Lateralization of Temporal Lobe Epilepsy using Resting State Functional Magnetic Resonance Imaging

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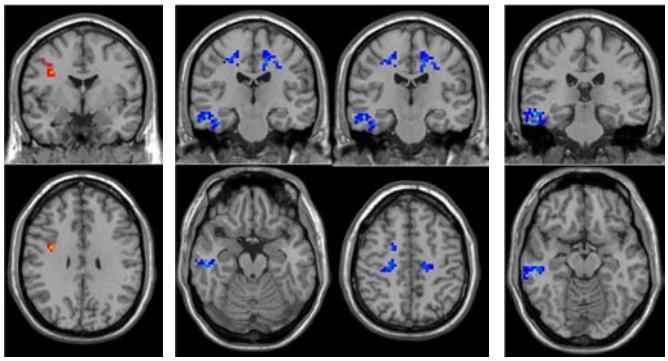
Introduction: Successful surgical intervention in temporal lobe epilepsy (TLE) relies on accurate lateralization of the seizure focus [1]. Resting state functional MRI (rfMRI), has been suggested as a viable method to detect the epileptogenic zone [2]. For example, asymmetrical hippocampal connectivity has been reported in mesial temporal lobe epilepsy [3]. Morgan *et al*. further identified that a resting-state functional network encompassing the right hippocampus and a small part of the right thalamus can be used to categorize patients into left or right TLE [1]. Besides FC among spatially segregated brain regions, regional homogeneity (ReHo) has also been used to localize TLE [4]. Unlike measuring the signal synchrony of low frequency fluctuation activities in different parts of the brain, ReHo is defined as the dependence of the resting state time course of a given voxel with those of its immediate neighbours [5]. Here we build on previous research to investigate a comprehensive set of measures of functional connectivity that may improve the localization of the seizure focus in TLE. These measures include amplitude of low frequency fluctuation (ALFF), fractional ALFF (fALFF), and voxel-mirrored homotopic connectivity (VMHC). ALFF measures the regional spontaneous activities and it was found being significantly larger than the global mean ALFF in vicinity of large blood vessels [6]. To overcome the issue of ALFF being sensitive to physiological noise, fALFF was proposed as the ratio between the total amplitude with low-frequency range (typically 0.01-0.08 Hz) to the total amplitude of the entire detectable frequency range [7]. VMHC is a voxelwise measure of function homotopy, *i.e.*, the synchrony of resting state FC between each voxel in one hemisphere and its mirrored counterpart in the other [8].



(a) FC (LH) (b) ReHo (c) ALFF

Fig. 1. Brain regions with significant differences (radiological view).

Table I. Details of brain regions with significant difference.

	Region	MNI	# Voxels	Peak *t*
FC-LH	Precentral gyrus right frontal lobe	36 -3 30	58	6.9
ReHo	Temporal lobe inferior right	54 -21 -18	99	-7.6
	Cingulate gyrus left frontal lobe	-15 -21 45	64	-5.2
	Medial gyrus left frontal lobe	27 -24 45	130	-7.0
ALFF	Inferior right temporal lobe	57 -27 -15	93	-13.8

Method: We studied the pre-surgical resting state brain activity of ten patients with TLE. Seven patients had left TLE (age 36.3±17.6 years) and three had right TLE (age 35.9±10.7 years). All MRI images were acquired on a Siemens Trio® 3T scanner. Functional MRI BOLD signal series in a 5 minutes time interval were obtained when patient was at rest with eyes closed. Imaging parameters are TR/TE 2500/34 ms, flip angle 90°, 36 slices with acquisition matrix 64×64 and FOV 1260×1260 mm^2, slice thickness 3.0 mm, and reconstructed voxel size 3.3×3.3×3.3 mm^3. The study was proved by the Human Research Ethics Committee of Queensland Health and written informed consent was obtained prior to scanning from each patient. DPARSF and REST software were employed for fMRI data processing [9]. The first 10 time points were removed to allow patient adaptation and signal stabilization. The time difference between slices was corrected and scans were checked for excessive head motion (> 2mm); no patients were excluded. Left and right hippocampus masks were created from the Automated Anatomical Labeling (AAL) atlas as seed regions for whole brain hippocampal FC analysis following a similar procedure as in [1]. ReHo, ALFF, fALFF, and VMHC were computed and compared statistically on the left against right TLE patients. Two sample t-tests results were corrected for multiple comparison error using AlphaSim (AFNI) method with cluster size of 54 voxels and 6-connections. Positive *t* values indicate the measurement in left TLE group is larger than that in right group, and vice versa.

Results & Discussion: The regions showing a significant difference between left and right TLE groups are illustrated in Fig. 1 and details of these regions are listed in Table I. The right precentral gyrus was found to have stronger connectivity to left hippocampus in left TLE group than right TLE group. However, there is no difference found in the right hippocampal FC between the groups, which was reported in [1]. There are three regions showing lower regional homogeneity in the left group compared to the right group. The ALFF in a region of inferior right temporal lobe was found to be lower in the left TLE patients than right TLE patients. No significant difference was identified in fALFF or VMHC between groups.

Based on our findings, not only the whole brain hippocampal FC, but also other high level features of resting state fMRI signal, such as ReHo and ALFF differ between left and right TLE groups. These results provide preliminary support for the hypothesis that the properties of the resting state signal may show differences according to the lateralization of epilepsy. Recently, pattern classification based on functional brain networks based has been used to search for informative neuroimaging markers in epilepsy patients [2]. The results of this study may be incorporated in pattern classification methods as prior knowledge to increase the classification accuracy. The inconsistency of the findings about the hippocampal FC between this study and that reported in [1] with similar sample size implied that a larger scale independent cohort is required for further validation on the findings presented.

References:

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