Hippocampal volume relates to white matter integrity and episodic memory in Multiple Sclerosis

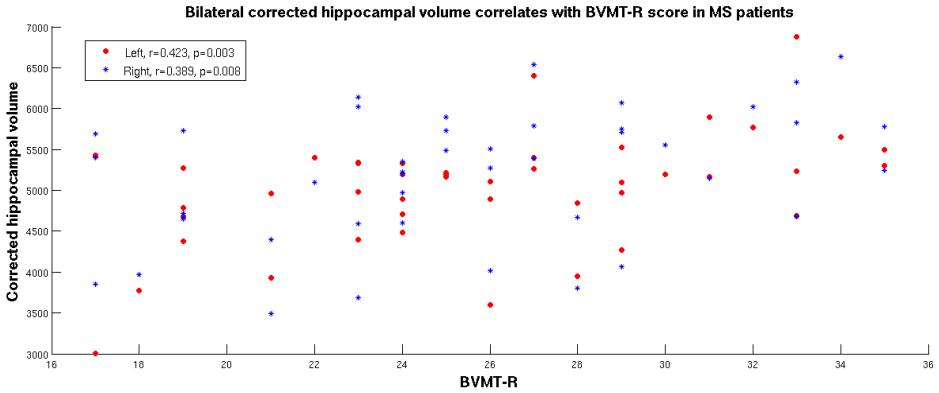
Katherine A Koenig[1], Ken E Sakaie[1], Mark J Lowe[1], Jian Lin[1], Lael Stone[2], Robert A Bermel[2], Erik B Beall[1], Stephen M Rao[2], Bruce D Trapp[3], and Micheal D Phillips[1]
[1]Imaging Sciences, Cleveland Clinic, Cleveland, OH, United States, [2]Neurological Institute, Cleveland Clinic, Cleveland, Ohio, United States, [3]Neurosciences, Cleveland Clinic, Cleveland, OH, United States

Target Audience: This work is of interest to researchers studying Multiple Sclerosis, DTI, and volumetric analysis.

Introduction: Recent research of the demyelinating disorder Multiple Sclerosis (MS) has focused on the role of hippocampal atrophy and demyelination in the loss of cognitive abilities. Hippocampal volume loss has been found to correlate with measures of episodic memory [1], and demyelinated hippocampi show decreased synaptic density and molecular changes hypothesized to underlie memory loss [2]. The current study compares hippocampal atrophy to episodic memory measures and to diffusion measures of the fornix, the largest efferent white matter tract from the hippocampus.

Methods: 47 MS patients (mean age 43.13 (9.16), mean EDSS 2.45, 13 male) and 24 healthy controls (mean age 40 (9.11), 9 male) were scanned in an IRB-approved protocol at 3T using a bitebar to reduce head motion, in a 12-ch receive head coil. Scans included a T1-MPRAGE (1x1x1.2mm) and a HARDI scan (FOV=192×192 mm2; matrix=192×192; 45 1-mm thick slices; TE/TR=90/7700 ms) 71 directions; 2 averages; 8 b=0 acquisitions per average.

HARDI postprocessing. Motion correction was performed with an iterative algorithm [4]. At each voxel, the diffusion tensor was calculated for each individual.



Hippocampal volumes. Bilateral hippocampi were identified on each subject using the T1-MPRAGE and the automated program FIRST from the FMRIB Software Library/FSL [6]. ROIs were manually checked and corrected by one trained expert. White matter (WM), gray matter (GM), and CSF masks were created using SPM8 [7] and manually checked for accuracy. For each subject, brain parenchymal fraction (BPF) was calculated according to the following formula: BPF=(GM+WM)/(GM+WM+CSF) and used as a correction for individual hippocampal volumes.

Cognitive tests. All subjects completed several tests of cognitive function, including the CVLT [8], a standard test of verbal episodic memory, and the BVMT-R [9], a test of visuospatial episodic memory.

Corrected hippocampal volume was compared between patients and controls using an unpaired t-test and was compared with measures of episodic memory and with fornicial diffusion measures used Pearson correlations.

	Patient		Control	
Right hip. volume	r	*p*	r	*p*
FA	0.3788	0.0094	0.3217	0.1667
MD	-0.4183	0.0038	-0.1104	0.6431
TD	-0.4455	0.0019	-0.1627	0.4931
LD	-0.3251	0.0275	0.0189	0.9370
Left hip. volume				
FA	0.3491	0.0174	0.2703	0.2492
MD	-0.3784	0.0095	-0.3958	0.0841
TD	-0.3945	0.0067	-0.3543	0.1254
LD	-0.3280	0.0260	-0.3694	0.1090

Table 1. Correlation of hippocampal volume with fornicial DTI measures.

Results: Corrected hippocampal volume was not different between patients and controls. In patients, all DTI measures were significantly correlated with hippocampal volume (Table 1), while no correlations reached significance in controls. In patients, performance on the BVMT-R was significantly correlated with hippocampal volume bilaterally (Figure), while there was no correlation with the CVLT. One patient was removed from the cognitive measures analysis due to cognitive scores that fell more than 2.5 standard deviations outside of the mean. Controls showed no correlation between hippocampal volumes and cognitive measures.

Discussion and conclusion: Though we found no between-group differences in overall hippocampal volume, measures of white matter integrity in the fornix and a measure of episodic memory were related to hippocampal volume only in patients. This bolsters the argument that hippocampal pathology contributes to memory loss in MS. The current patient sample has relatively low disease burden, and we expect that with the addition of subjects with a greater degree of cognitive impairment we would see both a significant hippocampal volume loss and a significant relationship between CVLT performance and hippocampal volume.

References:

[1] Sicotte et al. Brain. 2008;131(Pt 4):1134-41. [2] Dutta et al. Ann Neurol. 2011; 69(3): 445–454. [4] Sakaie et al. Magnetic Resonance Imaging. 2010; 28:290-6. [5] Basser et al. J Magn Reson B, 1994; 103:247-54. [6]Patenaude et al. NeuroImage. 2011;56(3):907-922. [7] Ashburner and Friston. NeuroImage. 2005; 26:839-851. [8] Delis et al. San Antonio, TX: Psychological Corporation, 1987. [9] Benedict. Odessa, FL: Psychological Assessment Resources, 1997.