142-54
  - Van Dijk KR, Sabuncu MR, Buckner RL. (2012) *The influence of head motion on intrinsic functional connectivity MRI*. Neuroimage. 59(1):431-8.
  - Satterthwaite TD, Wolf DH, Loughead J, Ruparel K, Elliott MA, Hakonarson H, Gur RC, Gur RE. (2012) *Impact of in-scanner head motion on multiple measures of functional connectivity: relevance for studies of neurodevelopment in youth*. Neuroimage. 2012 Mar;60(1):623-32
  - Power, J. D., Mitra, A., Laumann, T. O., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2014). *Methods to detect, characterize, and remove motion artifact in resting state fMRI*. Neuroimage, 84, 320-341.

Reading list (ii)

- What can we do about it?
  - Satterthwaite TD, Elliott MA, Gerraty RT, Ruparel K, Loughead J, Calkins ME, Eickhoff SB, Hakonarson H, Gur RC, Gur RE, Wolf DH. (2013) *An improved framework for confound regression and filtering for control of motion artifact in the preprocessing of resting-state functional connectivity data*. Neuroimage. 64:240-56.
  - Hang Joon Jo, Stephen J. Gotts, Richard C. Reynolds, et al., (2013) *Effective Preprocessing Procedures Virtually Eliminate Distance-Dependent Motion Artifacts in Resting State FMRI*. Journal of Applied Mathematics, 2013.
  - Hallquist MN, Hwang K, Luna B (2013) *The nuisance of nuisance regression: Spectral misspecification in a common approach to resting-state fMRI preprocessing reintroduces noise and obscures functional connectivity.* Neuroimage. 82:208-25.
  - Yan CG, Cheung B, Kelly C, Colcombe S, Craddock RC, Di Martino A, Li Q, Zuo XN, Castellanos FX, Milham MP. (2013) *A comprehensive assessment of regional variation in the impact of head micromovements on functional connectomics*. Neuroimage. 76:183-201.
  - Parkes, L., Fulcher, B., Yücel, M., & Fornito, A. (2018). *An evaluation of the efficacy, reliability, and sensitivity of motion correction strategies for resting-state functional MRI.* NeuroImage, 171, 415-436.

Reading list (iii)

- For task based analyses
  - Christodoulou AG, Bauer TE, Kiehl KA, Feldstein Ewing SW, Bryan AD, Calhoun VD. (2013) *A quality control method for detecting and suppressing uncorrected residual motion in fMRI studies*. Magn Reson Imaging. 31(5):707-17.

  - You can find the list (with PubMed links) here: **http://montilab.psych.ucla.edu/fmri-wiki**