Framework for Studying Changes in the Functional Connectivity Network After Stroke Using Resting state fMRI

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Introduction

Resting State connectivity using functional Magnetic Resonance Imaging (fMRI) has recently been used for evaluating the post stroke neuro-restoration and functional reorganization [1]. In resting state fMRI analysis, slow spontaneous fluctuations in the BOLD (Blood Oxygenation Level Dependent) signals are studied and the temporal correlation between different areas of the brain are calculated for determining the connectivity between these areas. Usually, these areas are identified using event-related fMRI scans [2] or by known anatomical landmarks [3]. In this study, we have defined a connectivity network in the brain in which every brain region is considered as a node and correlation is calculated between every two nodes in this network. The correlation between the temporal signals at every node in this network is calculated for normal subjects and is used as a reference for evaluation of the functional reorganization of the brain in stroke patients.

Materials and Methods

Functional MRI images were acquired on a GE 3.0-T whole-body magnet using a gradient echo EPI sequence for whole-brain BOLD fMRI with an FOV of 22X22cm on a 64x64 matrix (3.4375 mm×3.4375 mm in-plane resolution), 34 slices/3.5mm slice thickness with BW/px=7.8125 kHz/px, TR/TE=2000 ms/30 ms. For the resting state image set, 150 volumes (five minutes) were recorded while the subjects were lying quietly with eyes open inside the scanner and using ear plugs for minimizing the noise from the scanner. Keeping the eyes open eliminates the coherent activity in the occipital cortex. High resolution (IRSPGR) mages were also acquired to be used for segmentation. Respiration and cardiac data of the patient were recorded during the scan using a pneumatic belt and pulse-oximeter, respectively. This data was used in artifact removal prior to data analysis. Statistical parametric mapping (SPM2) (www.fil.ion.ucl.ac.uk/spm) was used for pre-processing the data, time-slicing correction, and realignment for correcting the motion artifact and spatial smoothing. The brain was segmented into 104 regions using the high resolution 3D IRSPGR image and the HAMMER software (University of Pennsylvania, Section of Biomedical Image Analysis, SIBA) and the temporal fMRI signals from all voxels in each segmented region were averaged to represent one signal for each region (Figure 1) and the physiological noise was removed using a linear regression model. These signals were low-pass filtered so that only signal components with frequencies less than 0.08Hz remain for further analysis. Then, cross correlation was calculated between these low frequency signals from each of these regions.

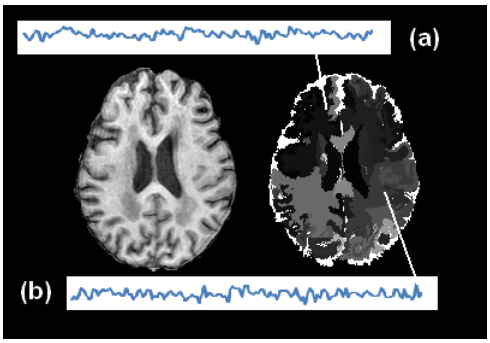

Figure 1. A slice of the IRSPGR (left) image and the segments (right). The resting state temporal fMRI signals corresponding to all the voxels from each segment (typically a and b) are averaged and processed for connectivity analysis

Eleven subjects with no prior history of neurologic or psychiatric disorders were scanned as normal controls with the procedure explained above for measurement and creating reference weights of the connectivity network. The same procedure was repeated for five stroke patients, three at the acute stage and two at 3 and 5 months after the stroke onset.

Results

Five segments of the brain including the ventricles were excluded from the analysis since they were not relevant to the study. The resulting 99X99 correlation coefficient matrix showing the cross-correlation between the temporal signals from every two regions was calculated for the normal cases and the mean and standard deviation of every coefficient was calculated between all the subjects. A similar matrix was created for each stroke patient. In order to detect the abnormal connections between the regions for these patients, the correlation coefficients that fell outside the range of mean±2std. were highlighted for further discussion. These include both higher and lower cross-correlation values. As an example, Table1 illustrates part of the matrix that shows the mean and standard deviation of cross correlation values for the normal subjects. Table 2 represents the same values for one of the stroke patients. The bold items in the table indicate values that fall outside the defined normal range.

Table 1. Mean and standard deviation of the cross correlation values from 11 normal subjects for 4 typical regions as follows: Superior Parietal Lobule, Superior Temporal gyrus, Supramarginal Gyrus and Temporal lobe white matter named Reg.1-4 respectively.

	Reg.1	Reg.2	Reg.3	Reg.4
Reg.1	1	0.81+/-0.14	0.86+/-0.12	0.86+/-0.08
Reg.2	0.81+/-0.14	1	0.86+/-0.09	0.91+/-0.09
Reg.3	0.86+/-0.12	0.81+/-0.09	1	0.82+/-0.09
Reg.4	0.86+/-0.08	0.91+/-0.09	0.82+/-0.09	1

Table 2. Cross correlation values in a stroke subject for the four regions mentioned in Table 1. The bold items show values outside the normal range

	Reg.1	Reg.2	Reg.3	Reg.4
Reg.1	1	**0.51**	0.61	0.79
Reg.2	**0.51**	1	**0.46**	**0.71**
Reg.3	0.61	**0.46**	1	0.89
Reg.4	0.79	**0.71**	0.89	1

Conclusions

The results show the feasibility of using the proposed method for studying changes in the functional connectivity network of the brain after stroke. The advantage of using the current framework is that no region will be left out for studying the brain function and no prior knowledge is needed for marking the brain regions. One of the features that can be studied using this framework is the long term effects of stroke on functional reorganization of the brain and studying neural compensation and recruitment after stroke. Longitudinal studies will be performed on patients and using this framework, neuro-restoration and changes in the functional network will be studied. Using a larger population of normal cases will help build a more reliable normal database. Consistency of the studies and image acquisition should be taken into consideration.

References

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