Resting State Preprocessing and Motion Artifacts

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BACKGROUND AND OBJECTIVES

• Resting state functional connectivity (RS-fc) relies on the correlation of residual time series to estimate the connection strength between brain regions and is thought to represent true functional relationships of brain organization.

• RS-fc preprocessing methods currently account for motion by rigid body realignment and linear regression of realignment parameters from RS data.

• Regression of these parameters may not remove all motion effects, due to "spin history" modulation. And despite these compensatory steps, subtle, motion-induced artifacts can systematically bias RS-fc in a way that covaries with the distance between regions [1-3].

• Although these motion effects have been reported in large, independent RS-fc data sets, all of these studies have used similar imaging sequences and preprocessing, both of which may affect the impact of motion on RS-fc [4-6].

•Our objective was to examine the impact of our processing stream on the relationship between motion and RS-fc using data acquired with an interleaved slice order and an ascending slice order.

PARTICIPANTS AND METHODS

Participants

• KKI cohort: 102 typically developing (TD) children, mean age 10.2 (±1.2) years.

• "Cohort 1" from Power et al. (2012): 22 TD children, mean age 8 (±1) years.

RS Acquisition

• KKI: Philips Achieva 3T scanner

•2D-SENSE EPI, 8-channel head coil, TR/TE = 2500/30 ms, flip angle = 70°
•47 contiguous **ascending** 3-mm slices
•5 min 20s – 6 min 30s

• "Cohort 1": Siemens MAGNETOM Tim Trio 3T scanner

•BOLD contrast sensitive EPI,12-channel head coil, TR/TE = 2500/27 ms (N=20), 2200/27 ms (N=2), flip angle = 90°
•32 contiguous **interleaved** 4-mm slices
•10 min 30s – 18 min over 2 (N=12), 3 (3), 4 (3) and 6 (4) runs in 1 (N=14) or 2 (N=8) sessions.

Data Preprocessing

• All data was preprocessed using SPM8 [7] and custom Matlab scripts. A schematic of all participant-level processing operations is presented in **Figure 1**.

• Nuisance regressors included the 6 motion parameter estimates and their derivatives (computed by backward differences), mean global signal, CSF and WM signals.

• WM and CSF masks were defined using a 99% probability threshold on the participant-specific segmented MPRAGE. aCompCor was used to estimate principal components that explained 96% of the WM/CSF signals separately [8].

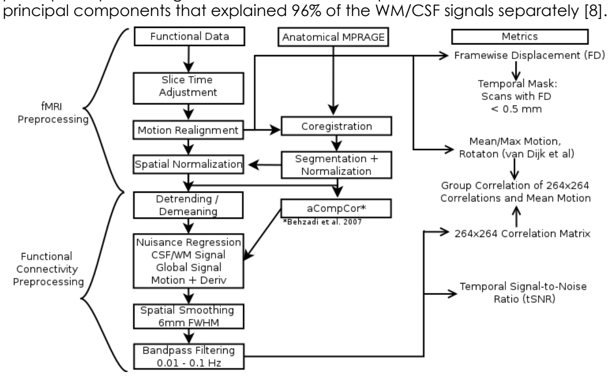

Figure 1. Processing Stream

Statistical Analysis

• A correlation matrix of 264 seeds [9] covering a majority of functional areas of the brain was calculated to represent a commonly used fc metric.

• Motion derivatives were used to calculate **framewise displacement** (FD), the sum of the absolute value of the 3 translational and 3 rotational (x head radius, 50 mm) derivatives [1], and **mean motion**, the root mean square (RMS) of the 3 translational derivatives [2]. See **Figure 2** for distributions of mean motion.

• Prior to fc preprocessing, a global measure of signal change, **DVARS** [1], the RMS of the RS-fMRI derivative, was calculated and compared to FD (**Figure 2**).

• To examine the association between motion and data quality, the correlation between temporal signal-to-noise ratio (tSNR) [2] and mean motion were calculated (**Figure 3**).

•Within each cohort, the correlation between mean motion and each seed-pair correlation was calculated [3] and analyzed as a function of distance between seeds (**Figure 4**).

• A **"scrubbed" correlation matrix** was generated, removing scans with **FD>0.5 mm** [1], as well as 1 preceding and 2 proceeding scans, to determine the effect of potentially motion-contaminated scans on these correlations with respect to the distance between seeds. The average group differences between the scrubbed matrix and the original correlation matrix are shown in **Figure 5**.

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RESULTS

• **Figure 2 (left)** illustrates the distribution of mean motion across cohorts. Although the mean of the distribution is higher for Cohort 1 (0.135 vs. 0.092, p=0.012), this may be due to some "high movers". The **right** panel displays the reduction in the correlation of FD and DVARS after processing and that the distribution of correlations are similar across cohorts, and around zero.

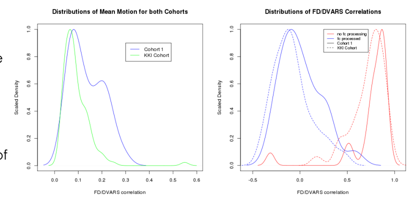

Figure 2: Motion distributions were higher for Cohort 1. A stronger relationship exists between motion and % MRI signal change before fc processing.

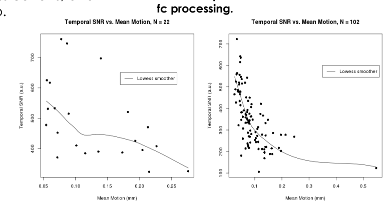

Figure 3. Increased mean motion corresponds to decreased temporal SNR for fc processed data. Data undergoing only fMRI preprocessing had a similar relationship.

• **Figure 3** demonstrates that motion is related to SNR even after standard fc processing (Cohort 1: Spearman's rho=-0.54, p=0.011, KKI: rho=-0.73, p < 0.001). This indicates that motion may still be a problem in fc analysis, but it is unclear how this would bias the results.

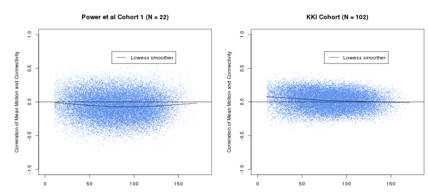

Figure 4. The effect of motion does not seem to be modulated by inter-node Euclidean distance.

• **Figure 4** shows that, for both cohorts, specific seed pair correlations have a high correlation with mean motion, but on average, these correlations are not systematically high or low with respect to inter-seed distance.

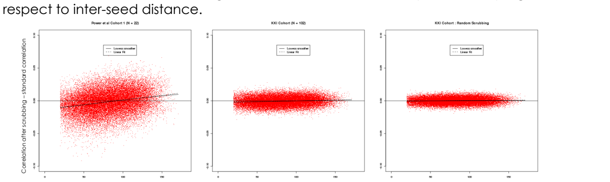

Figure 5: Scrubbing high-motion scans did not have a distance-dependent impact on inter-seed correlation.

• **Figure 5** illustrates a positive relationship between the effect of scrubbing and distance between seeds in fc processed data for Cohort 1, but not to the extent presented in [1]. The relationship does not suggest scrubbing would affect the relationship of the distance of the seeds and the correlation between seeds. The slope of the regression line for Cohort 1 (left) was 1.5e-4 (r^2 = 0.0645), and was 0.24e-4 (r^2=0.0115) for the KKI Cohort (right). Random scrubbing was done (right) to see the effect of scrubbing if random (non-motion related scans) were removed.

DISCUSSION

• Few studies have examined the optimal acquisition and fc processing stream to minimize the impact of motion on RS-fc measures.

• Although we observed a relationship between motion and frame-by-frame changes in the rs-fMRI signal prior to fc processing in both cohorts, we did not observe the same strong relationships between changes in inter-seed correlations and inter-seed distance as previously published [1, 3].

• Motion artifacts may still be present in our RS-fc data. Thus, when evaluating fc, it is important to use these motion metrics to examine the extent of motion in a sample and account for motion differences across samples when comparing RS-fc measures.

• Overall, the results are promising but inconclusive due to main limitations of lack of ground truth and the absence of accurate motion simulation models.

REFERENCES

1. Power, J.D. and Barnes, K.A. and Snyder, A.Z. and Schlaggar, B.L. and Petersen, S.E. Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. NeuroImage 2011; 59(3):2142-54.
2. Van Dijk, K.R.A. and Sabuncu, M.R. and Buckner, R.L. The influence of head motion on intrinsic functional connectivity MRI. NeuroImage 2012; 59(1):431-438.
3. Satterthwaite, T.D. and Wolf, D.H. and Loughead, J. and Ruparel, K. and Elliott, M.A. and Hakonarson, H. and Gur, R.C. and Gur, R.E. Impact of in-scanner head motion on multiple measures of functional connectivity: Relevance for studies of neurodevelopment in youth. NeuroImage 2012;60(1):623-632.
4. Landman, B.A. et al. Multi-parametric neuroimaging reproducibility: A 3-T resource study 2011; 54(4):2854-2866.
5. Weissenbacher, A. and Kasess, C. and Gerstl, F. and Lanzenberger, R. and Moser, E. and Windischberger, C. Correlations and anticorrelations in resting-state functional connectivity MRI: a quantitative comparison of preprocessing strategies. NeuroImage 2009;47(4):1408-1416
6. Carp, J. Optimizing the order of operations for movement scrubbing: Comment on Power et al. NeuroImage 2011.
7. Wellcome Center for Neuroimaging, London, UK.
8. Behzadi, Y, et al. A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. NeuroImage 2007;37(1):90-10.
9. Power, J.D. ,et al. Functional network organization of the human brain. Neuron 2011;72(4):665-78.

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