Function Lateralization through Measuring Coherence Laterality

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Introduction

Function lateralization is important for basic science researches and clinical practices. Functional MRI (fMRI) has been increasingly assessed as a noninvasive alternative to the current clinical standard, the intracarotid amobarbital testing (IAT) procedure[1] for presurgical brain function evaluations. With fMRI, the function laterality is most widely determined via comparing activation in homologous ROIs in each hemisphere. However, the task induced activations are usually assessed using the univariate general linear model (GLM). So that there is no control for performance effects or variations in hemodynamic response function (HRF) [2] due to underlying pathology. A data driven approach may offer a more robust alternative to the GLM based lateralization. Regional coherence is a model free measure for assessing brain activities during resting state or behavioral state. Instead of comparing activation in homologous ROIs in each hemisphere as in the GLM based method, a completely data-driven approach to determine functional laterality can be achieved via checking the coherence difference in the bilateral homologous ROIs. In this work we assessed the utility of the coherence laterality (CL) approach to determine function laterality first by examining motor laterality in normal subjects' data acquired both at rest and with a simple motor task and second by examining mesial temporal lobe memory laterality in normal subjects and patients with temporal lobe epilepsy. The results were compared to a standard laterality index based on GLM [3] (termed GLMLI in the following text).

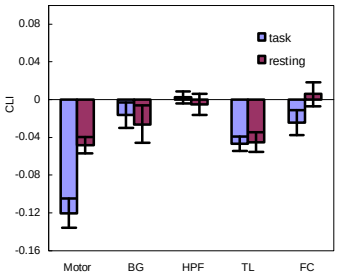

Fig. 1. CLIs calculated from the resting and sensorymotor fMRI data within the 5 ROIs. Motor, BG, HPF, TL, and FC mean motor cortex, basal gangalia, hippocampus-parahippocampus-fusifor m, temporal lobe, and frontal cortex, respectively.

Materials and Methods

Seventeen young healthy subjects were scanned with signed consent form approved by IRB. MR imaging was conducted in a Siemens 3T whole-body scanner. High resolution structural images were acquired for spatial brain normalization using a 3D MPRAGE sequence. Gradient-echo echo-planar imaging sequence was used for BOLD fMRI data acquisition with TR=3s, TE=30 ms, FOV = 220x220 mm^2, matrix=64x64, 40 slices with a thickness of 3 mm. Four dummy scans were performed at the beginning of the acquisition to allow magnetization to reach a steady state. During the resting scan (220 TRs), each participant was asked to lie in the scanner at rest and keep eyes open. The same subjects were asked to perform a self-paced left hand fingertapping task when they see a flashing black and white checker board during the sensorymotor fMRI session. A block design was used, consisting of 5 task blocks separating by a baseline block. Each block lasted for 1 min. The visual stimuli during the task state was an 8.33 Hz reversing black and white checkerboard. CL index (CLI) was also evaluated for memory lateralization using previously reported data from 14 epilepsy patients (6 had TLE localized to the right temporal lobe, and 8 to the left temporal lobe) [4]. For this particular cohort, memory lateralization via IAT pointed to the same side of seizure for the patients with unilateral epilepsy.

All data preprocessing was performed in batch mode with SPM5 software (http://www.fil.ion.ucl.ac.uk/ spm) based batch scripts [5], including realignment, coregistration, smoothing with an isotropic Gaussian filter (FWHM=6 mm), low-pass filtering with a Butterworth filter (cutoff frequency = 1/8 Hz), a high-pass Butterworth filtering (cutoff frequency = 1/128 Hz), spatially normalization to the MNI 152 standard brain, and GLM analysis. All ROIs except the motor cortex ROI were defined using the Wake Forest Pick atlas utility [6]. For resting and sensorymotor fMRI data, 6 ROIs were defined in the motor cortex (MC), basal ganglia (BG), hippocampus-parahippocampus-fusiform (HPF), temporal lobe (TL) and the frontal cortex (FC). MC was defined from the random effect analysis results of the sensorymotor fMRI with a threshold of P<0.01 (FWE correction) and was used to assess the task effects on the brain activity coherence and the associated CLI. BG and TL were used as control ROIs. Memory laterality was determined using the scene-encoding fMRI data within HPF and BG. Kendall's coefficient of concordance (KCC) [7] was used to measure the coherence of fMRI signal in each side of the chosen ROIs. The time series at each voxel were ranked from 1 to n (n=220 for the sensorymotor data, and 168 for the scene-encoding data), and the KCC was then calculated as $W = (\sum (R_i)^2 - n(\bar{R})^2) / \frac{1}{12}k^2(n^3 - n)$, where R_i is the rank sum of the i-th voxel's rank series; $\bar{R} = ((n+1)k)/2$ is the mean of all R_i's; k is the number of voxels within the measured ROI. KCC ranges from 0 to 1 with 0 meaning completely incoherent and 1 meaning completely coherent. After getting KCC from the left and right side (LW and RW), the CLI was calculated as: CLI=(LW-RW)/(LW+RW). A positive CLI indicates left lateralization and vice versa for a negative CLI.

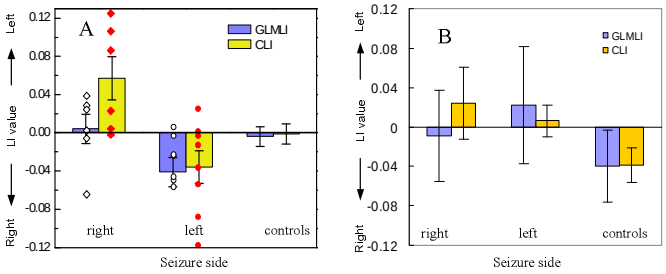

Fig. 2. CLI and GLMLI distributions of the epileptic patients and normal controls calculated from the scene-encoding fMRI data within A) HPF and B) BG. The "right" and "left" unilateral epilepsy patient groups are subdivided according to their side of seizure. "controls" means normal healthy subjects. The scattered points overlapped on the bars are LIs of the right (diamonds) and the left patient group (circles).

Results and discussions

Fig. 1 shows the CLIs calculated from the resting and sensorymotor fMRI data of the same group of normal subjects. As compared to the resting state, performing sensorymotor task only significantly increased coherence laterality (P<0.02, paired t-test) in task related MC and FC, suggesting a valid and effective CL-based functional lateralization using the functional ROIs. Fig. 1 showed no prominent coherence laterality in HPF of the normal health brain. A symmetric distribution was also found in the HPF CLI calculation using normal subjects' scene-encoding fMRI data (Fig 2), suggesting no functional lateralization in HPF of the normal brain using the scene-encoding task. In Fig. 2, CLI of the right side seizure group (n=6) calculated from the HPF ROI (Fig. 2A) was significantly greater than 0 (P=0.049, only 1 patient was lateralized to the wrong side using CLI). For the left side group (n=8), the mean HPF CLI was less than 0 (P=0.075, 2 of the 8 patients were lateralized to the wrong side using CLI). As compared to GLMLI, CLI presented better performance for seizure side/IAT laterality prediction for the right side seizure group, while similar performance for the left side group. However, CLI significantly (P=0.0059, two sample t-test, 2-tailed) differentiated the right side group and the left side group. For normal controls, both GLMLI and CLI yielded a symmetric distribution around zero, meaning no memory laterality found by either LI. In the non-task-involved BG ROI, GLMLI and CLI were symmetrically distributed for both patients (the right side and left side unilateral epilepsy patients) and controls as shown in Fig. 2B. These findings are quite encouraging for using CLI as a tool for function lateralization. It's also worth to note that the application to memory lateralization for epilepsy patients was limited by the small number of patients assessed in this paper. Particularly, for this particular epilepsy patient cohort, IAT memory laterality was determined to be same as the seizure side for every patient with unilateral seizure. It's worth noting that CLI was more effective than GLMLI for the right side seizure group and its performance for the left side patient group was largely affected by one outlier. A larger sample size is basically required to further verify the usefulness of CLI for memory lateralization in future work,

Reference [1] Wada et al., J Neurosurgery, 1960, 17:266-282. [2] Friston et al., Human Bra Map, 1994,1:153-171. [3] Rabin et al., Brain, 2004, 127(10): 2286-98. [4] Narayan et al., 2003, 57th American Epilepsy Society meething. [5] Wang et al., MRI, 200, 26(2): 261-269. [6] Maldjian et al., NeuroImage, 2003, 19(3):1233-9. [7] Kendall et al., Rank correlation Methods, 1990, Oxford Univ Press.

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