

Study on gray and white matter changes in ALS with voxel-based morphometry using DARTEL

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Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease with both upper and lower motor neuron involvement [1]. Standard voxel-based morphometry (VBM-STANDARD) has demonstrated the gray and white matter loss in ALS [2]. In order to evaluate the efficacy of voxel-based morphometry with DARTEL algorithm (VBM-DARTEL) [3] in the detection of brain structural changes in ALS, both VBM-DARTEL and VBM-STANDARD were performed and the results were compared.

Methods: High resolution three-dimensional T1-weighted fast spoiled gradient recalled echo (3D T1-FSPGR) images were acquired from 30 ALS patients, including 14 with mild cognitive impairment (ALS/MCI), 16 with cognitively normal state (ALS/CN) according to cognitive state, and 6 bulbar-onset patients (ALS/Bulbar) and 24 limb-onset patients (ALS/Limb) according to clinical onset, and also from 30 age and sex matched controls. Voxel-based analysis was applied and statistical parametric mapping was generated using a analysis of covariance (ANCOVA). Voxel-wise correlation was performed between volumetric changes and ALS functional rating score (ALSFRS). Significance was set to a P value of < 0.001. The minimal number of contiguous voxels was set at 20.

Results: VBM-DARTEL revealed gray matter deficits in bilateral inferior frontal gyri, precentral gyri, parahippocampal gyri, right anterior cingulate gyrus, right middle and superior temporal gyrus, right sub-lobar extra-sub-gyral region and left frontal sub-gyral region in ALS compared with control, while VBM-STANDARD showed less region of deficits, especially bilateral precentral gyri (Fig.1). VBM-DARTEL also demonstrated marked white matter deficits in bilateral corticospinal tract regions, frontotemporal white matter, and sub-lobar white matter in ALS compared with control (Fig.2), while VBM-STANDARD only showed scattered deficit regions (Fig.3). Using VBM-DARTEL, we further showed gray matter loss in right medial frontal gyrus and bilateral postcentral gyri and no white matter loss in ALS/MCI compared with ALS/CN (Fig.4), and gray matter deficits in frontal lobe, temporal lobe, parietal lobe, limbic and insula (Fig.5) and white matter deficits in right centrum semiovale and right periventricular white matter (Fig.6) in ALS/Limb compared with ALS/Bulbar. Voxel-wise correlation analysis showed no significant correlation between volumetric changes and ALSFRS.

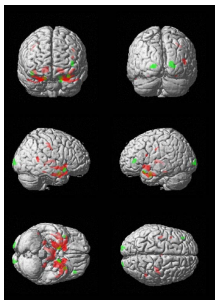


Fig.1 Gray matter loss in ALS compared with control using VBM-DARTEL (red) and VBM-STANDARD (green).

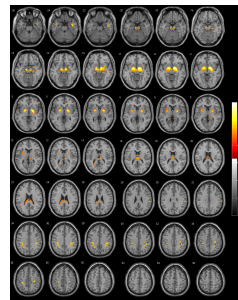


Fig.2 White matter volume deficits in ALS compared with control using VBM-DARTEL

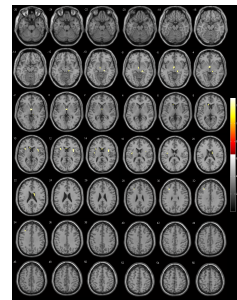


Fig.3 White matter volume deficits in ALS compared with control using VBM-STANDARD

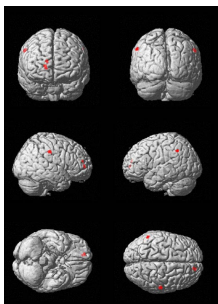


Fig.4 Gray matter loss in ALS/MCI compared with ALS/CN using VBM-DARTEL

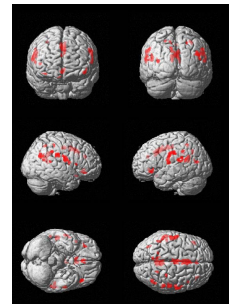


Fig.5 Gray matter loss in ALS/Limb compared with ALS/Bulbar using VBM-DARTEL

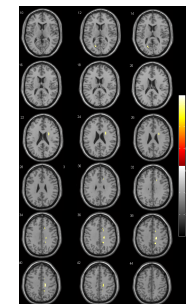


Fig.6 White matter loss in ALS/Limb compared with ALS/Bulbar using VBM-DARTEL

Discussion: VBM-DARTEL may be more accurate and reliable than VBM-STANDARD in performing volumetric studies and in detecting the regional volume loss of gray and white matter in ALS. Regional patterns of gray and white matter atrophy in ALS detected by VBM-DARTEL provided a better understanding of pathophysiological changes of brain structures in ALS and supported that ALS is a multisystem degenerative disease.

References:

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- [2] Grosskreutz J, *et al.* BMC Neurol, 2006, 6: 17.
- [3] Ashburner J. Neuroimage, 2007, 38: 95-113.