SHIFTING CHARACTERISTICS OF UPPER MOTOR NEURON REVEALED BY VOXEL-BASED MORPHOMETRY IN AMYOTROPHIC LATERAL SCLEROSIS

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Introduction

Amyotrophic lateral sclerosis is characterized by progressive deterioration of upper and lower motor neurons. The survive time after diagnosis is less than 5 years, death occurs when degenerative course affects neuron that control respiration, which was thought not the true end of disease process. The pathological changes and neuron degeneration procedure remain unclear, especially for upper motor neuron (UMN). Therapies could be applied regionally at early stages to suppress spread and efforts to spare the critical neurons that control respiration had been speculated, based on motor neuron degeneration procedure[1], which has not yet been confirmed by valid research. So, in this work, we aim to found the topography of gray matter changes through voxel-based morphometry (VBM), to explore spread characteristics of upper motor neuron.

Materials and methods

Twenty-seven sporadic patients with ALS were enrolled in this study (17 men, mean age 54.3±7.9 years), according to the revised EI Escorial criteria. Twenty-seven age and gender matched healthy volunteers (14 men, mean age 50.7±9.2 years) served as controls. Three-dimensional T1-weighted images were acquired on a GE 3T HDxt scanner equipped with an eight-channel head coil, using fast spoiled gradient echo (FSPGR; TR/TE: 10.8ms/4.8ms, acquisition matrix:256×256, voxel= 1×1×1 mm^3). We used FSL-VBM[2] (http://www.fmrib.ox.ac.uk/fsl/fslvbm/index.html) to evaluate gray matter differences between groups, with demeaned age, sex, and total intracranial volume (TIV) as covariates in general linear model. Region of interest (ROI) analysis was performed in seven brain regions, including bilateral precentral gyrus, postcentral gyrus, superior, inferior, middle and medial frontal gyrus and insular cortex. Mean gray matter density of ROIs showing significant group differences were extracted and regressed against ALS clinical measurements.

Results

Regional gray matter volume reduced in left precentral gyrus, postcentral gyrus and superior frontal gyrus in whole brain analysis (P<0.05, FWE corrected). Two additional brain regions were found by ROI analysis, including right precentral gyrus and left insular (P<0.05, FWE corrected). No statistical significant correlation between mean gray matter intensity and clinical index of ALS were detected.

Discussion and conclusions

In this study, we found predominant volume reduction in the left hemisphere and insignificant changes in contralateral regions. The left hemisphere dominance in our study, especially for the profound precentray gyrus volume reduction, was in keep with the clinical observation that more than half of patients were right limb motor deficits. Gray matter loss in left postcentral gyrus, SFG and insular, reflected cortical level changes due to progressive degeneration of the ipsilateral upper motor neuron in precentral gyrus[3]. However, slight reduction of gray matter volume in right precentral gyrus, may account for a minority of ALS patients with left limb-onset, or a consequence caused by striking left precentral gyrus degeneration procedure, transmitted through impaired corpus callosum, which was proved to be a consistent involvement in ALS[4]. Correlation analysis failed to identify significant relationship, was in keep with other morphometry studies that VBM was not sensitive enough to detect minimal changes in later stages of ALS[3, 5], but reliable method to reveal intense changes occurred before, while ALS clinical characteristics changed remarkably as assessments of life quality. So, we concluded that the topography of gray matter changes revealed by VBM was a more stationary results which was a proper representation of upper motor neurons degeneration process in ALS. And this topography here also tend to support that at UMN level, spread is first to the contiguous ipsilateral foot/leg and subsequent spread to the contralateral hand/arm areas, which will be useful for determination of therapy strategies[1].

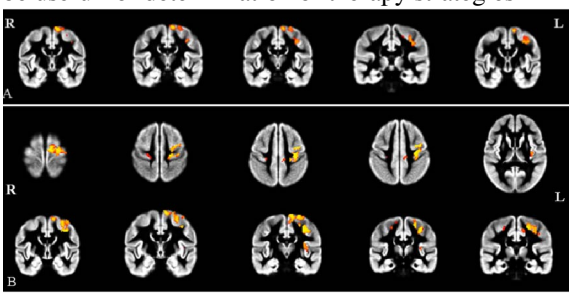

Fig A, whole brain VBM analysis showed gray matter loss in left precentral gyrus, superior frontal gyrus and left postcentral gyrus. (P<0.05, FWE corrected) Fig B, ROI analysis revealed gray matter volume reduction in left precentral gyrus, superior frontal gyrus, postcentral gyrus, left insular and right precentral gyrus. (P<0.05, FWE corrected)

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