Hippocampus volume in trauma-exposed veterans: What are the associated psychological processes?

Reduced hippocampal volume has been observed in posttraumatic stress disorder (PTSD)1, but the exact processes associated with hippocampal alterations in PTSD remain unclear. Given the role of the hippocampus in contextual representations and episodic memory formation2, and a recently reported relationship between perceived stress and hippocampal volume3, we investigated relationships between retrospectively reported subjective threat perception, combat exposure, and hippocampal volume.

We analyzed MRI data from 51 male, combat-exposed veterans of Operations Enduring Freedom/Iraqi Freedom with a broad spectrum of PTSD symptoms. On the basis of total Clinician-Administered PTSD Scale (CAPS) scores, veterans were divided into a PTSD-symptoms (PTSS) group (CAPS ≥ 20; N=34) and a combat-exposed control (CEC) group (CAPS < 10; N=17).

Previous studies have mainly compared hippocampal volume in groups with and without PTSD. Here, we looked at hippocampal volume as a function of continuous variability in distinct PTSD symptom clusters, and in relation to individual differences in a construct that we call Perceived Threat Bias.

Perceived Threat Bias (PTB)

A new construct for PTSD research.

Previous research has demonstrated that the impact of combat exposure on PTSD symptoms is mediated by individual differences in perceived threat4. We quantified the relationship between these measures by creating a measure of Perceived Threat Bias (PTB). After z-transforming scores on the Combat Exposure Scale5 and Perceived Threat from the Deployment Risk and Resilience Inventory (DRRI)6, we subtracted the former from the latter. The resulting metric reflects, in standard deviation units, over- or under-estimates of perceived threat relative to the reported frequency and severity of combat exposure.

PTSD numbing/avoidance symptoms are inversely related to hippocampus volume

Increasing PTSD symptoms were associated with smaller hippocampus volume across the entire sample (r(49) = -0.30, p = 0.030) and in the PTSS group alone (r(32) = -0.35, p = 0.040).

PTB and numbing/avoidance symptoms are uniquely associated with reduced hippocampus volume

Across the entire sample, PTB was correlated with CAPS:C symptoms (r(49) = 0.31, p = 0.024) but not other CAPS clusters (r < 0.07).

Conclusions

We extend previous reports of smaller hippocampus volume in PTSD, showing a continuous relationship with symptom scores, particularly avoidance/numbing symptoms. We report a novel relationship between Perceived Threat Bias and reduced hippocampus volume, irrespective of PTSD symptom severity. These factors explained unique variance in hippocampal volume, suggesting that independent processes are related to structural alterations in trauma-exposed veterans.

References

Freesurfer hippocampus segmentation

Cortical reconstruction and volumetric segmentation was performed with the Freesurfer image analysis suite (http://surfer.nmr.mgh.harvard.edu/). Processing included motion correction, skull removal, intensity normalization, registration, segmentation of subcortical white and deep gray matter structures, white matter and pial surface tessellation, and cortical surface parcellation. Bilateral hippocampus volumes were extracted for the automatically segmented structure for each subject.

Freesurfer hippocampus segmentation

This relationship was present for both the PTSS (r(32) = -0.38, p = 0.025) and CEC groups (r(15) = -0.48, p = 0.051), suggesting that trauma-related hippocampal alterations may be observed in the relative absence of PTSD symptoms.

Across the entire sample, increases in perceived threat bias were associated with smaller hippocampus volume (r(49) = -0.42, p = 0.0021).

The relationship with hippocampus volume was strongest for CAPS avoidance/numbing symptoms (Cluster C; (r(49) = -0.38, p = 0.0066; FTSS r(32) = 0.44, p = 0.0084). CAPS:C symptoms predicted unique variance in hippocampus volume in a multiple regression analysis including all 3 symptom clusters.

Although the two groups reported equivalent levels of combat exposure (r(49)=1.11, p=0.26), the PTSS group reported significantly greater perceived threat during combat exposure, relative to the CEC group (r(49) = 3.03, p = 0.004). Scores on both scales showed approximately normal distribution across the entire sample.

A plot of combat exposure vs. perceived threat, with the dashed line indicating zero PTB. Individuals above this line reported elevated perceived threat relative to the amount of combat experienced and thus have positive PTB, whereas individuals below the line have negative PTB.

The CEC group had numerically but not significantly lower PTB than the PTSS group (r(49)=1.48, p=0.10). In the 17 PTSS participants with positive PTB (PTSSHigh), there was no relationship between combat exposure and perceived threat (r=0.08, p=0.25). However, there was a strong relationship between these measures in the 17 symptom participants with negative PTB (PTSSLow): r=0.87, p=0.001 and in the CEC group (r=0.70, p=0.002).

Across the entire sample, increases in perceived threat bias were associated with smaller hippocampus volume (r(49) = -0.42, p = 0.0021).

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Across the entire sample, PTB was correlated with CAPS:C symptoms (r(49) = 0.31, p = 0.024) but not other CAPS clusters (r < 0.07).

Despite this shared variance, and common inverse correlations with hippocampus volume, PTB and CAPS:C each predicted unique variance in hippocampus volume in a simultaneous linear regression model.

Funding support provided by an NSF graduate research fellowship, the Dana Foundation, the UW Institute for Clinical and Translational Research, NIH/NIMH (R01-MH043454 and T32-MH19381), and NICHD (1R01HD033522). Thanks to Regina Lapate, Drew Fox, Stacey Schaefer, Joe Wielgus, & Kate Rifken.