Thalamic activation during verbal encoding is related to episodic memory in MS

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Target Audience: This work is of interest to researchers studying Multiple Sclerosis, memory, and fMRI.

Purpose: Patients with Multiple Sclerosis (MS) frequently show impairments in episodic memory (EM)[1]. Recent work suggests that encoding difficulties play a role in verbal EM impairment[2]. In the current study, we investigate functional activation during the encoding phase of an EM task in MS patients with intact cognition and with impaired EM. We hypothesize that functional activation during an EM task will be related to disease status and to EM performance.

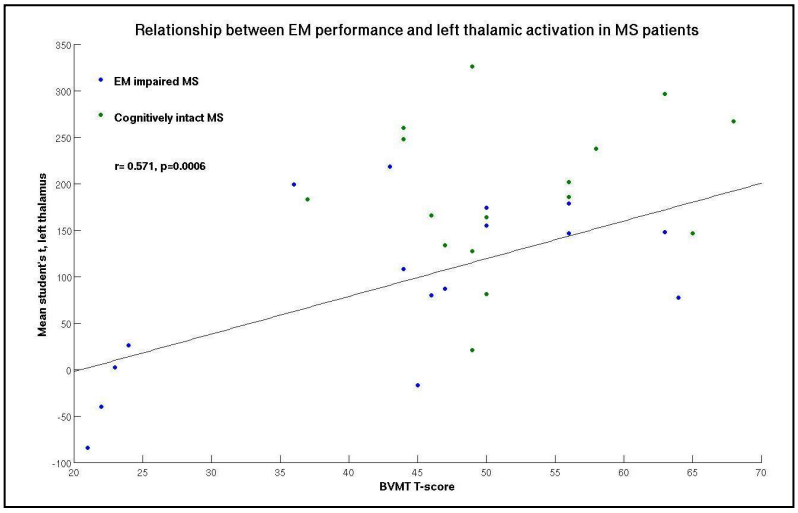
Methods: Thirty two patients with MS and 16 age- and education-matched healthy controls were scanned at 3T, in a 12-ch receive head coil. Scans included a T1-MPRAGE (1x1x1.2mm) and two event-related verbal EM fMRI tasks, encoding and retrieval, (described in [3]), both at 2x2x4mm voxels, 1954 Hz/pix BW, 31 axial slices, TR/TE/FA=2800/29/80. Remembered and non-remembered words from the encoding task were identified using responses on the retrieval task and encoding student's t-maps were produced using the AFNI program 3dDeconvolve[4]. Anatomical volumes and a volumetric scaling factor were estimated using FSL[5]. All volumes were corrected for head size using the volumetric scaling factor.

Scores on two measures of EM, the California Verbal Learning Test (CVLT-II) and the Brief Visual Memory Test (BVMT-R) were used to group MS patients into two age- and education-matched groups (Table 1). Student's t-maps from the correct encoding condition were stereotactically transformed and averaged in each group. Group maps were thresholded at p=0.0005 and added across groups to create an "OR" mask, including all regions that were significant in any group. The mask was transferred to individual space for each subject, and individual maps were inspected to ensure ROIs were located entirely in tissue. Mean student's t for each region was calculated. A one-way ANOVA was used to compare anatomical volumes and student's t scores for each ROI across the three groups.

	MS		
	Cognitively Intact	EM Impaired	Control
n	16 (4 males)	16 (5 males)	16 (3 males)
Age	43 ± 9.6	42.8 ± 9.6	43.3 ± 9.9
Edu	15.6 ± 2.1	14.5 ± 1.3	15.6 ± 1.6
EDSS	1.75 (1-6)	1.75 (1-6.5)	-

Table 1. Demographic information. Age and education mean and st. dev.; EDSS median and range.

Results: The left thalamus showed a significant group difference in mean signal (p=0.013), and a post-hoc analysis revealed that EM-impaired MS subjects showed lower activation as compared to cognitively intact MS subjects. In patients, mean signal in the left thalamus was related to delayed recall and total scores on the BVMT (p<0.009). EM-impaired MS subjects showed significantly smaller left thalamic volumes than both cognitively intact MS subjects and controls (p =0.0005). In patients, left thalamic volume was significantly related to mean activation in the left thalamus (r=0.499, p=0.003), delayed recall and total scores on the BVMT (p<0.032), and to total score on the CVLT-II (r=0.445, p=0.011). Controls did not show relationships between cognitive tasks, activation, and left thalamic volume.



Discussion: We found strong relationships between left thalamic volume, mean activation, and EM performance in patients with MS but not in controls. A number of previous studies have found increased functional activation in MS patients during memory task performance, thought to be related to compensatory mechanisms[5,6]. We found that thalamic activation decreased as MS patients showed greater EM impairment. In addition, thalamic atrophy was related to activation level and EM impairment. Thalamic atrophy has previously been related to cognition in both adult and pediatric MS[7,8,9].

Conclusion: Our findings show that performance on an EM task is related to functional activation of the thalamus in MS. Further, thalamic atrophy is related to both cognitive performance and functional activation. A larger sample and longitudinal measures are required to clarify the temporal relationship of these measures.

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