TEST-RETEST RELIABILITY OF FUNCTIONAL MOTOR CONNECTIVITY

A. B. McMillan1, S. Roys1, N. Shah1, A. Roy2, J. D. Greenspan1, and R. P. Gullapalli3

1University of Maryland School of Medicine, Baltimore, MD, United States, 2University of Maryland Baltimore County, Baltimore, MD, United States, 3University of Maryland Dental School, Baltimore, MD, United States

Introduction: Functional connectivity MRI (fcMRI) is used to measure inter-regional similarities in the time-varying BOLD signal across the resting brain and can yield important information about the connectivity of functional anatomy, e.g., the motor system1,2. However, the reproducibility of these resting state networks both within and across sessions has yet to be clearly quantified, particularly with special consideration to physiological noise. In this study, we evaluate the consistency of resting state networks in five regions of the motor system: the primary motor cortices (LM1, RM1), the supplementary motor area (SMA), and the pre-motor areas (LPMA, RPMA), both within and across sessions for multiple participants using both voxel-wise and ROI-based approaches.

Methods: All imaging was performed on a Siemens 3T MRI scanner using an 8-channel receive-only head coil. Seven healthy participants (4 males, 3 females, mean age: 32±11 years) were imaged. T1-weighted images were acquired using a single-shot EPI sequence (TE = 30 ms, TR = 2000 ms, FOV = 220 mm, resolution = 64 x 64) with 24 axial slices (sl. thick. = 6 mm) over 6 min 42 s that yielded 171 time points. A high resolution T1-weighted MPAGE (TE = 3.44 ms, TR = 2250ms, TI = 900ms, flip angle = 9º, resolution = 256 x 256 x 96, FOV = 22 cm, sl. thick. = 1.5 mm) was also acquired for anatomic examination. Physiological data (cardiac and respiratory) was acquired during image acquisition using the output of an Invivo monitoring system (Invivo Corporation, Pleasanton, CA) which was digitized using a USB data acquisition module DT9801 (Data Translation, Marlboro, MA) connected to a Windows PC running customized software.

Each participant was imaged across three separate sessions. In each session, three resting state fcMRI acquisitions were acquired, with each being separated by two block-design fMRI acquisitions (motor and visual activation paradigms - 8 On-Off blocks of 20 seconds-On and 20 seconds-Off). During the motor activation experiment, the participant performed a self-paced finger-thumb apposition task.

Data were analyzed using AFNI (Robert Cox, NIH) and MATLAB (MathWorks Inc., Natick, MA). Each subject’s functional images were corrected for slice timing, optionally filtered to remove physiological artifacts1, and registered to the first functional scan from their first session. A 6mm FWHM Gaussian blur was applied to the registered functional scans. To chosen seed voxels for the fcMRI analysis, each subject’s functional motor scan from their first session was deconvolved with the motor task function. The motor activation t-statistic image was then thresholded so that the single most active cluster in the LM1 contained 50 voxels. The time series obtained from these seed voxels in the LM1 were averaged and used for deconvolution with the resting state data of the whole brain to obtain fcMRI images (R' images thresholded at 0.4). This process was repeated for the physiological filtered resting state data. Spherical ROIs were manually drawn in the LM1, RM1, RPMA, LPMA, and SMA and masked with the fMRI image generated from the concatenation of the resting data from the first session. These composite regions were used to extract average time series from each ROI within the resting-state scans for further statistical analysis.

The statistical methodology was based upon large sample theory of stationary signals. Given that the signal lengths are relatively large, we estimated the exact asymptotic variance matrix for the cross-correlations of the stationary signals. We used the asymptotic variance to normalize the cross-correlations to obtain approximately independent normal varimates. Within each subject the signals were taken to be potentially dependent, whereas across subjects they are independent. We looked at the pairwise connections and tested for differences against the null hypothesis of absence of connection, and scan effects. We performed a two-way MANOVA using PROC GLM in SAS (SAS Institute, Inc., Cary, NC) to identify session and scan effects. Due to the exact normalization of the signals the observations for individual connections become approximately independent allowing us to choose a threshold of 0.0051 after adjusting for multiple comparisons.

Table 1. p-value tables of two-way MANOVA for inter-regional connectivity. Upper-left: Session effect, Upper-right: Scan effect, Lower-left: Session*scan effect, Lower-right: Subject effect. High p-values (>0.005) indicate highly reliable functional connectivity.


Figure 1. % overlap of fcMRI acquisitions for a representative subject over 9 resting state scans during 3 separate sessions.