High Resolution MRI Neuromorphometric Assessment of the Hippocampal Subiculum in Mood Disorders

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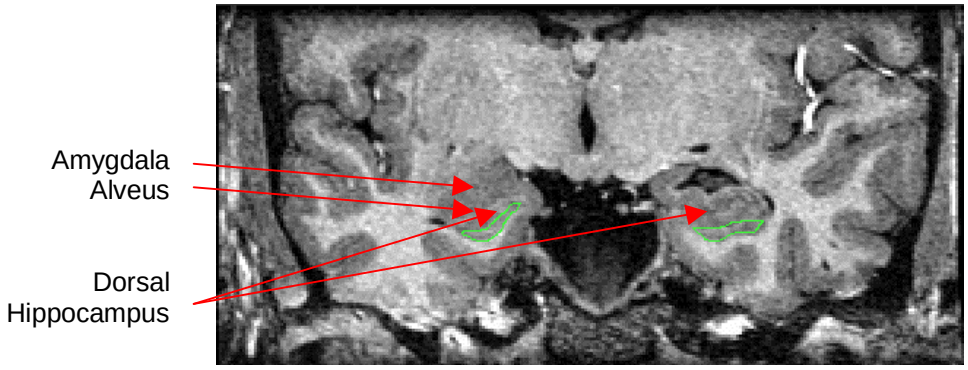
Background: Neuromorphometric MRI studies report reductions in hippocampal volume in mood disorders, although differences relative to control samples have been subtle, and were not confirmed by most replication attempts. Two post mortem studies of bipolar disorder (BD) found abnormal reductions of synaptic proteins in the subiculum (Eastwood et al 2000) and of the spine density on pyramidal cell apical dendrites in the subiculum and CA1 (Rosoklija et al 2000), which did not extend to other hippocampal subregions. Changes in neuropil, which occupies most of the grey matter volume, may thus be regionally specific, and volumetric measures of the entire hippocampus may reduce sensitivity to this difference. The current study investigated whether the subiculum can be reliably segmented in MRI images, and compared mean subiculum volumes between bipolar and control samples..

Methods: Medically healthy subjects ages 19 to 60 who were psychiatrically healthy (n=34; 25 female; mean age = 38.56 ± 10.8) or had bipolar disorder type II (n=17; 12 female; mean age =39.2 ± 9.5) were imaged using a GE 3T MRI scanner, running an MP-RAGE pulse sequence optimized for tissue contrast resolution, and voxel size of 0.6 x 0.6 x 0.6 mm. Between two and four 11.5 min scans were acquired and summed. The subiculum was manually segmented by a rater blind to diagnosis in coronal planes using MEDx 3.4.1. The subiculum was segmented using the anatomical landmarks of Duvernoy (1998), as grey matter ventral to the uncal sulcus or to the white matter lining that sulcus, from the anterior-most section where it appeared ventral to amygdala, through the head of hippocampus, ending caudally one plane before the hippocampal body separated from the head. To assess the specificity of findings in the subiculum/ventral CA1, the volumes of the remainder of the hippocampal head, entire hippocampus, and whole brain were also measured.

Results: Assessments of intrarater reliability (same image segmented by same rater on 2 separate days) showed mean volumes in mm^3 (SD) for measurements 1 and 2 were 392 (40) and 398 (42) on the left, respectively, and 415 (35) and 411(39) on right, respectively, with correlation coefficients for day 1 vs 2 measures of: left, r =0.826; right, r =0.820. Correlation coefficients for the hippocampal head and entire hippocampus all exceeded r =0.95. The mean volume of the left subiculum was significantly smaller in BD subjects than controls (p = 0.013). This difference remained after normalizing subicular volume by whole hippocampal volume and whole brain volume (p = 0.038 and 0.051, respectively). Neither the right subicular volume, nor the volumes of the control regions in the left hippocampal head minus subiculum, the entire left or right hippocampus or whole brain, significantly differed between BD and control samples.

Discussion: The volume of the human subiculum/ ventral CA1 region can be reliably measured in high resolution 3T MRI images, although the validity of this measure depends upon correlation between macroscopically evident anatomical landmarks with microscopically based cytoarchitectonic distinctions The abnormal reduction in the left subiculum/CA1 region volume in BD is consistent with reports from *post mortem* studies of BD that synaptic markers are reduced in the subiculum/ ventral CA1 region, but not in other hippocampal subregions, because the associated reduction in neuropil would presumably be evidenced by a corresponding reduction in grey matter volume.



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