Detection of epileptogenic zone and its dynamics by database-approach of resting-state BOLD-based fMRI in Brain Cloud

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Background:

There are 20 - 30% of patients with epilepsy refractory to all forms of medical therapy. These medically intractable patients are candidates for surgical treatment in an attempt to achieve better seizure control. But two-thirds of patients with focal epilepsy there are no identifiable brain lesions on conventional MR imaging, and it is sometimes difficult to identify the source of epileptic discharges with scalp EEG. Resting-state blood-oxygenation-level-dependence (BOLD) functional MRI (rs-fMRI) was proposed to detect the epileptogenic zone (EZ), irritative zone (IZ), pacemaker zone (PZ) or ictal symptomatic zone (ISZ) based on local functional connectivity of inter-ictal neuronal discharge (1). In this study, the database-approach of "Brain Cloud" was tested using the rs-fMRI of on-site or web-site database of rs-fMRI. Correlation with electrocorticography (ECoG) was applied for verification, and time-lag functional network of rs-fMRI was derived for mapping the dynamics of zones related to seizure.

Methods:

From1000 Functional Connectomes Project, three databases using protocols of whole brain BOLD-based studies of 3T MRI scanner were selected as (1) Cleveland [n = 31 (11M/20F); ages: 24-60; TR = 2.8s; slice number (SN) = 31; repetition number (RN) = 127], (2) Leipzig [n = 37 (16M/21F); ages: 20-42; TR = 2.3s; SN = 34; RN = 195)] and (3) Oulu [n = 103 (37M/66F); ages: 20-23; TR = 1.8s; SN = 28; RN = 245). On-site databases of two 3T MRI scanners (NYMU and VGHTPE) were acquired as (1) NYMU [n = 40 (5M/35F); ages: 20-30; TR = 2s; slice number (SN) = 40; RN = 200] and (2) VGHTPE [n = 161 (86M/75F); ages: 20-30; TR = 2s; SN = 40; RN) = 200]. For on-site databases, whole-brain rs-fMRI with eye fixation and response to end of fMRI sessions was obtained with on-line real-time fMRI for verification of head motion (translation < 1 mm and rotation < 1 degree). Standard Spm8 preprocessing was done with (1) normalization to EPI (echo planar image) template (3x3x3 mm), (2) detrend, (3) band-pass filtering (0.01-0.08 Hz), (4) local functional connectivity (LFC) by summated correlation analysis of 26 neighbor voxels, and (5) 6x6x6 mm smooth. The feature of LFC (average/one standard deviation) was calculated using the mask of grey matter (GM) (probability > 0.5, FSL). Rs-fMRI data of two patients with epilepsy (ages: 18–28 years; 2 men) were analyzed with data acquired by VGHTPE. The patients were undergoing routine pre-surgical evaluation prior to grid implantation for localization of epileptic discharges. The VGHTPE database (N-161) was used as a normative comparison sample to identify aberrant connectivity patterns.

Dynamics of epileptic activity was explored by ICA (independent component analysis) detecting 40 spatial components using informax ICA of group ICA fMRI toolbox (GIFT). By spatial correlation with the aberrant LFC maps (correlation coefficient > 0.2), segmented temporal course (NR=50 with 40% overlap) of selected components was applied for group analyses of maximal lag correlation among components using (1) interval of time lag = -3 to +3 seconds and (2) one-sample t-test with statistical criteria of $p<0.05$. Group comparison was conducted using two-sample t test with adjusting the degree of freedom.

Results:

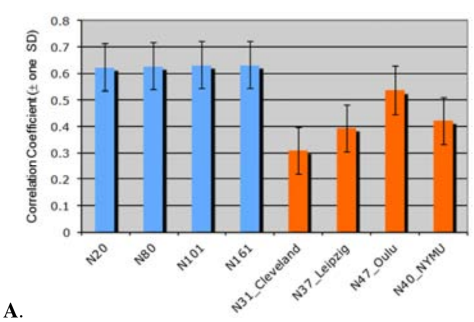
Stability of LFC was demonstrated using the database of VGHTPE with N=20, 80, 101 and 161, respectively, with significant higher LFC within GM as compared with Oulu (p=0.05), NYMU (p=0.006), Leipzig (p=0.001) and Cleveland (p=0.00001) groups (Figure A). The LFC of one patient with pathologically proved focal cortical dysplasia (FCD) of left frontal lobe was evaluated using VGHTPE database (N-161) with normative comparison. Areas of increased and aberrant LFC with normalized z values > 3 were labeled as red regions (Figure B, left) and verified as epileptogenic zone by ECoG and depth electrodes (Figure B, right). GIFT-derived dynamics of seizure was compatible with the results of LFC, and component of FCD (component 26 in Figure C) showed highest outbound centrality among spatially selected components. The patients were post-surgically followed with seizure free in two years.

Conclusion:

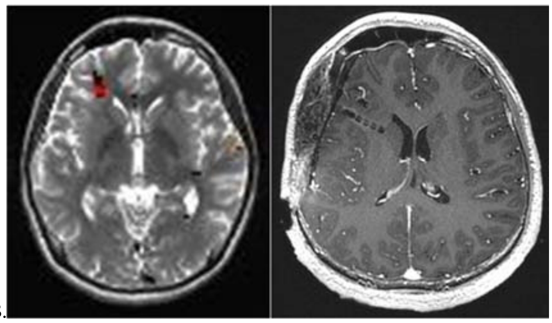
Platform specificity of LFC interfered the normative comparison with change of sensitivity/specificity in detecting aberrant LFC via "Brain Cloud" approach, e.g. users upload their data of rs-fMRI to VGHTPE database for tele-medical analysis. Spatial specificity and temporal dynamics of aberrant LFC well correlated with ECoG, surgical pathology and model of connectivity.

Reference:

(1) Stufflebeam SM et al., J Neurosurg 114 (2011) 1693-1697.



A.



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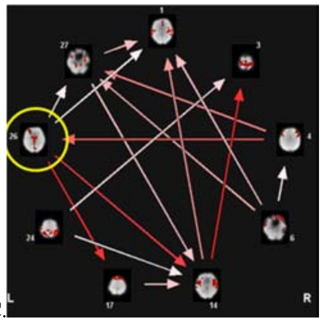

C.

Figure A :
Stability (average/one standard deviation) of LFC within GM was summarized for various databases of VGHTPE, Cleveland, Leipzig, Oulu and NYMU.

Figure B :
The LFC of one patient with FCD of right frontal lobe was evaluated using VGHTPE database (N-161) with normative comparison. A cluster of aberrant LFC with normalized z values > 3 was labeled as red regions (Figure B, left, superimposed on a T2-weighted image). By implantation of grid and two depth electrodes, the area of aberrant LFC was verified as epileptogenic zone by ECoG (Figure B, right, a contrast-enhanced T1-weighted image).

Figure C :
Lag-based connectivity demonstrated the dynamics among selected components from ICA of segmented rs-FMRI. 2D image with the maximal correlation was shown for each selected components based on spatial correlation to aberrant LFC maps (the yellow circle indicated the component best fitted to LFC results as Figure B). The lag time (0~3 seconds) with maximal correlation between components was color-coded as white to red.