Reliability of Intrinsic Networks over 128 Weeks

Ann S Choe[1,2], Suresh E Joel[3,4], Craig K Jones[3,4], John Muschelli[5], Visar Belegu[1,2], John W McDonald[1,2], Brian S Caffo[5], Peter C.M. van Zijl[3,4], and James J Pekar[3,4]
[1]Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, United States, [2]International Center for Spinal Cord Injury, Hugo Moser Research Institute, Kennedy Krieger Institute, Baltimore, MD, United States, [3]Russell H. Morgan Department of Radiology and Radiological Science, Johns Hopkins University School of Medicine, Baltimore, MD, United States, [4]FM Kirby Research Center for Functional Brain Imaging, Kennedy Krieger Institute, Baltimore, MD, United States, [5]Department of Biostatistics, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, United States

Introduction: The ability of resting state fMRI (rs-fMRI) to probe multiple intrinsic functional networks of the brain without requiring subjects to perform explicit tasks has strong clinical appeal, as it allows use of an identical protocol for patients in various stages of diseases, regardless of their degree of cognitive or physical limitation. This is especially important for conditions that affect motor functions, such as spinal cord injury[1] and Parkinson's disease[2]. There is growing interest in using rs-fMRI derived parameters as functional correlates to monitor disease progression, and responses to therapeutic interventions. Several studies have investigated the reliability of rs-fMRI derived measures across participants and found them to be stable and reproducible[3-5]. In this study, we extend this approach through the use of a longitudinal dataset that covers the span of 128 a weeks with weekly repeat measure to investigate the intra-subject inter-session reproducibility of rs-fMRI derived parameters.

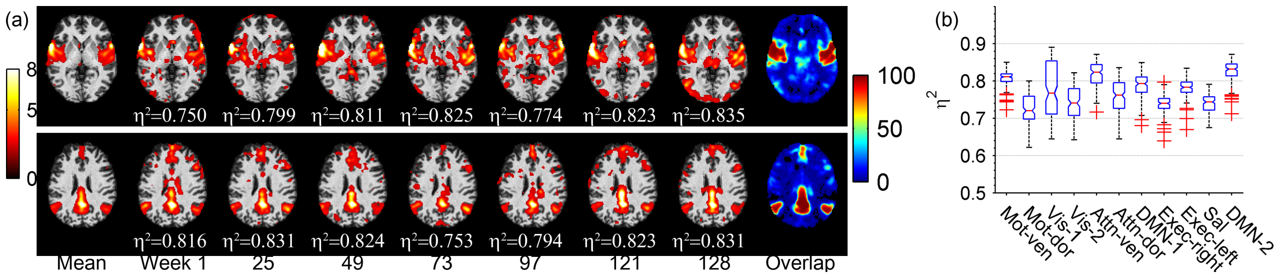

Figure 1. Network spatial stability over 128 weeks. (a) Group mean maps (left most column), single session maps (middle columns), and overlap maps (right most column) for the primary motor (top row), and default mode (bottom row) networks. Units are z-score for the spatial maps, and percentage for the overlap maps. (b) Spatial similarity of single session networks as measured by η^2. Boxplots show median (red bar), inter-quartile range (blue boxes; 25 and 75 percent), 1.5 times interquartile range (black lines), and outliers (red crosses)

Methods: A healthy participant underwent an MRI session at 3T (Philips Healthcare) weekly at a regular basis for 128 weeks, that included a 7 min rs-MRI scan (multi-slice SENSE-EPI, TR/TE=2000/30 ms, flip angle=75°, 37 axial slices, resolution = 3x3x3 mm^3, 1 mm gap). Preprocessing included: 1) slice time correction; 2) motion correction; 3) co-registration; 4) unified segmentation-normalization[6]; 5) high pass filtering with 0.005 Hz cutoff; 6) spatial smoothing using 6 mm full-width at half-maximum Gaussian kernel. Principal component analysis was performed, followed by group independent component analysis (GICA)[7] using GIFT (http://mialab.mrn.org/software/gift). A total of 30 independent components were initially estimated and 11 components were retained as functional networks; the remainder were rejected as non-neuronal (*e.g.*, head motion, cardiac pulsation). The spatial correspondence of the backreconstructed[7] single-session maps for each of the 11 networks and the corresponding group mean maps was computed using η^2, a measure of spatial similarity[8]. Each single session map was thresholded at Z=1, and the resulting binary maps were summed to create corresponding overlap maps, as shown in Figure 1(a). Between-network connectivity (BNC)[9, 10] between pairs of networks was computed for each session as the Pearson correlation coefficient of the network time courses and hierarchical clustering was applied to the resulting BNC matrices to group similar networks together, as shown in Figure 2(a) .

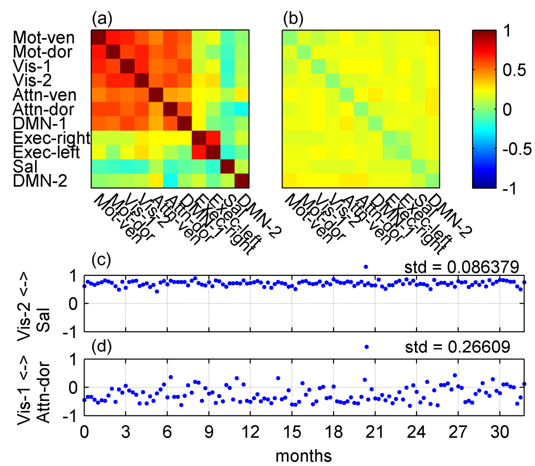

Figure 2. 128 weeks stability of single session BNC measurements. (a) Mean BNC matrix. (b) Standard deviation of the BNC values. (c, d) Time course of BNC across 128 weeks for the secondary visual-salience network and primary visual-attention dorsal network pairs, respectively.

Results: The spatial stability of the single session network maps was high, reflected by η^2 values ranging from 0.62 to 0.89, as shown in Figure 1. The degree of spatial correspondence was not the same for all networks (group ANOVA, p<0.001). The most stable networks were primary motor (median=0.811, std=0.0213) and default mode networks (median=0.832, std=0.0298), and the most variable network was the primary visual network (median=0.767, std=0.0739). The reproducibility of single session maps are illustrated for the primary motor and default mode networks in Figure 1(a). Stability of the single session BNC measurements was also high, reflected by the small standard deviation values of the BNC measurements (Figure 2(b)). The most stable network pair was the secondary visual and salience networks (std=0.0864) and the least stable network pair was the primary visual and dorsal attentional networks (std=0.266), as shown in Figure 2(c) and (d). BNC values between networks of similar functions (motor, visual attention, and executive control networks) were found to be high (r-values significantly higher than 0.5), as shown using hierarchical clustering in Figure 2(a).

Discussion: This high repeat measure study provides insight into the stability of rs-fMRI outcome measures over 128 weeks, a time frame relevant for disease progression and therapeutic intervention. Some networks are more stable than others. For example, since the primary motor and default networks are more stable, they may be better suited for the detection of changes due to diseases, while the more variable networks such as visual networks may be better suited for correlational studies exploiting network variability.

Conclusions: GICA derived rs-fMRI outcome measures for spatial network maps and between-network connectivity are stable over a period of approximately two and a half years. The most spatially stable network was the primary motor network and the most stable BNC was between the secondary visual and salience networks.

Acknowledgements: This work was supported in part by grants from the DOD (W81XWH-08-1-0192) and NIH (R21 EB006120-01A2 and P41-EB-015909).

References: [1] Choe AS. *Proc Intl Soc Mag Reson Med*.19:2875,2012. [2] Helmich RC, *Cereb Cortex*.20:1175,2010. [3] Wang JH, *PLoS One*.6:e21976,2011. [4] Chou YH, *AJNR Am J Neuroradiol*.33:833,2012. [5] Guo CC, *Neuroimage*.61:1471,2012. [6] Ashburner J, *Neuroimage*.26:839,2005. [7] Calhoun VD, *Hum Brain Mapp*.14:140,2001. [8] Cohen AL, *Neuroimage*.41:45,2008. [9] Jafri MJ, *Neuroimage*.39:1666. [10] Joel SE. *Proc Intl Soc Mag Reson Med*.18:3497, 2010.