

Morphometric and Functional Connectivity Correlates of Hippocampal Changes in Migraine Frequency

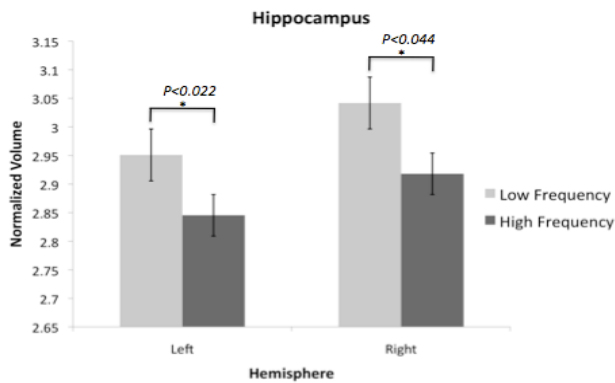
N. Maleki¹, G. Pendse¹, L. Nutile², R. Burstein³, L. Becerra^{1,4}, and D. Borsook¹

¹P.A.I.N. Group, Brain Imaging Center, McLean Hospital, Department of Psychiatry, Harvard Medical School, Belmont, MA, United States, ²Department of Psychology, Villanova University, Villanova, Pennsylvania, United States, ³Department of Anesthesia and Critical Care, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, ⁴Department of Radiology, Massachusetts General Hospital, Charlestown, MA

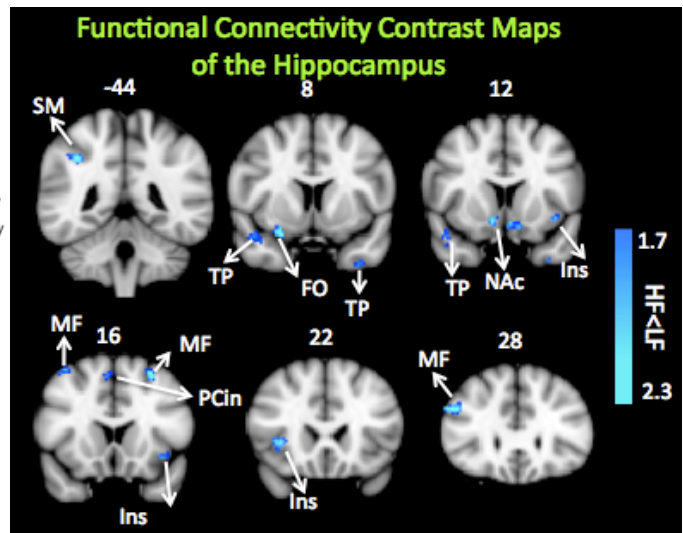
Introduction: The hippocampus is normally involved in memory and seizure activity. It also has been intimately associated with stress and stress hormones, which may alter hippocampal structure both functionally and anatomically (1). The hippocampus has recently been found to play a role in pain processing (2). However, the role of the hippocampus in migraine has not been well characterized. In this study we assessed whether there are any anatomical changes in the hippocampus in migraine patients based on the frequency of their migraine attacks and what the corresponding functional connectivity correlates are.

Methods: The study was approved by the IRB and all subjects gave informed consent prior to the scanning session. Two groups (N=10 in each) of migraineurs broken down by frequency of migraine attacks (low frequency: 1-2 attacks/month, high frequency 10-14 attacks/month) were recruited; all had suffered from migraine for 3 years or longer. High resolution, T₁-weighted datasets were collected from each patient using a 3D MPRAGE pulse sequence (TR/TE/TI=2100/2.74/1100ms, FA=12, 128 sagittal slices, res = 1.33 x 1.0 x 1.0 mm³). Subjects also underwent functional scans (TR/TE=2500/30ms, 41 coronal slices, res=3.5 x 3.5 x 3.5 mm³) as a thermal stimulus (3 noxious stimuli at pain threshold +1°C (Thr+1°C)) was applied to the dorsum of the hand (migraine side). For the data processing, anatomical volumes were segmented using Freesurfer image analysis software (<http://surfer.nmr.mgh.harvard.edu/>). A univariate analysis of variance for the hippocampus was used to assess the differences between the two cohorts while accounting for the differences in the total intracranial volume (3). fMRI analysis was carried out using FSL 4.1.2 (www.fmrib.ox.ac.uk/fsl). Functional maps were corrected using General Mixture Model analysis (GMM) (4).

Results: There were no significant differences in age or age of migraine onset between the two cohorts. High frequency migraine patients showed a decrease in volume in bilateral hippocampus (left hippocampus, p<0.022 and right hippocampus, p<0.044) relative to the low frequency migraine patients. Significantly reduced functional connectivity with hippocampus was observed in high frequency vs. low frequency migraine patients in contra-lateral supra marginal (SM) gyrus, bilateral temporal pole (TP), contra-lateral fronto-orbital, bilateral nucleus accumbens (NAc), bilateral insula (Ins), bilateral middle frontal (MF) gyrus, and contra-lateral para cingulate (PCing).



Hippocampal volumetric differences in high vs. low frequency migraine subjects. (Volumes have been normalized to the total intracranial volume to scale for the brain sizes).



Co

Conclusion: These findings suggest that there seems to be an association between the reduction of hippocampal volume and its functional connectivity changes with specific regions involved in pain processing that is associated with the frequency of migraine attacks.

Functional connectivity contrast of the hippocampus during intermittent heat stimuli (pain threshold +1°C on hand) in high frequency – low frequency migraine patients.

Acknowledgements: Supported by NIH grants to DB (K24NS064050 and R01NS056195) & by an unrestricted grant to DB from Merck & Co.

References: [1] Rothman and Mattson, 2010, Neuromolecular Med [2] Liu and Chen, 2009, Neurosci Bull [3] Buckner et al. 2004, NeuroImage, [4] Pendse et al, 2009, NeuroImage