Regional atrophy demonstrated in Alzheimer's disease and mild cognitive impairment (MCI) using minimal post-processing time

D. L. Henderson[1], J. F. Schenck[2], N. A. Staples[1], and E. A. Zimmerman[3]

[1]Bioinformatics, General Electric Global Research, Niskayuna, New York, United States, [2]Imaging Technology, General Electric Global Research, Niskayuna, New York, United States, [3]Neurology, Albany Medical College, Albany, New York, United States

Introduction

Quantitative imaging techniques, such as T2 mapping, hold great promise for enhancing the evaluation of neurodegenerative diseases. Because T2 effectively separates fluid from tissue in brain images, changes in T2 distribution resulting from tissue loss and replacement by cerebrospinal fluid (CSF) can be used as a surrogate measure for brain atrophy. While the link between regional brain atrophy in early Alzheimer's disease and mild cognitive impairment (MCI) is well established[1-3], the techniques for measuring it typically require extensive manual image analysis by analysts trained in neuroanatomy. Before widespread clinical applications of these techniques can occur, there must be a great increase in the speed and ease with which quantitative information (both global and regional) can be extracted from the images. However, these semi-automated techniques must have sufficient accuracy to capture the significant signs of disease. We present here a semi-automated technique that we have evaluated on 3-tesla images of normal controls and of patients with Alzheimer's disease and mild cognitive impairment (MCI). We hypothesized that semi-automated approximate segmentation based on a standard atlas might provide a clinically feasible and useful method for quantifying regional variations in T2 associated with brain atrophy.

Methods

T1 and T2-weighted MRI images were collected for 56 subjects with AD, 7 with MCI, and 33 normal controls in an IRB-approved study. T1-weighted images were mapped to Talairach coordinates[4] by manually defining landmarks using AFNI[5]. Regional T2 distributions were extracted from the co-registered T2 images using the atlas as a mask and quantified as the percentage of voxels with T2 above 80 ms (Fig 1). The results were compared for the AD, MCI and control groups.

Results

Significant increases in high-T2 voxels in AD were found in several areas including the left and right hippocampus and parahippocampal gyrus. A comparison of the fraction of voxels with T2 > 80 ms in the left hippocampus of normal controls, MCI, mild AD (CDR < 1) and advanced AD (CDR ≥ 1) is shown in Fig 2. A trend of increasing frequency of high-T2 voxels accompanies the increasing disease severity from normal to advanced AD, with significant differences between normal controls and AD. The MCI group is intermediate between the normal controls and AD, but did not reach significance, in part because of the small sample size. Preliminary longitudinal analysis of 4 MCI subjects who later progressed to AD showed significantly higher rate of increase in high-T2 voxels in the left hippocampus (5%/year) vs. controls (0.6%/year) (p=0.04). These results suggest increased atrophy in the left hippocampus in subjects with MCI and AD relative to controls of similar ages. The results were obtained in only 10-15 minutes of postprocessing time per case by a technician without specific neuroanatomy training. This compares to the 4-5 hours required for a trained neuroanatomist to complete a precise manual segmentation and analysis. Thus, these results support the contention that clinically relevant T2 mapping can be achieved in a semi-automated fashion, greatly enhancing the possibility of its widespread clinical use.

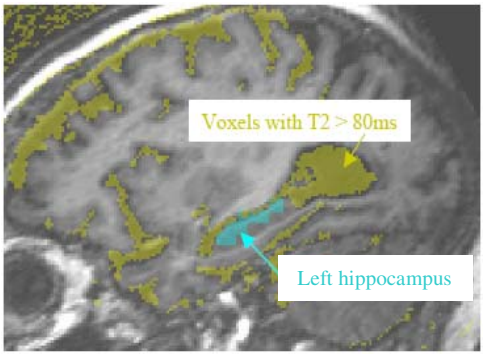

Figure 1. Voxels with T2 > 80ms superimposed on the left hippocampus as defined by the Talairach atlas.

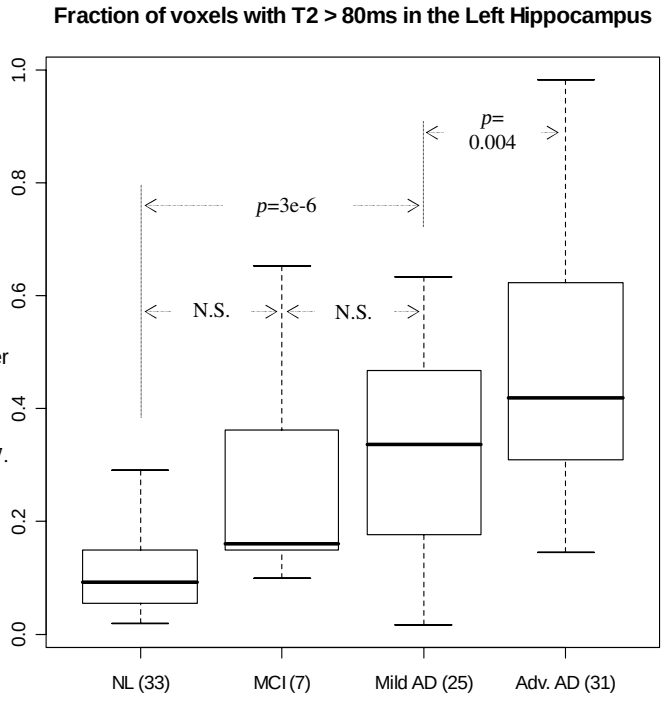

Figure 2. Comparison of high T2 (>80ms) voxels in the left hippocampus in normal controls, MCI and AD.

Acknowledgement

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