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Relationship of hippocampal volumes and posttraumatic stress disorder symptoms over early post-trauma periods

Hong Xie, MD, PhD.,

Department of Neurosciences, University of Toledo, Toledo, OH

Meredith Claycomb Erwin, MA.,

Department of Psychology, University of Toledo, Toledo, OH

Jon D. Elhai, PhD.,

Department of Psychology, University of Toledo, Toledo, OH

John T. Wall, PhD.,

Department of Neurosciences, University of Toledo, Toledo, OH

Marijo B. Tamburrino, MD.,

Department of Psychiatry, University of Toledo, Toledo, OH

Kristopher R. Brickman, MD.,

Department of Emergency Medicine, University of Toledo, Toledo, OH

Brian Kaminski, DO.,

Department of Emergency Medicine, ProMedica Toledo Hospital, Toledo, OH

Samuel A. McLean, MD.,

Department of Anesthesiology, University of North Carolina at Chapel Hill, Chapel Hill, NC

Israel Liberzon, MD., and

Department of Psychiatry, University of Michigan, Ann Arbor, MI

Xin Wang, MD, PhD.

Department of Psychiatry, University of Toledo, Toledo, OH

Abstract

Background—Smaller hippocampal volume is associated with more severe posttraumatic stress disorder (PTSD) symptoms years after traumatic experiences. Posttraumatic stress symptoms appear early following trauma, but the relationship between hippocampal volume and PTSD symptom severity during early post-trauma periods is not well understood. It is possible that the inverse relationship between hippocampal volume and PTSD symptom severity is already present

Corresponding author: Xin Wang, Department of Psychiatry, MS#1193, the University of Toledo, 3000 Arlington Ave. Toledo, OH 43614 Phone: 419-383-4452. Fax: 419-383-3008. xin.wang2@utoledo.edu.

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soon after trauma. To test this possibility we prospectively examined the association between hippocampal volumes and severity of PTSD symptoms within weeks to months after trauma due to motor vehicle collision (MVC).

Methods—Structural MRI scans of 44 survivors were collected about 2 weeks and again at 3 months after MVC to measure hippocampal volumes. The PTSD checklist (PCL) was used to evaluate PTSD symptoms at each scan time. Full (n=5) or partial (n=6) PTSD was evaluated using CAPS at 3 months.

Results—Left hippocampal volumes at both time points negatively correlated with PCL scores, and with subscores for re-experiencing symptoms at 3 months. Left hippocampal volumes at 3 months also negatively correlated with hyperarousal symptoms at 3 months. Finally, neither left nor right hippocampal volumes significantly changed between 2 weeks and 3 months post trauma.

Conclusions—The results suggest that small hippocampal volume at early post-trauma weeks is associated with increased risk for PTSD development. Furthermore, the inverse relationship between hippocampal volume and PTSD symptoms at 3 months did not arise from post-trauma shifts in hippocampal volume between 2 weeks and 3 months after trauma.

Keywords

motor vehicle collision; PCL; re-experiencing; longitudinal; acute trauma; structural MRI

Introduction

Posttraumatic stress disorder (PTSD) is a debilitating condition with a major public health impact as reflected by findings that about 7% of the U.S. population suffers from PTSD at some point in life (1). PTSD involves major financial and societal costs (2). Existing pharmacological and behavioral treatments are only partially effective and often leave residual symptoms (3). PTSD symptoms involve persistent re-experiencing of the trauma, avoidance of trauma-related circumstances, hyperarousal, and negative alterations in mood and cognition lasting more than a month after experiencing a traumatic event that threatens one's life or bodily integrity. Understanding how PTSD symptoms develop may provide clues for understanding PTSD pathophysiology and a potential basis for developing early interventions to prevent PTSD. Identification of early post-trauma brain factors that are associated with PTSD symptom development is thus emerging as an important goal that has major public health implications.

Human brain imaging studies have shown associations between chronic PTSD symptoms and structural and functional alterations in brain regions involved in the processing and regulation of emotions (4, 5). Among brain structural alterations, unilateral or bilateral hippocampal volumes are commonly reported to be smaller in adult patients who suffer from chronic PTSD as compared to non-PTSD adult trauma survivors (6–9). Hippocampal volumes in adult PTSD patients negatively correlate with chronic PTSD symptom severity (6, 10–12), particularly the severity of re-experiencing symptoms. Rodent and human studies of hippocampal function suggest the hippocampus plays a key role in contextual learning and modulation of fear responses (13, 14). Hippocampal volume also negatively correlates with memory deficits in adult PTSD patients (15, 16). Together, these findings could suggest

that small hippocampal volumes in adult chronic PTSD patients may be related to abnormal contextual processing of trauma related cues, which in turn results in failure to inhibit fear responses in safe environments (13, 14). Interestingly, recent studies suggest that PTSD patients who respond poorly to prolonged exposure therapies have smaller hippocampal volumes compared to patients who respond well or to non-PTSD controls (17, 18). Conversely, hippocampal volumes in PTSD patients may increase after some treatments that reduce PTSD symptoms (19, 20). These findings suggest that hippocampal volume may be associated with mechanisms that have therapeutic effects on PTSD symptoms.

Trauma survivors often have PTSD symptoms soon after a traumatic experience (21, 22), but time periods when small hippocampal volumes become associated with PTSD symptoms have received little study (10, 23). One twin study of veterans and their homozygous twins reported that smaller hippocampal volumes were seen in both veterans with PTSD and in their non-combat-exposed twins who did not have PTSD (10). This suggests that smaller hippocampal volumes in the veterans with PTSD may have been a pre-existing, potentially genetic-related condition already present prior to trauma exposure in adulthood. Another study reported smaller hippocampal volumes in adult PTSD patients with a previous history of childhood abuse relative to healthy controls with no history of childhood abuse (23). This could suggest that smaller hippocampal volumes might be related to early life trauma. However, other findings on the relationship between hippocampal volumes and pediatric PTSD appear inconsistent with this thinking (24). It remains possible that genetic factors and/or early life trauma may contribute to a smaller hippocampal volume and subsequently to a higher PTSD risk after adult trauma. If a smaller hippocampal volume is indeed a risk factor for PTSD that exists prior to trauma exposure in adulthood, it might contribute to development of PTSD symptoms during early post-trauma periods.

Given the above possibility, it is surprising that little attention has been paid to relationships between hippocampal volume and PTSD symptoms at early post-trauma periods. A single study in 2001 in 11 PTSD and 27 non-PTSD trauma survivors reported no differences in hippocampal volumes at both 1 week and 6 months after trauma and no relationship between hippocampal volume and PTSD symptoms over these periods (25). In the 16 years since that study, improved MRI techniques and automated analytical approaches have greatly increased sensitivity of neuroimaging methods to provide better detection of hippocampal changes. The importance of the issue, limited existing studies, and current technical advancements clearly justify re-examination of relationships between hippocampal volumes and PTSD symptoms at early post-trauma periods.

Based on existing findings of an inverse relationship between hippocampal volume and PTSD symptoms in adult chronic PTSD patients, we hypothesized that hippocampal volumes are inversely associated with PTSD symptom severity in early weeks to months after trauma. To test this hypothesis, we recruited survivors of motor vehicle collision (MVC) trauma from Emergency Departments (EDs) and examined hippocampal volume and PTSD symptoms during the initial 2 weeks to 3 months after this trauma.

Methods and Materials

Subjects

Adults (18–60 years old), admitted to hospital EDs within 48 hours of MVCs were recruited. The MVCs caused significant trauma, as indicated by the facts that most vehicles were no longer drivable; moreover, all subjects had physical injuries that were considered threatening to well-being by first responders and, thus, required immediate medical attention in EDs. Subjects were excluded if they were pregnant, under the influence of alcohol or recreational drugs at the time of MVC, suffered from major injuries or moderate to severe traumatic brain injury (TBI), had conditions that precluded either assessment in the ED or MRI procedures, or had major medical problems affecting general health. An initial sample of 78 survivors who gave written informed consent underwent a first MRI scan about 2 weeks after MVC. Fifty-three returned for a follow-up scan at 3 months. Forty-four had useable structural MRI data at both time points and were included in the final analyses. Loss of subjects was due to self-withdrawal (n=3), loss of contact (n=22), changes in physical condition (e.g., pregnancy, surgery, or re-injury)(n=7), or scan motion artifacts (n=2). The study was approved by The University of Toledo Institutional Review Board.

Psychological and other assessments

To assess PTSD symptoms, survivors completed the self-report PTSD Checklist-Stressor Version (PCL) questionnaire at 2 weeks and 3 months after MVC. Subscores of individual clusters of re-experiencing, avoidance, and hyperarousal symptoms were also derived from the PCL. Except for one subject who missed the initial PCL, all survivors completed the PCL at both time points. The PCL provides valid measures of PTSD symptoms (26), and a cutoff score of 44 has been employed for PTSD diagnosis after MVC (27). In addition, subjects were interviewed at 3 months by a clinical psychology PhD candidate supervised by a clinical psychologist (author JE), using the Clinician Administered PTSD Scale (CAPS) and the Mini-International Neuropsychiatric Interview (M.I.N.I. Version 6.0.0)(28). The MVC was specified as the index trauma in the PCL questionnaire and CAPS interview. CAPS was used to diagnose PTSD (1 re-experiencing, 3 avoidance/numbing, and 2 hyperarousal symptoms) according to DSM-IV-TR criteria (29), or partial PTSD (1 re-experiencing, and either 3 avoidance/numbing or 2 hyperarousal symptoms)(30). Partial PTSD was identified because partial PTSD with impairment of social function often requires clinical intervention (31). Acute MVC related pain was evaluated using the Numeric Pain Scale (NPS) at ED admission. Survivors completed the Rivermead Post-Concussion Symptoms Questionnaire (RPCSQ)(32). A mild TBI (mTBI) diagnosis was assessed by application of the criteria of the American Congress of Rehabilitation Medicine to ED medical records and RPCSQ (33). Psychotropic medication use was identified from ED medical records and self-report surveys.

Data acquisition and structural MRI processing

Subjects were scanned using a 3T General Electric Signa HDx MRI scanner. A high-resolution T1-weighted structural MRI image was obtained using a previously validated 3-D Volume Inversion Recovery Fast Spoiled Gradient Recall Echo (IR-FSPGR) protocol (repetition time = 7.9 milliseconds, echo time = 3 milliseconds, inversion time = 650

milliseconds, field of view = 25.6×25.6 cm, matrix= 256×256 , slice thickness=1 mm, voxel dimensions= $1 \times 1 \times 1$ mm, 164 contiguous axial slices)(34). MRI images were reviewed by a radiologist and no qualitative brain abnormalities were found.

Hippocampal volume and intracranial volume (ICV) were derived using automated FreeSurfer programs (<https://surfer.nmr.mgh.harvard.edu>)(35). Measures of hippocampal volume were based on 3D whole-brain segmentation and labeling according to a probabilistic atlas. FreeSurfer measurements of hippocampal volumes accurately correlate with manual measures (36) and have been shown to have high reproducibility (37). FreeSurfer segmentation was visually verified by an inspector blinded to psychological assessments.

Statistical analyses

First, progressive changes in hippocampal volume and PCL scores between 2 weeks and 3 months were tested across all subjects using repeated measures ANOVA (RM-ANOVA), with controls for age and gender. An additional covariate for RM-ANOVA of hippocampal volumes was ICV (average of the two-time points), while acute NPS scores were used for the RM-ANOVA of PCL scores. Acute NPS scores were considered because chronic PTSD increases with acute pain (38). Second, we examined correlations between (a) hippocampal volumes at 2 weeks and PCL scores at 2 weeks and at 3 months, and (b) hippocampal volumes at 3 months and PCL scores at 3 months. We also reexamined the above correlations of hippocampal volumes and PCL scores with partial correlations, controlling age, gender, ICV and NPS scores. A Bonferroni adjusted $P < 0.008$ (multiple comparisons of six correlations from a starting $P < 0.05$) was accepted as significant. Finally, if hippocampal volume on a given side significantly correlated with PCL total scores in the partial correlation analyses, post hoc partial correlations between hippocampal volumes and PCL subscores of individual symptom clusters at both time points were performed. A Bonferroni adjusted $P < 0.005$ (multiple comparisons of nine correlations from a starting $P < 0.05$) was considered significant for this analysis. Hippocampal volumes and PCL scores and subscores were normally distributed, falling within benchmarks of skewness (< 2) and kurtosis (< 7)(38). Statistical analyses were conducted using SPSS23, and data are reported as means ($\pm$ standard deviation).

Results

Sample characteristics are presented in Table 1. Mean NPS score in the ED (7.3) suggested MVC survivors experienced severe acute pain. At 3-month follow-up, 41 (93% of 44) survivors completed CAPS interviews, and 11 met diagnosis of full ($n=5$) or partial ($n=6$) PTSD. Eleven subjects reported one or more other psychiatric conditions, or use of psychotropic medications excluding pain medications (Table 1).

PCL scores at 2 weeks and 3 months

RM-ANOVA of PCL scores across all subjects indicated PCL scores did not significantly differ at 2 weeks and 3 months ($F(1, 39) = 0.421$, $p = 0.520$). This was likely due to relatively stable PCL scores in the subgroup of 11 survivors who developed PTSD

(Supplemental Results). Acute NPS scores significantly affected PCL scores ($F(1, 39) = 15.165, p < 0.001$). There were no significant effects of age and gender on PCL scores and no interaction effects of time with age, gender, and acute NPS on PCL scores.

Hippocampal volumes at 2 weeks and 3 months

RM-ANOVA of hippocampal volumes across all subjects indicated left and right hippocampal volumes did not significantly change from 2 weeks to 3 months (left: $F(1, 40) = 2.387, p = 0.130$; right: $F(1, 40) = 0.251, p = 0.619$). Effects of ICV on hippocampal volumes were significant (left: $F(1, 40) = 12.073, p = 0.001$; right: $F(1, 40) = 11.696, p = 0.001$), but effects of age and gender on hippocampal volumes were not significant nor were any interaction effects of time with age, gender, and ICV. In additional analyses in a subgroup of 41 subjects who completed CAPS, left hippocampal volume was significantly smaller in the PTSD vs. non-PTSD group at both time points; the interaction of time by diagnosis group was not significant (Supplemental Results).

Correlations between hippocampal volumes and PTSD symptom severity

Hippocampal volumes at 2 weeks were not significantly correlated with PCL scores at 2 weeks (Table 2). In contrast, left hippocampal volumes at 2 weeks significantly negatively correlated with PCL scores at 3 months ($r = -0.478, p = 0.001$, Bonferroni corrected; Fig. 1A; Table 2). This likely mainly reflected a negative correlation between volumes of the left CA1 sub-region and PCL scores (Supplemental Results). The respective correlation for the right hippocampus was not significant. Left hippocampal volumes at 3 months also significantly negatively correlated with PCL scores at this time ($r = -0.467, p = 0.001$, Fig. 1B; Table 2), but the respective correlation for the right hippocampus was not significant ($r = -0.279, p = 0.067$). The significant finding regarding left hippocampal volumes at 3 months likely reflected mainly significant negative correlations of the volumes of left CA1 and molecular layer sub-regions with PCL scores (Supplemental Results). In addition, changes from 2 weeks to 3 months in left hippocampal volume vs. PCL scores were not significantly correlated ($r = -0.084, p = 0.610$).

Because RM-ANOVAs indicated hippocampal volumes were affected by ICV and PCL scores were affected by NPS scores, we tested the relationship between hippocampal volume and PCL scores when controlling for ICV and NPS scores (in addition to age and gender) with partial correlation analyses. Left hippocampal volumes at both 2 weeks and 3 months remained significantly negatively correlated with PCL scores at 3 months (2 weeks: $r = -0.430, p = 0.006$; 3 months: $r = -0.444, p = 0.004$, Bonferroni corrected; Table 2: *partial correlation*). Correlations between hippocampal volumes and acute NPS scores were not significant. In addition, smaller left hippocampal volumes at 2 weeks predicted higher CAPS scores at 3 months (correlation $r = -0.446, p = 0.003$; partial correlation $r = -0.428, p = 0.008$; Bonferroni corrected; $n = 41$). Other correlations between hippocampal volumes and CAPS scores were not significant.

Given the above significant partial correlations with overall PCL scores, we examined the association between left hippocampal volume and PCL subscores for the 3 individual clusters of re-experiencing, avoidance, and hyperarousal symptoms. Left hippocampal

volumes at 2 weeks were significantly negatively correlated with re-experiencing symptoms at 3 months (partial correlation $r = -0.465$, $p = 0.002$, Bonferroni corrected; Fig.2A). Similarly, left hippocampal volumes at 3 months were significantly negatively correlated with re-experiencing symptoms at 3 months ($r = -0.444$, $p = 0.004$; Fig.2B). Finally, left hippocampal volumes at 3 months were significantly negatively correlated with hyperarousal symptoms at 3 months ($r = -0.453$, $p = 0.003$; Fig.2C). Left hippocampal volumes at 2 weeks were not correlated with any subscores at 2 weeks, and all other correlations were not significant.

Discussion

Hippocampal volume has been frequently studied in chronic PTSD patients, however, little work has been directed at potential relationships between hippocampal volumes and PTSD symptoms during early post-trauma periods. We found that left hippocampal volumes at both 2 weeks and 3 months following trauma were inversely associated with severity of PTSD symptoms reflected by PCL scores at 3 months. These findings suggest that trauma survivors who have smaller left hippocampal volumes during initial weeks and months after trauma may exhibit more severe PTSD symptoms within initial post-trauma months. The inverse relationship between left hippocampal volume and PTSD symptoms was not present at 2 weeks, but became apparent at 3 months. Symptom cluster analyses revealed significant negative correlations between left hippocampal volumes at both 2 weeks and 3 months vs. re-experiencing symptom severity at 3 months, and between left hippocampal volumes at 3 months and hyperarousal symptom severity at 3 months. The current findings differ from findings of a previous report that found no relationship between hippocampal volumes and PTSD symptoms from 1 week to 6 months after trauma (25). In further contrast to that report, we found left hippocampal volumes in survivors with PTSD were significantly smaller at both 2 weeks and 3 months than those of non-PTSD survivors. The reason for differences in findings is unclear. One possibility is methodological differences in the two studies, including, for example, differences in magnetic field strength, imaging resolution, use of automated volume measurement techniques, and/or the greater homogeneity of trauma conditions in the present study. In addition, we found no significant change in PTSD symptoms from 2 weeks to 3 months across all survivors, which may have been due to unchanging higher levels of symptoms in survivors who developed PTSD. Finally, hippocampal volumes did not change between 2 weeks and 3 months. Together, these results suggest an association between left hippocampal volume in early weeks to months after trauma and severity of early PTSD symptoms by 3 months after trauma, especially re-experiencing and hyperarousal symptoms. This could reflect a “failure to recover” from early post-traumatic responses in subjects with a smaller hippocampus. We interpret these findings to indicate that small hippocampal volume at early post-trauma periods is associated with development of PTSD symptoms in adult trauma survivors.

Negative correlation of left hippocampal volumes with severity of PTSD re-experiencing symptoms 3 months after trauma

Previous studies have reported a negative relationship between hippocampal volume and chronic PTSD symptoms over years following trauma (39, 40). The current finding that left

hippocampal volumes at 2 weeks and 3 months were negatively correlated with severity of re-experiencing symptoms at 3 months could suggest that re-experiencing symptoms might be related to early post-trauma hippocampal memory dysfunction linked to a smaller hippocampus. Studies show hippocampus is involved in the formation of memories (41), and larger hippocampal volume has been linked to greater ability to discriminate between different memory contexts (42). Both extinction recall and fear renewal involve context dependent memory processes, and chronic PTSD patients have deficits in fear extinction recall and fear renewal (13) that are associated with reduced activation in the hippocampus (43). In addition, a pilot study involving a 1 year administration of selective serotonin reuptake inhibitor in chronic PTSD patients suggested that increases in hippocampal volume after treatment were associated with improvement in memory and PTSD symptoms (19). This is consistent with potential links between hippocampal volume and both memory function and PTSD recovery. If smaller hippocampal volume is related to deficits in contextual memory processing that lead to intrusive symptoms, the current symptom and hippocampal volume findings could suggest that hippocampal related memory processing deficits were present or developed within weeks to months following trauma.

Left hippocampal volumes negatively correlated to hyperarousal symptoms 3 months after trauma

We also found that left hippocampal volume at 3 months negatively correlated with severity of hyperarousal symptoms 3 months after trauma. Functional imaging studies suggest that PTSD hyperarousal symptoms are associated with hypoactivity in prefrontal emotion regulation regions, including prefrontal and anterior cingulate cortical regions, which, in turn, may underlie failure to inhibit negative emotion responses (4, 44). Further studies suggest that hippocampal activation is positively coupled to prefrontal activation (13, 45). Thus alterations in hippocampus may also affect emotion regulatory functions of prefrontal cortex. Given this, smaller hippocampal volume following trauma might be associated with less efficient emotion regulatory function due to deficient contextual processing or other dysfunctions. A previous report indicated the volume of the left superior frontal gyrus progressively decreased over 2 weeks to 3 months in MVC survivors who met PTSD criteria at 3 months after MVC (34). These findings suggest prefrontal regions may also be affected over the same early post-trauma period during which the negative association between hippocampal volume and hyperarousal symptoms is developing. Further studies are needed to examine relationships between hippocampal volume and activation in hippocampus, prefrontal cortex, and related emotion regulation pathways.

Hippocampal volumes during early post-trauma

We found hippocampal volumes did not change from 2 weeks to 3 months. This is consistent with a previous report of no changes in hippocampal volumes in PTSD patients from a week to 6 months after trauma (25). Although a twin study has suggested that pre-existing smaller hippocampal volume may predispose to PTSD (10), other studies suggest that smaller hippocampal volume or decreased grey matter density may develop slowly over long post-trauma periods in both chronic PTSD patients and trauma survivors without PTSD (46, 47). For example, a voxel-based morphometry study reported no change in hippocampal grey matter density from pre-earthquake to 3–4 months after earthquake trauma in survivors who

did not have PTSD (48); however, a significant decrease in hippocampal grey matter density appeared in these survivors a year after the earthquake (46). This raises the possibility that changes in hippocampal structure may develop slowly and gradually over the year following trauma. It is possible that persistent high stress symptoms in PTSD patients contributed to more gradual hippocampal volume reduction over the course of a year or longer. Consistent with this possibility, animal studies suggest that persistent stress alters brain neurochemistry including, e.g., levels of glucocorticoids and brain derived neurotrophic factor (BDNF)(5, 49). Hippocampus may constitute one target of stress hormones, and high levels of glucocorticoids and low BDNF can reduce synaptic density, number of glial cells, and neurogenesis in hippocampus (50). These mechanisms might lead to changes in hippocampal volume that arise over long intervals. Future studies with longer post-trauma periods may reveal a progression of changes in hippocampal structure. The present results suggest that the inverse relationship between hippocampal volume and PTSD symptoms at 3 months could be accounted for either by a pre-existing small hippocampal volume at the time of MVC, or by a decrease in hippocampal volume within the post-trauma days prior to our initial 2 week observations, or both. Future research could longitudinally examine hippocampus volume prior to trauma and within days after trauma to address this question.

Clinical relevance

To better target treatment resources to trauma survivors at high risk, there is substantial interest in early clinical identification of individuals who are vulnerable to PTSD development. Current understanding does not permit early identification (51). The present findings suggest PTSD symptoms may be related in part to early post-trauma structural properties of the hippocampus. Our findings introduce the issue of using hippocampal volume, either alone or in conjunction with other factors, in early days after trauma to identify survivors at high risk for PTSD. Additional work is required to test this possibility.

Limitations

The present study has the following limitations. First, we had a relatively small sample. Larger samples are needed to confirm the current findings. Second, we used PCL to measure PTSD symptoms. Use of PCL is appropriate to evaluate early posttraumatic stress symptom severity before a PTSD diagnosis can be established after the required one-month period, but questions regarding the specificity of PCL as compared to structured clinical interviews can be raised (26). We confirmed that left hippocampal volumes at 2 weeks negatively correlated with CAPS scores at 3 months in a subgroup of subjects. This provides additional confidence in our findings. Third, a majority of our subjects did not meet full PTSD diagnosis at 3 months after MVC. This potentially limits the findings to survivors with mild to moderate PTSD symptoms. In addition, the use of DSM-IV measures may limit generalization of the findings to DSM-5 diagnosis. Fourth, small hippocampal volumes have been linked to depression and other psychiatric symptoms (52, 53). We have begun to explore the specificity of the present findings to PTSD symptoms in analyses which exclude all subjects with other psychiatric conditions and who were taking psychotropic medications. The negative correlations of left hippocampal volumes at both 2 weeks and 3 months with PCL scores at 3 months remain significant at trend levels even after these exclusions (Supplemental Results). The specificity of the present findings needs further

examination. Fifth, PTSD symptoms may also be associated with other brain structures. For example, although correlations of amygdala volumes and PCL scores were not significant after controlling for effects of age, gender, ICV, and acute pain, i.e. as was done in hippocampal analyses, some correlation coefficients in amygdala analyses approximate correlation coefficients in hippocampus (Supplemental Results). Further study of amygdala and other structures is needed. Finally, potential risk factors for PTSD involving childhood trauma history were not studied.

Conclusion

The findings suggest that left hippocampal volumes at early post-trauma weeks may predict severity of PTSD symptoms, particularly re-experiencing symptoms, over subsequent post-trauma months. This supports a hypothesis that structural brain properties, like hippocampal volume, are associated with early post-trauma predispositions for PTSD symptom development and maintenance. Further studies of these associations can test the usefulness of structural measures for early identification of trauma survivors at high risk for PTSD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig 1.
Negative correlations between PCL scores at 3 months and left hippocampal volumes at (A) 2 weeks and (B) 3 months (n=44).

Fig 2.

Negative correlations between PCL re-experiencing subscores at 3 months and (A) left hippocampal volumes at 2 weeks, and (B) left hippocampal volumes at 3 months. (c) Negative correlation between PCL hyperarousal subscores at 3 months and left hippocampal volumes at 3 months (n=44).

Table 1

Demographics and symptoms

	mean±SD	range
Number of survivors	44	
Male/Female (m/f)	13 (30%)/ 31(70%)	
Age (years)	32.8 ± 11.3	19 – 58
Post-MVC days of first scan	10.3 ± 5.1	2 – 25
Post-MVC days of second scan	109.2 ± 14.1	85 – 147
NPS scores at ED	7.3 ± 2.1	1 – 10
PCL scores within 2 weeks	42.0 ± 15.8	17 – 77
PCL scores at 3 months	36.3 ± 15.6	17 – 70
CAPS scores at 3 months (n=41)	24.4 ± 23.6	0 – 76
CAPS diagnosis (n=41)	11 (27%) PTSD (5 full / 6 partial)	
Other psychiatric conditions ^a (number of survivors) (n=41)	MDD history (2), GAD (4), OCD (4), life time PTSD (3), substance dependence (1)	
psychotropic medications (number of survivors)	Pain medications (17)	
	Prozac/Xanax (1), Valium (2), Celexa (1), Trazadone (1)	
mTBI evaluation (n=38)	13 (34%) met MTBI criteria	

^a Other psychiatric conditions include generalized anxiety disorder (GAD), obsessive-compulsive disorder (OCD), major depressive disorder (MDD) history, life time PTSD, and substance dependence. Subjects could have more than one condition.

Table 2

Hippocampus volumes and correlations with PCL scores in all survivors

volume (mm ³)		correlation with PCL scores		correlation with PCL scores	
2 weeks	3 months	2 weeks	3 months	2 weeks	3 months
mean (SD)	mean (SD)	r (P)	r (P)	r (P)	r (P)
Left 4049.4 (389.1)	4059.2 (415.3)	-0.358 (0.018)	-0.478 (0.001)*	-0.467 (0.001)*	-0.467 (0.001)*
Right 4172.3 (365.5)	4168.5 (371.5)	-0.176 (0.258)	-0.261 (0.087)	-0.279 (0.067)	-0.279 (0.067)
<i>Partial correlation</i>					
Left		-0.324 (0.044)	-0.430 (0.006)*	-0.444 (0.004)*	-0.444 (0.004)*
Right		-0.031 (0.854)	-0.172 (0.288)	-0.224 (0.165)	-0.224 (0.165)

Partial correlations controlled for age, gender, ICV, and acute NPS scores.

* : significant at a Bonferroni adjusted p<0.008 (multiple comparisons of six correlations from a starting P<0.05)