Gray Matter Thinning Demonstrated in ALS Using Novel Thickness Maps

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Introduction

Amyotrophic lateral sclerosis (ALS) is a devastating disease that preferentially attacks motor functions. Currently, there is no non-invasive method to identify and evaluate pathological changes in the brain in ALS. Our resent study on nine ALS subjects revealed a conspicuous loss of T1 contrast in the focal area within the primary motor cortex (PMC), in addition to atrophy. These findings suggest a potential utility of using gray matter (GM) thickness as a quantitative and sensitive method to assist diagnosis of ALS.

Figure 1: 3-D rendering of gray matter thickness image of an ALS patient. Red areas are the thinnest, yellow areas are mid-range, and green is thickest. Note the prominent thinning in the primary motor cortex.

Method

Nine ALS subjects (7 male and 2 female, average age 55.8) and eight age/sex-matched controls (6 male and 2 female, average age 59.4) received a whole brain T1-weighted 3D MDEFT (TE=3.14ms, TR=10.55ms, TI=680ms, SENSE factor=2, 20° flip angle) scan on a Philips Intera 3.0 T system with isotropic 1mm voxel size. Mean symptom duration for ALS subjects was 42 months (range: 19 – 76). Five subjects had mixed upper motor neuron (UMN) and lower motor neuron (LMN) involvement and the remaining four subjects showed LMN signs only. Images were smoothed and segmented into GM, white matter, and cerebrospinal fluid using the FMRIB Software Library (FSL) [1]. GM thickness was calculated from the segmented GM images using a novel method based on the Euclidian distance filter developed at our institution. To highlight brain areas with significant thinning, the GM thickness maps were displayed such that 1mm areas were marked in red, 2mm areas marked in yellow, and everything greater than 2mm was marked as blue.

Results

Figure 1 shows the GM thickness map of an ALS subject overlaid on the 3D brain image. A striking GM matter thinning is revealed in the focal area in the PMC. All ALS patients with primarily LMN signs showed extensive thinning of the PMC. Two of the five patients with mixed symptoms also showed thinning. Figure 2 shows a comparison of an age/sex-matched control and ALS thickness maps in three orthogonal plans cutting through the PMC. The pathological change associated with the disease is detected and clearly presented in the thickness maps. In addition, the two bulbar patients showed thinning in the PMC area associated with mouth motor function.

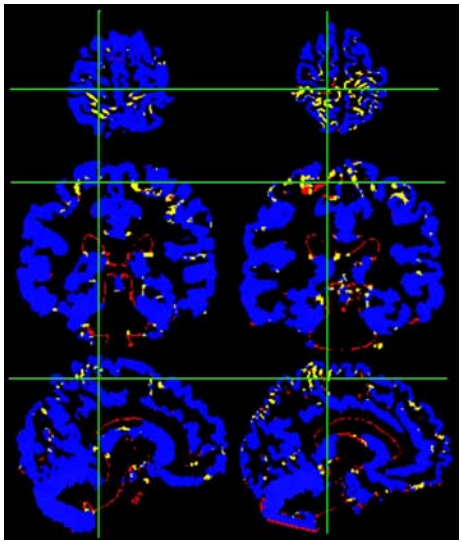

Figure 2: Three orthogonal projections of thickness images for 40 year old sex-matched control (left) and ALS subject (right). Top is axial, middle is coronal, and bottom is sagittal. The green cross-hairs indicate the positions of the slices. Red is 1mm, yellow is 2mm, and blue is greater than 2mm. The ALS subject has greater thinning in the primary motor cortex.

Discussion

These preliminary results suggest that thinning in the PMC may be useful for diagnosis of ALS and its progression. ALS is a rapid developing neurodegenerative disease with a wide degree of clinical presentation. We demonstrated that this brain imaging and analysis method has the ability to identify and quantitatively evaluate pathological changes in an ALS brain.

In addition to the apparent cortical thinning, ALS patients may experience a series of pathological changes in the brain associated with the disease progression. A further longitudinal study is necessary to characterize the corresponding changes in contrast and morphology. GM thinning is also confounded with age and must be accounted for when comparisons are made between controls and ALS patients [2]. Combining a normative data cortical thickness and variation with age, our method can be an effective tool for the study of other neurodegenerative diseases.

References

[1] S. M. Smith, et al., *NeuroImage*, vol. 23, pp. S208-S219, 2004.
[2] D. H. Salat, et al., *Cereb. Cortex*, vol. 14, pp. 721-730, 2004.