Mapping Brain Entropy using Resting State fMRI: Part I

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Introduction. Entropy indicates system irregularity [1] and is minimized in complex systems. The human brain requires low entropy to function normally [2]. Characterizing brain entropy (BEN) may provide new insights into brain organization and function. The purpose of this study was to map BEN derived from resting BOLD fMRI data using a large sample size.

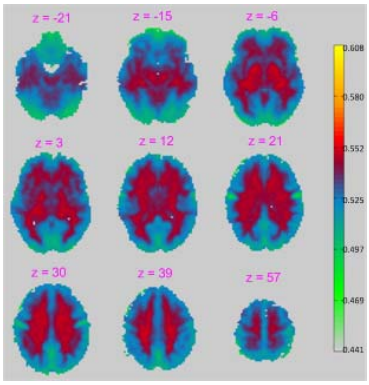

Fig. 1. Average resting BEN map of 1049 normal subjects.

Materials and Methods. 1049 usable data with demographic information (age and gender) were identified from the 1000 functional connectivity project (FCP) database [3]. rsfMRI images were acquired with: a duration of 4.15~9.8 min; voxel size: 2~4mm within plane; slice thickness, 3~5.5 mm. Repeat rsfMRI data were found from 50 subjects. fMRI data were first motion corrected, spatially smoothed, temporal filtered with a passband of 0.01 Hz to 0.12 Hz, first and second order detrended, nuisance corrected for removing motion artifacts, global WM signal, and global CSF signal , and registered with the structural images.

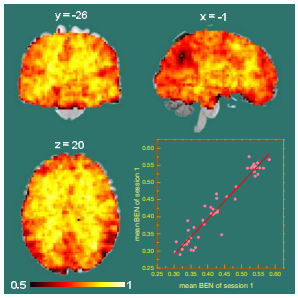

Fig. 2. The correlation coefficient map of 50 subjects' BEN maps of two different sessions. The inset plots the session 1 versus session 2 global BEN curve and the fitted relations.

BEN was mapped at each voxel by calculating sample entropy (SampEn)[4, 5] of that voxel's rsfMRI time series using in-house software written in C++. SampEn is a state-of-art approximate entropy measure [4, 5], which depends on two pre-defined parameters: the embedded dimension m and tolerance r. With a series of validations, we chose m=3 and r=0.8 of the standard deviation of the data, respectively. The resulting BEN map was divided by its grand mean and subtracted by 1 to get a relative BEN (rBEN) map, which was registered into the MNI space using the transform derived from each subject's structural image using FNIRT [6] provided in FSL. A one-sample t-test using the rBEN maps was performed to evaluate the spatial distribution of BEN during rest state. A multiple regression model including age and gender as two independent variables was used to assess the effects of age and gender on resting BEN.

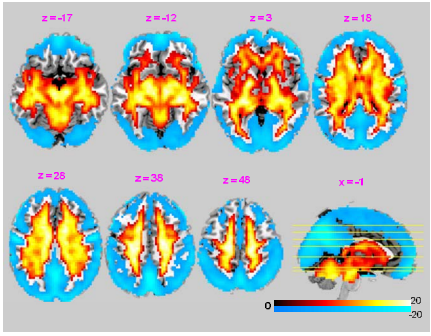

Fig. 3. Resting BEN distribution. Hot and cool color indicate HBEN and LBEN network. The text above each axial slice indicates the slice location in the MNI space.

Results and Discussion. No age and gender effects on resting BEN were found. Fig. 1 shows the mean BEN map. Neocortex showed lower entropy than white matter (WM), and the subcortical gray matter regions. BEN in neocortex was inhomogeneous. (Note that in a previously reported pilot study [7], motor cortex (MC) artificially showed higher than average BEN, due to the sensitivity to data preprocessing of the entropy measure used therein) BEN mapping using SampEn showed high test-retest stability (Fig. 2, CC >0.5 for all intracranial voxels and was 0.978 for the whole brain mean BEN (the insect)). Fig. 3 shows the spatial BEN distribution patterns defined with p<0.01 (FWE corrected). The entire brain was segregated into a lower than average BEN network (LBEN) and a higher than average BEN network (HBEN). Similar to that shown in Fig. 1, LBEN consists of the entire neocortex, while HBEN consists of WM, the limbic area, cerebellum, and brain stem. BEN in neocortex showed large heterogeneity across different cortical areas, with the 5 lowest BEN located in the precuneus, followed by bilateral motor cortex, orbito-frontal cortex and visual cortex (Figs. 1, 3), meaning a higher brain activity regularity in those areas, which has been partly supported by prior rsfMRI-based resting state studies [8-10]. This study demonstrates the successful generation of reproducible BEN maps based on resting BOLD fMRI data. BEN maps show spatial features consistent with known brain organization. BEN provides a novel, data-driven approach for examining regional brain function in health and disease.

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