Motor Functional Plasticity in Patients with Brain Tumor: The fMRI study

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Introduction: Brain plasticity may take place during oncogenesis, infections or following injuries. Resting-state functional connectivity MRI (fc-MRI) is an effective method to study impaired brain plasticity. This method has been widely used to investigate the brain network correlated fluctuations over the past few years [1-3]. Functional connectivity of motor regions in the resting brain has been reported in both healthy controls and patients with brain tumor [4, 5]. Presence of tumor in the primary motor cortex or adjacent to this area may disrupt the functional connectivity of the brain even in asymptomatic patients. The underlying reason may be oncogenesis; however the exact reason is still unclear. The aim of this study is to better understand the mechanism of motor functional plasticity and disrupted functional connectivity induced by brain tumors, and provide the possible guidance for surgical resection. To observe the changes in motor functional plasticity of patients with brain tumor, we compared the functional connectivity between bilateral primary motor cortex (PMC) and supplementary motor area (SMA) of healthy controls and patients with brain tumor. Furthermore, we studied the effect of two different types of tumor on the connection pattern between PMC and SMA.

Figure 1: Schematic of the SMA and PMC connectivity maps in (a) healthy controls and (c) patients with brain tumors; correlation analysis of the LPMC-SMA and RPMC-SMA in (b) controls and (d) patients.

LPMC= left primary motor cortex; RPMC= right primary motor cortex; SMA= supplementary motor area

Materials and Methods: Fifteen patients with brain tumor, (right-handed, 5 male and 10 female, age ranged from 27~65 years, mean age 45± 0.9 years), lesion located in or close to the motor cortex and 11 healthy volunteers (right-handed, 5 male and 10 female, age ranged from 27~58 years, mean age: 42±0.9 years) were enrolled in this study. The following tumor types were included: astrocytoma=7 and meningioma=8. We employed 3.0-T GE scanner equipped with an eight-channel head coil. Both structural images (3D FSPGR 1x1x1 mm3, 140 slices) and BOLD EPI data (TR/TE = 2500/40 ms, flip angle=90°, 3.75x3.75x3mm^3) were acquired. In our experiment, each subject did a resting-state block (150 volume, 6.15 minutes, eyes closed) initially followed with fist-movement task that consisted of five 30s blocks of movement task and six 30s fixations, the total time was 5.5 minutes.

Motor task fMRI data was analyzed with FSL software. The first 4 scans were discarded then motion correction was processed using FLIRT. Spatial smoothing was performed at 6-mm FWHM. The functional images were normalized to the MNI152 standard brain space. General linear model (GLM) analysis was carried out using FSL FEAT. Higher-level analysis was carried out using FLAME. Z statistic images were thresholded using clusters determined by Z >2.3, a corrected cluster significance threshold of p<0.05. For the resting state fMRI, analysis was performed in AFNI and FSL software. Pre-processing consisted of motion correction, temporal band-pass filtering (0.008Hz<f<0.08Hz), spatial normalization to standard brain space and spatial smoothing (Gaussian, FWHM 6mm). Several sources of nuisance covariates (six head motion parameters, signal from the white matter and the CSF) were eliminated using linear regression. The key motor regions included LPMC, RPMC and SMA based on motor task functional mapping. The 3 key motor regions were defined as a spherical region with a radius of 10mm. Then ROIs' mean time series were estimated by averaging the time series of all voxels in these regions. The pearson's correlation coefficients were computed between each pair of brain regions for each subject. For further statistic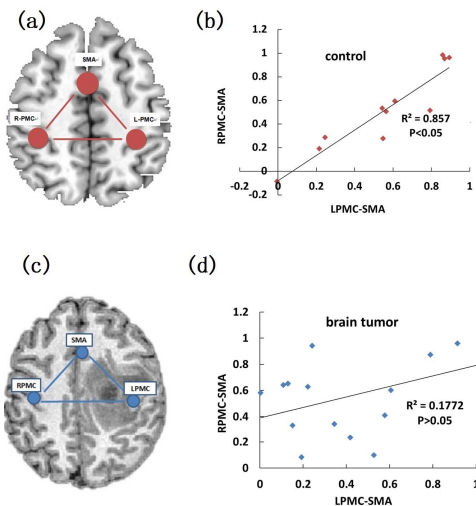al analysis, a Fisher's r-to-z transformation was applied to improve the normality of the correlation coefficients. We further performed the two-sample t tests on pairwise correlation of inter-region motor regions between tumor patients and normal subjects to evaluate the alteration of functional connectivity within key motor regions. In addition, we calculated the correlation between inter-region functional connectivity.

Results: A significant linear correlation between LPMC-SMA and RPMC-SMA was presented in the normal control group (Fig. 1b). However, no significant correlation was observed between LPMC-SMA and PRMC-SMA in the patient group (Fig. 1d). Our preliminary result showed significant statistical difference in the functional connectivity of LPMC-RPMC between the healthy controls and patients with brain tumor (P<0.05) (Fig. 2). In addition, the LPMC-RPMC functional connectivity revealed no statistical difference between patients with meningioma and astrocytoma.

Discussion: In this study, both healthy controls and patients with brain tumor performed resting-state and task-based fMRI scans. Three seed areas were selected based on the activation volumes of LPMC, RPMC and SMA which were identified by the bilateral fist-movement (closing and opening) task response. We used this method to avoid possible shift of functional areas caused by the tumor. The results from two different types of brain tumor patients demonstrated that tumor type (i.e. histological type) had no direct correlation with the functional connectivity between PMC and SMA which was consistent with previous findings [6]. By comparing the connectivity strengthens of RPMC-SMA and LMPC-SMA between the healthy controls and patients with brain tumor, a linear correlation was only found in the control group. Our results showed that the functional connectivity between bilateral PMC and SMA in the tumor patients was significantly different from that in the normal controls. This might be due to the processing of tumor growth and functional plasticity of the brain. However, this study has the limitation of small dataset and the time of tumor incidence was not taken into account. The future work will be a longitudinal study of preoperative and postoperative evaluation of patients with brain tumor, and observe the remodeling and postoperative functional network recovery. We suggest that the functional imaging can be a possible approach to understanding the brain reorganization and functional plasticity in patients with brain tumor and guides the operation.

Figure2: Box plots of interhemispheric connectivity between LPMC and RPMC in control group, patients with meningioma and astrocytoma.

References: [1] Biswal B., et al. MRM, 1995, 34:537-541. [2] Cordes D., et al. AJNR, 2000, 21:1636-1644. [3] Duffau H., Lancet Neurol, 2005, 4: 476-486. [4] Hampson, M., Hum Brain Mapp, 2002, 15: 247-262. [5] Marc L.O, et al. Brain 201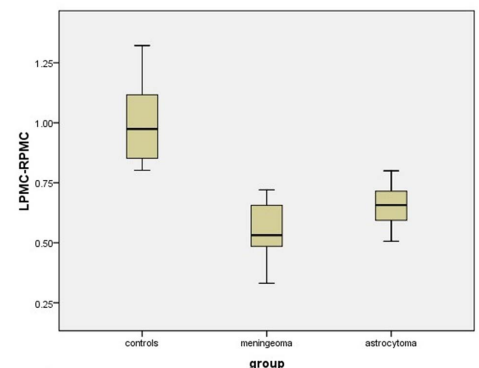2, 135:1017-1026. [6] Hou L.B, et al. ISMRM, 2009, 17:3356.