Less dynamic functional brain network in schizophrenia

Hu Cheng[1], Sharlene Newman[1], Joaquin Goni Cortes[1], Jerillyn S. kent[1], Josselyn Howell[1], Amanda Bolbecker[1], Aina Puce[1], Brian F. O'Donnell[1], and william P. Hetrick[1]
[1]*Indiana University, Bloomington, IN, United States*

INTRODUCTION

Functional network (FC) derived from resting state fMRI time series has become an attractive tool to explore the brain functions from a network perspective**.** The data are composed of correlations of time courses between different brain regions. Alterations in the functional network have been found in individuals with brain disorders or neurodegenerative diseases[1,2]. Recent studies found higher correlation between functional network and structural network in schizophrenia (SZ)[3], suggesting less dynamic brain function in those patients. Because head motion and other confounds can affect the FC and its variability[4], investigation of FC dynamics by directly comparing FC over time can be invalid. We propose a method to tackle this problem. By constructing two FCs from interleaved time points of the resting state time course, we can extract the variance of FC irrelevant to brain dynamics, and use it as a baseline in the evaluation of FC change. Using this approach, we found that the schizophrenia patients exhibited smaller variations of functional network compared to normal controls (NC).

METHODS

MRI data acquisition: 19 SZs (12 male, mean age 33.1 ± 10.9 years) and 29 NCs (13 male, mean age 27.8±8.5 years) were recruited. SZ diagnosis was determined using the Structured Clinical Interview for the DSM-IV (SCID-IV) and medical chart review. Subjects were scanned on a Siemens TIM Trio 3 T scanner using a 32-channel headcoil. The high resolution (1 mm3) anatomical scan was performed with an MP-RAGE sequence. This was followed by the eye-closed resting state fMRI scan performed with EPI sequences (TR/TE = 2500/30 ms, FOV = 220 mm, 128×128 matrix, iPAT2, 200 volumes).

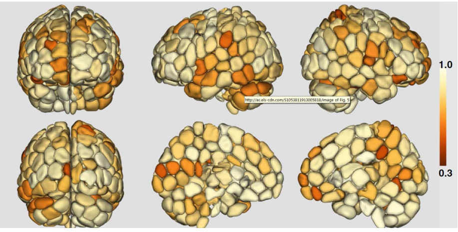


Fig. 1. Parcellation schem with 278 regions. The cross-subject reproducibility is indicated by the shading of each subunit in the parcellation.

Head motion characterization: All functional data were motion corrected in FSL (http://fsl.fmrib.ox.ac.uk/). We computed the translation motion and rotational motion from the output of motion correction[4]. The mean translation or mean rotation is computed as described in Eq. 1, where N is the number of volumes and a, b, c are the three degree of freedom for translational motion or rotational motion.

Functional network: Aided by the anatomical image, the functional images were parcellated using a new parcellation scheme[5] based on functional homogeneity of resting state functional data of 79 healthy subjects. After regressing out head motion, white matter and the CSF time signal, and band-pass filtering between 0.01-0.10 Hz, time courses were extracted from 278 brain ROIs and averaged. The functional network was obtained from a weighted correlation matrix for the 278 ROIs. For each constructed network, first we computed the mean of the weight of positive edges, and used this as a threshold to remove all edges with weights smaller than the mean. This step can effectively minimize the contribution of variance of the overall correlation strengths of the subjects due to motion or other data acquisition factors.

$$Trans(Rot) = \frac{1}{N-1}\sum_{i=1}^{N-1}\sqrt{(a_{i+1}-a_i)^2+(b_{i+1}-b_i)^2+(c_{i+1}-c_i)^2} \qquad (1)$$

$$VON = \frac{std(net1-net2)}{\sqrt{2}} \qquad (2)$$

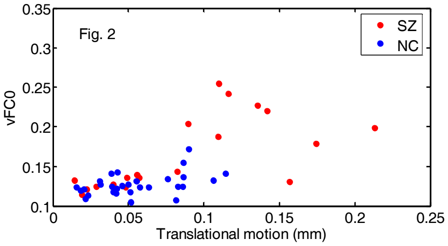
$$vFC_C = \sqrt{vFC^2 - \alpha \cdot vFC_0{}^2} \qquad (3)$$

Equations

Variance of FC: The variance of network (VON) is characterized by the standard deviation of the difference between two networks according to Eq. 2. First we constructed two FCs, one from the odd number of time points, and the other from the even number of time points. VON was computed; we called it variance of FC induced by motion or noise (vFC_0). To characterize the dynamics, we divided the time course into four segments (2 minutes each) and computed a FC from each segment. VON between the four FC was computed (vFC). The corrected variance of FC (vFC_c) was derived from previously computed vFC and vFC_0 according to Eq. 3, where α is a constant to correct for different number of time points between vFC and vFC_0 ($\alpha = 2$ in our case). Two sample t-tests were performed to compare vFC_c between two groups.

RESULTS

Figure 2 displays the scatter plot of translational motion and vFC0, showing a strong correlation between vFC0 and motion. The correlation coefficient is 0.46 for normal controls and 0.65 for SZ. The mean value of motion is 0.055 mm for NC and 0.088 mm for SZ subjects. As a result, the vFC_0 is higher for SZ (mean value 0.165 vs. 0.127). The correlation between vFC and motion was negligible for NC (0.01 in average) but still high for SZ (0.37 in average). Therefore, it is important to take this difference into account when comparing the dynamics of functional network. The mean variances of network between FCs at different time periods (1, 2, 3, and 4) are shown in table 1. For both NC and SZ, the variance tends to increase with the time lag of the FC pair. NC has relatively larger variance than SZ, with most P values of the two-sample t-test smaller than 0.5.



DISCUSSION

Our results show that the functional network is very dynamic. Within a short period of time of two minutes, the variance is comparable to the baseline variability. Based on our simple model, the schizophrenia subjects show less dynamic functional network compared to normal controls. However, the validity of our model at higher motion needs further investigation.

Table 1. Mean variance between pairs of FC for SZ and NC subjects, and corresponding P values for two-sample t-test of VON between the two groups.

	(1,2)	**(1,3)**	**(1,4)**	**(2,3)**	**(2,4)**	**(3,4)**
Mean vFC_c (SZ)	0.232	0.246	0.252	0.224	0.242	0.221
Mean vFC_c (NC)	0.259	0.278	0.287	0.259	0.273	0.263
P value	0.144	0.025	0.013	0.036	0.045	0.001

REFERENCES

1. Lynall M. et al., J. Neurosci. 2010; 10:829–843. 2. Pievani M. et al., Lancet Neurol. 2011; 30:9477–9487. 3. Van den Heuvel, M.P. et al., JAMA Psychiatry. 2013; 70:783-792. 4. Van Dijk K.R., et al., Neuroimage. 2012; 59:431-438. 5. Shen X., et al., Neuroimage. 2013; 82:403-415.