

Altered Default Mode Network Functional Connectivity in Amyotrophic Lateral Sclerosis

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Introduction

Default Mode Network (DMN) is a brain system that encapsulates a set of interacting brain regions that are functionally connected and distinct from other networks in the brain, and it has shown decreased activity during external stimuli task when compared with baseline condition [1-4]. Characterization of the default mode network (DMN) as a complex network of functionally interacting dynamic systems has received great interest for clinical application [5-6]. Amyotrophic lateral sclerosis (ALS) is a progressive disease that is associated with motor disorder. Little is known about how ALS affects the default mode network. The aim of this study is to assess the complex network of DMN while in the resting state, which can provide greater insight into how DMN functional networks are affected by ALS.

Methods

MRI acquisition: Seven patients with ALS and Seven age-matched control groups participated in this study. A 3.0 T GE scanner equipped with an eight-channel multi receive system was used. Structural images (3D FSPGR 1x1x1 mm³, 140 slices) and BOLD EPI data (TR/TE = 2500/40 ms, flip angle=90°, matrix size=64x64, 3mm slice thickness) were acquired. For the resting state fMRI data acquisition, each participant kept their eyes closed and not think of anything in particular. **fMRI data Analysis:** All fMRI image processing and analysis were performed with AFNI and FSL. The first four volumes were excluded from analysis to allow for initial stabilization of the fMRI signal. For each subject, motion correction was performed 3D image realignment with the program 3dvolreg, which uses a weighted least squares rigid-body registration algorithm, spatial normalization to standard Talairach space. For each subject, the data were spatially smoothed using a Gaussian kernel of FWHM 6mm. Prior to performing functional connectivity (fcMRI) analyses, several processing steps were used to condition the fMRI data for analysis of voxel-based correlations, temporal band-pass filtering (0.01 Hz < f < 0.08 Hz) was used to reduce the effect of low frequency drift and high frequency physiological noise. Several sources of nuisance covariates were eliminated using linear regression: 1) 6 rigid body motion correction parameters, 2) signal from the white matter, the signal from a ventricle region of interest and whole brain global mean signal. Here, we used priori regions of interest (ROI) to define the default network as previous studies [7], the each of 11 default mode network ROI was defined as a spherical region with a radius of 8mm. Then ROI mean time series was estimated by averaging the time series of all voxels in each region. The Pearson's correlation coefficients were computed between each pair of brain regions for each subject, and then correlation matrix (11x11) for each subject was constructed. For further statistical analysis, a Fisher's r-to-z transformation was applied to improve the normality of the correlation coefficients. Finally, we characterized the DMN by using binary complex network analysis approach [8].

Results and Discussion

We compared DMN network measures between the ALS and normal subjects. For each participant, we calculated the each DMN region mean clustering-coefficient and local efficiency. The patients with ALS PCC show significant mean clustering-coefficient decrease ($p < 0.05$, see Fig.1). The mean clustering-coefficient is a measure of segregation, which reflects the inter-region information communication ability. Our results indicate that ALS patients PCC interaction with other subnetwork of DMN decrease. We also found that PCC and LSupF DMN nodes locally efficiently show significant difference between ALS and normal subjects (see Fig.2, $p < 0.05$). The previous study has indicated the PCC as the hub of DMN [6]. Our results show PCC node clustering-coefficient and local efficiency significantly decrease in ALS patients. This study of ALS patients demonstrates DMN network topology changes associated with ALS disease. Our results suggest that DMN complex network measures have the sensitivity and objective assessment in patients with ALS.

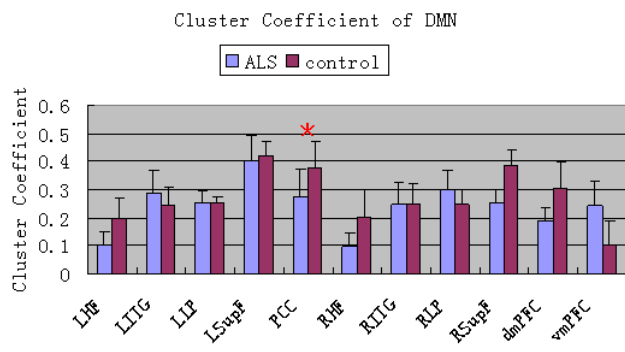


Fig.1 The DMN network measures: clustering-coefficient of ALS and normal subjects

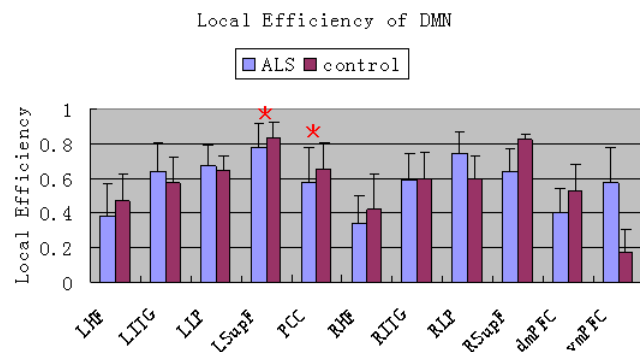


Fig.2 The DMN network measures: Local efficiency of ALS and normal subjects

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