A Voxel-Based Morphometric Analysis of Clinically Isolated Syndrome Patients

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Introduction

Clinically isolated syndromes (CIS) are isolated events typically involving lapses in sensory function and are the earliest signs of the possible onset of Multiple Sclerosis (MS). MRIs of these patients often show lesions in the white matter of the brain that indicate damage to myelinated axons, but few studies have focused on changes in gray matter. Localized concentration and volume of gray matter can be compared in a voxel-wise manner between groups of subjects using voxel-based morphometry (VBM) [1]. The high-resolution subject images are normalized into the same stereotactic space that is defined by a template created from an average of the subject scans [2]. Statistical parametric mapping (SPM) [3] enables the comparison of this data between groups as well as the correlation with certain patient factors such as age, expanded disability status scale (EDSS), and sensory grade at the time of exam.

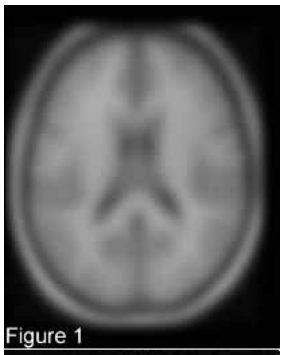
Figure 1

Methods

T1-weighted SPGR volumes, 1 x 1 x 1.5 mm resolution were acquired on a 1.5 T GE scanner on 93 subjects ages 21-63, 32 of them CIS patients (scanned within 4 months of clinical symptoms) and 61 control subjects. Figure 1 shows a local study template image that was created from the average of the images from all the subjects. Lesions appearing on the scans were encircled with ROIs and verified by an experienced neurologist as shown in Figure 2. The scans were segmented into gray matter, white matter, and CSF [2] and normalized by 12 point affine transform to a template created from the average of the high-resolution scans of each subject. The normalization of the CIS patient scans were weighted by a smoothed mask derived from the ROI lesion definitions, thereby annulling the distorting effect the lesions typically have on the normalizing cost function [4]. The resulting gray matter images were modulated to retain pre-normalization volume information and stored in the intensity of the voxels as shown in Figure 3. The procedure was repeated without the masking of lesions during normalization for comparison. Regions of significant grey matter atrophy between CIS patients and control subjects were analyzed with sex and age as nuisance variables.

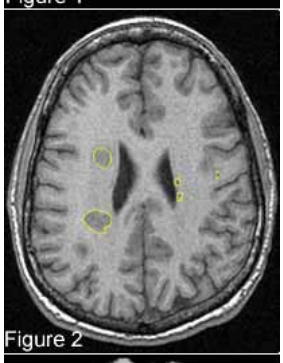
Figure 2

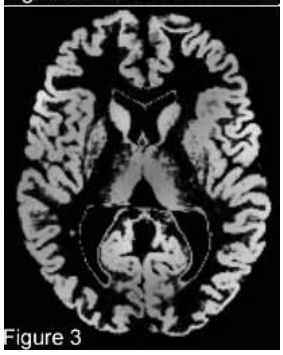
Figure 3

Results and Discussion

Analysis in SPM showed a significant decrease in volume in two clusters in the thalamus bilaterally from control subjects to CIS patients after a Family-wise Error correction, p=0.01 as shown in Figure 4. The results from the procedure without the lesions masked returned results in the same structure but with low significance. A voxel-based morphometric analysis has never been performed on CIS patients before. The masking of lesions in the white matter showed an improvement in stereotactic normalization and increased the significance of the results. The decrease in volume in the thalamus of CIS patients shows that there may be early grey matter involvement in patients at risk of developing Multiple Sclerosis. One other study has been performed using VBM on MS patients [5], with a different algorithm during segmentation to avoid lesion distortion; this study did not detect thalamic volume changes. However, our results are in line with recently published reports suggesting grey matter degradation in the thalamus of MS patients [6] [7] [8] [9] [10] [11].

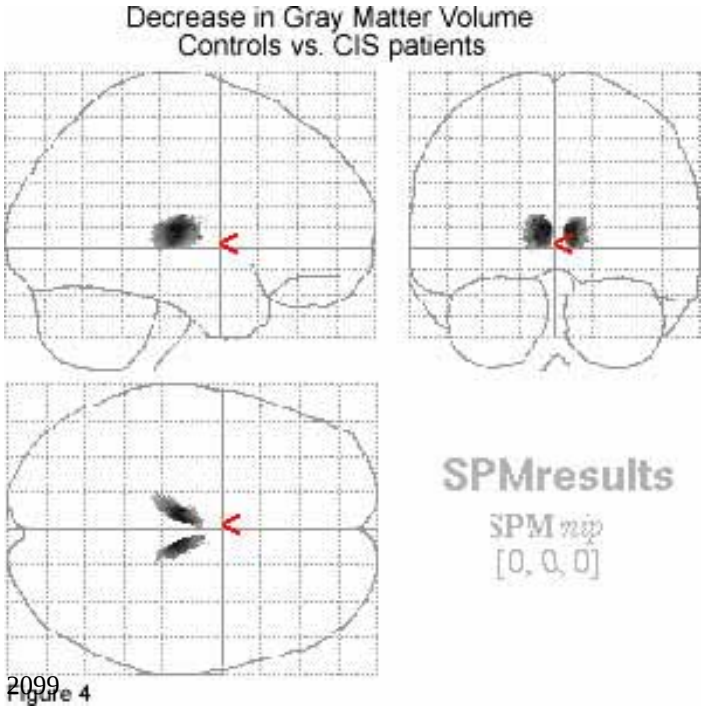

Figure 4

References

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