Memory Impairment in MS Correlates to Hemodynamic Response in Event-related fMRI of Incidental Encoding

K. A. Koenig[1], B. Mathew[1], J. Lin[1], L. Stone[2], S. Rao[3], M. Phillips[1], and M. J. Lowe[1]
[1]Imaging Institute, The Cleveland Clinic, Cleveland, OH, United States, [2]Mellen Center, The Cleveland Clinic, Cleveland, OH, United States, [3]Schey Center, The Cleveland Clinic, Cleveland, OH, United States

Introduction

An estimated 40-50% of MS patients have some cognitive deficit, with memory deficits included as a common manifestation of cognitive dysfunction [1]. In previous studies of healthy controls engaged in word recognition tasks, functional differentiation has been found between novel words and previously presented works [2]. Furthermore, one study investigated the correlation between the California Verbal Learning Test (CVLT) and functional activation differences. For novel words, CVLT performance showed a significant positive correlation with the right anterior hippocampus. For previously seen words, activation in the right dorsolateral prefrontal cortex was positively correlated with CVLT performance [3].

In addition to investigating recognition, researchers have also looked at stimuli encoding. Activation differences on incidental encoding tasks have been shown to predict performance on word recognition tasks [4,5]. In an encoding task using rapidly presented words, Wagner and colleagues found several frontal regions, including the left inferior frontal gyrus and the frontal operculum, which showed greater activation in response to remembered (“encoded”) vs. forgotten (“non-encoded”) words. Temporal regions also showed greater activation for encoded words, including the parahippocampal gyrus, the fusiform gyrus, and portions of the inferior temporal gyrus [4].

Because of the increased incidence of memory decline and the neuroanatomical degeneration inherent in MS, we hypothesize that brain regions involved in the performance of an incidental encoding task will have a hemodynamic response that is directly related to the degree of memory impairment. Specifically, we expect that activation in medial temporal lobe structures such as the parahippocampal gyrus, and frontal lobe areas such as the BA 45 and other prefrontal regions will correlate with performance on the CVLT.

Methods

The following scans were performed on sixteen female and two male right-handed subjects with MS (mean age 45.28 (9.07); mean EDSS 2.68 (1.57)). Anatomic whole-brain T1-weighted inversion recovery turboflash (MPRAGE): 120 axial slices, thickness 1.2mm, Field-of-view (FOV) 256mm x 256mm, matrix=256 x 128. Resting state whole-brain EPI scan: 132 volumes of 31-4mm thick axial slices TE/TR/flip=29ms/2800ms/80, matrix=128 x128, 256mm x 256mm FOV, BW=250KHz. In addition, three whole-brain EPI scans were run while subjects engaged in each of two tasks: First, an incidental encoding task (WE), during which subjects were shown 60 words for 2000ms each asked to decide if each word was abstract or concrete. Subjects were told that they would be asked about the words later. After twenty minutes, two word retrieval (WR) scans were used to measure recognition memory for words seen in the WE scan [4]. All subjects were also administered the CVLT, a test of verbal learning and memory [6].

Corrections include slice average covariate removal and physiologic noise correction using PESTICA [7] and RETROICOR [8], motion correction, a regression of the second order motion parameters of each voxel [9], and spatial filtering with a 2D hamming filter [10]. Finally, all timeseries were detrended and digitally filtered to remove fluctuations above 0.08Hz [11].

Analysis

WE events were split into “encoded” and “non-encoded” words for each subject based on responses during the WR task. “Encoded” words were those that were correctly identified, while “non-encoded” words were those that were identified as having not been seen in the WE task. The correlation between the fit hemodynamic response amplitude during the WE task and CVLT score was calculated for all 18 subjects for both the encoded and non-encoded words.

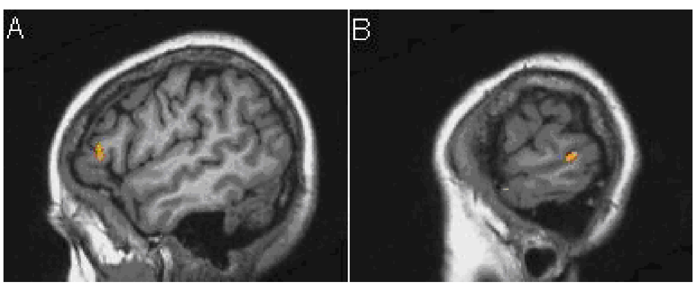

Fig 1. Correlation between CVLT scores and hemodynamic response amplitude for non-encoded words for A. DLPFC and B. left middle temporal gyrus.

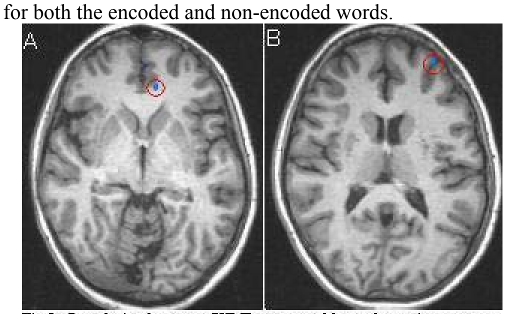

Fig 2. Correlation between CVLT scores and hemodynamic response amplitude for encoded words for A. the anterior cingulate cortex and B. the superior frontal gyrus.

Results

For the non-encoded words, areas that showed significant positive correlation with CVLT performance ($p<10^{-4}$, uncorrected) included BA 37, the left fusiform gyrus [-45 -42 -19], BA 9, the left dorsolateral prefrontal cortex [-40 27 32], BA 45, the left ventrolateral prefrontal cortex [-50 27 6], and BA 21 in the left middle temporal gyrus [-62 -42 4] and [-61 -7 -14].

For the encoded words, areas that showed significant negative correlation with CVLT performance ($p<10^{-6}$, uncorrected) included BA 10, the most rostral portions of the superior and middle frontal gyri [-32 54 13], and BA 32, the rostral portion of the anterior cingulate cortex (acc) [-9 38 0].

Discussion/Conclusion

For non-encoded words, positive correlations with CVLT score indicate brain regions involved in failed encoding for subjects with good verbal memory performance. These brain regions may reflect diminished concentration or distraction or possibly a failure of compensatory mechanisms demonstrated across multiple systems by previous investigators.

The encoded words which were negatively correlated with CVLT scores indicate brain regions which are relatively deactivated during successful encoding by subjects with good memory performance. These regions may reflect improved focus or concentration possibly resulting in decreased activation of brain regions not directly involved in the task. Alternatively, findings may reflect compensatory strategies such as mnemonic devices which may have resulted in a decrease in the amount of rehearsal used to keep information in memory.

Studies were supported by a grant from the National Multiple Sclerosis Society, RG4110-A2.

References[1] Rao et al. (1991) *Neurology*, 41(5):685. [2] Saykin et al. (1999) *Brain*, 122(10):1963. [3] Johnson et al. (2001*) J Int Neuropsychological Society*, 7(1):55. [4] Wagner et al. (1998) *Science*, 281(5380):1188. [5] Cabeza et al. (2001) *PNAS*, 98(8):4805. [6] Delis et al. (1987). *The California Verbal Learning Test*. New York: Psychological Corporation. [7] Beall & Lowe, *NeuroImage,* 37, 1286, 2007. [8] Glover et al., *Magn. Reson. Med.* 44, 162, 2000. [9] Bullmore et al., *Hum Brain Mapp*, 7, 38, 1999. [10] Lowe & Sorensen, *Magn. Res. Med*., 37, 723, 1997. [11] Biswal et al., *Magn Reson Med*, 34, 537, 1995.