

Hippocampal Volumes in a Sample of Trauma Patients: A Possible Neuro-Protective Effect of Dissociation

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Abstract: *Background:* We sought to determine hippocampal volumes in a sample of inpatients in a Trauma Program specializing in posttraumatic stress disorder and dissociative disorders.

Methods: We measured whole brain and left and right hippocampal volumes on MRI in a sample of 20 inpatients in a Trauma Program and 20 controls.

Results: There were no differences between the two groups. Nineteen inpatients also completed a set of diagnostic and symptom measures; 16 met criteria for posttraumatic stress disorder (PTSD); the average score on the Dissociative Experiences Scale was ($M = 45.4$, $SD = 20.1$); and the average score on the secondary features of dissociative identity disorder section of the Dissociative Disorders Interview Schedule was ($M = 9.1$, $SD = 4.9$).

Conclusion: We hypothesized that dissociation may have a neuro-protective effect, which accounts for the normal hippocampal volumes in the patients, despite their PTSD and trauma histories.

Keywords: Childhood trauma, dissociation, dissociative disorders, hippocampal volume, MRI, posttraumatic stress disorder.

BACKGROUND

Hippocampal volumes have been measured in a variety of different diagnostic groups including schizophrenia and first episode psychosis [1], schizotypal personality disorder [2], depression [3, 4], obsessive-compulsive disorder [5, 6], borderline personality disorder ([7, 8], posttraumatic stress disorder (PTSD)) [9-15], and dissociative identity disorder (DID) [16], and also in additional traumatized populations [17-21]. In many of these studies, but not all, hippocampal volumes have been reduced compared to normal controls.

In one prior study on patients with DID [16], hippocampal volumes were reduced by 19.2% in patients compared to controls, but this difference disappeared when age was controlled for as a covariate. In an additional study [22] there were no differences in hippocampal volume between patients with dissociative disorders and controls, while in a third [23] there was reduced hippocampal volume in patients with DID and dissociative disorder not otherwise specified.

Despite the negative findings in two out of three prior studies of hippocampal volume in individuals with dissociative disorders, we hypothesized that we would find reduced hippocampal volumes on MRI in a sample of Trauma Program inpatients with PTSD, high levels of dissociation, and severe childhood trauma, compared to a non-clinical control group. Although we could not test this hypothesis with our methodology, we assumed that the reduced hippocampal volume we would observe would have

been caused by the biology of reactions to psychological trauma. We were especially interested in conducting future research trying to determine whether reduced hippocampal volumes in the patients would normalize during the process of recovery, as observed by Ehling, Nijenhuis and Krikke [23].

In this context, we were struck by the fact that in the PTSD literature, reduced hippocampal volume is assumed to be due to the psychophysiology of trauma: one mechanism of this effect is thought to be based on increased levels of cortisol that occur in response to trauma; the cortisol affects gating mechanisms in hippocampal neurons; this results in toxic products of brain metabolism entering the cells, which in turn causes cell damage and death [24]. Additional mechanisms such as a neurotoxic effect of excitatory neurotransmitters like glutamate may also contribute. This hypothesis is supported by controlled animal studies [25].

In contrast, in the literature on hippocampal volume in schizophrenia, depression and obsessive-compulsive disorder [1-6], PTSD and trauma are not mentioned, and the implicit assumption is that reduced hippocampal volume is due to endogenous disease. We made an additional hypothesis, not tested in the present study, that reduced hippocampal volume in these other disorders is due to chronic trauma experienced by a subgroup of the individuals with these diagnoses.

We assume that there is a range of endogenous vulnerabilities, but that reduced hippocampal volume rarely occurs in the absence of environmental trauma. Thus, a genetic predisposition to hippocampal atrophy is a necessary but not a sufficient cause of reduced hippocampal volume in most cases, irrespective of diagnosis. There is a subset of cases, we assume, in which the endogenous predisposition is so strong that minimal or no trauma is required for

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expression of the phenotype (reduced hippocampal volume). In contrast, at the opposite end of the spectrum of genetic predisposition, there could be cases of reduced hippocampal volume with a normal genotype if the dose of trauma is severe enough. The genetic predisposition, we assume, based on the evidence to date, is not specific to any DSM-5 diagnostic category, and usually but not always requires trauma for the phenotype to be expressed. Thus, in any diagnostic category, we expect to find cases with and without hippocampal volume reduction, depending on the mix of genetic vulnerability and trauma exposure.

In the context of this thinking and this literature, we expected to find severe trauma histories and therefore marked hippocampal volume reduction in our sample of psychiatric inpatients.

MATERIALS AND METHODOLOGY

Participants

Participants were 20 inpatients in a hospital Trauma Program and 20 controls. The inpatients were consecutively admitted patients who consented to participate and who were able to travel to the MRI facility immediately after discharge. There were 17 women and 3 men in the patient sample with an average age of 40.9 years ($SD = 10.1$). The 20 controls were staff at the outpatient Neurology Clinic where the MRI's were performed. All were female and their average age was 37.4 years ($SD = 12.3$). The two groups did not differ on age or gender using a t test for age and a chi square analysis for gender, with significance set at $p < .05$. All participants gave written informed consent and the study was approved by the Medical Staff Committee of the hospital, which acts as the Internal Review Board. The control group did not complete any of the clinical study measures, and one patient did not complete the clinical diagnostic and symptom measures.

Measures

Of the 20 patients, 19 completed a set of measures that included: the Structured Clinical Interview for DSM-IV (SCID) [26]; the Dissociative Disorders Interview Schedule (DDIS) [27]; the Dissociative Experiences Scale (DES) [28]; the Hopkins Symptom Checklist-90-Revised (SCL-90-R) [29]; the Childhood Trauma Questionnaire (CTQ) [30]; the Somatoform Dissociation Scale (SDQ) [31]; the Beck Hopelessness Scale (BSS) [32]; the Beck Suicide Scale (BSS) [33]; and the Beck Depression Inventory (BDI) [34]. All these measures have established reliability and have been widely used in mental health research.

Procedures

The MRI procedure in this study included a coronal 3D T1-weighted image taken using a 1.5T machine (imaging parameters were TR/TE/TI = 10.1/4.3/450 msec, 15° flip angle, 240 × 240 mm field of view, 192 × 192 matrix, 180 1.2-mm slices). Hippocampal volume was measured using a semi-automatic atlas based non-linear warping method [35]. The atlas was based on healthy elderly subjects [36] and each subject's 3D T1-weighted volume image was used to

compute a high dimensional deformation field that maps voxels in the atlas volume to voxels in the subject volume. This deformation field was then used to transform a hippocampus surface defined in the atlas into the subject space bounded by hippocampus landmarks defined by the readers. Twenty-two landmarks around the hippocampus for each side (i.e. left and right) were assigned by the readers. They included a) head and tail of hippocampus and b) lateral, medial, superior, and inferior aspects of the hippocampus for 5 slices between head and tail. The readers reviewed the tracing results, and manually edited any region that needed improvement if needed. The region of interest was limited strictly to the hippocampal gray matter.

Analyses

The patients and controls were compared on whole brain volume, left hippocampal volume and right hippocampal volume using t tests, with significance set at $p < .05$. Average values for symptom scores and number of participants positive for dichotomous variables were tabulated for the clinical measures. A Pearson correlation matrix was constructed that included the symptom measures, left and right hippocampal volume and whole brain volume, with significance set at $p < .05$.

RESULTS

Average whole brain volumes were ($M = 1,165.235 \text{ cm}^3$, $SD = 106.836$) for the patients and ($M = 1,108.645 \text{ cm}^3$, $SD = 101.866$) for the controls ($t = 0.230$, NS). Average left hippocampal volumes were ($M = 2,417.425 \text{ mm}^3$, $SD = 207.422$) for the patients and ($M = 2,352.255 \text{ mm}^3$, $SD = 236.856$) for the controls ($t = 0.926$, NS). Average right hippocampal volumes were ($M = 2,545.55 \text{ mm}^3$, $SD = 319.757$) for the patients and ($M = 2,460.365 \text{ mm}^3$, $SD = 239.159$) for the controls ($t = 0.954$, NS).

On the SCID, 16 out of 19 (84.2%) patients met criteria for PTSD. Of the 19 patients completing the DDIS, 4 met criteria for somatization disorder, 11 met criteria for substance abuse, 17 met criteria for major depressive episode and 10 met criteria for borderline personality disorder. On the symptom sections of the DDIS, average scores were: somatic symptoms ($M = 10.8$, $SD = 7.8$); Schneiderian symptoms ($M = 3.6$, $SD = 2.1$); secondary features of dissociative identity disorder (DID) ($M = 9.1$, $SD = 4.9$); borderline diagnostic criteria ($M = 4.1$, $SD = 1.8$); and ESP/paranormal experiences ($M = 2.9$, $SD = 2.3$).

Average scores on the symptom measures for the patients were: DES ($M = 45.4$, $SD = 20.1$); BDI ($M = 35.6$, $SD = 12.3$); BSS ($M = 15.4$, $SD = 10.7$); BHS ($M = 11.0$, $SD = 6.1$); SDQ ($M = 41.3$, $SD = 13.0$); and the SCL-90-R ($M = 2.1$, $SD = 0.49$).

On the DDIS, 17 patients reported childhood physical abuse, 18 reported childhood sexual abuse, and all 19 reported physical and/or sexual abuse. The average duration of the physical abuse was ($M = 10.2$ years, $SD = 5.8$); the average number of physical abusers reported was ($M = 1.6$, $SD = 1.1$); the average duration of the sexual abuse was ($M = 10.0$ years, $SD = 4.4$); the average number of sexual abusers reported was ($M = 1.9$, $SD = 1.1$); and the average number of

types of sexual abuse reported was ($M = 4.9$, $SD = 3.1$). The average score on the CTQ was ($M = 84.6$, $SD = 19.3$).

There were no significant correlations between left and right hippocampal volume, whole brain volume and any of the symptom measures.

DISCUSSION

Contrary to our predictions, there were no differences between patients and controls on whole brain, left hippocampal or right hippocampal volumes. Initially we thought of these results as a failure to replicate and a false negative finding, however we then reconsidered this view in light of the fact that three out of four studies of hippocampal volumes in highly dissociative patients, including the present study, have shown no volume reduction compared to controls.

Perhaps, we thought, dissociation has a neuro-protective function. Clinically, one finds attachment, trust, joy and spontaneity preserved in a child alter personality in individuals in treatment for DID. These qualities have been preserved because they have been insulated from the toxic effects of the childhood environment. Although the dissociation in DID has a cost in terms of symptoms and dysfunction, it is psychologically protective in that it preserves positive, adaptive traits and qualities. This is true despite the fact that there are not literally separate “personalities” present – the existence of separate “people” inside does not have to be literally true for the dissociation to serve a protective function.

In mammals, the evolutionary imperative of survival requires attachment to an adult caretaker: when the primary attachment figures are also perpetrators of abuse and neglect, dissociation protects the attachment systems, maintains bonding to the perpetrator parents, and therefore facilitates survival, as stated in Freyd’s [37] betrayal trauma theory. The image of good, safe parents is preserved in child alter personalities who maintain the attachment, while the negative feelings, perceptions, thoughts and attitudes towards the perpetrator parents are encapsulated in dissociated identities within the mind. Additionally, as stated in structural dissociation theory [38], dissociation is rooted in mammalian defense responses. In humans, the basic freeze response is elaborated into a more complex psychology in which executive function is preserved while traumatic affect and defensive reactions are encapsulated in child ego states or emotional personalities.

We hypothesized that, in parallel to the psychology of structural dissociation, dissociation may have a neuro-protective function. It may down-regulate the toxic effects of cortisol, glutamate and other trauma-driven inputs to the hippocampus, thereby conserving hippocampal volume, at the functional cost of fragmentation of memory. This may be true in both DID and PTSD. Based on this hypothesis, we predict that in these two diagnostic categories, individuals with comparatively minimal trauma and individuals with extensive trauma but high levels of dissociation will tend to have normal hippocampal volumes. Reduced hippocampal volume will be most evident in individuals with high trauma exposure but low levels of dissociation. Our data cannot test

this hypothesis, but we advance it for consideration by future researchers.

Our hypothesis is consistent with the observation that a high-dissociation subgroup of PTSD is characterized by low resting serum cortisol levels and an altered cortisol response to stress [39, 40]. Rather than representing an exhausted hypothalamic-pituitary-adrenal (HPA) axis, these results might represent an adaptive trauma survival strategy. In a situation of acute danger, it makes sense for a mammal to activate cortisol and the sympathetic nervous system, and to shunt blood away from digestion and reproduction to the muscles. For a child trapped in inescapable, chronic childhood trauma, however, neither fight nor flight are realistic options. Resources are shunted to the parasympathetic nervous system and digestion, and away from the HPA axis, that is, towards freeze and dissociation. This would result in a low-cortisol, high-dissociation, normal hippocampal volume subgroup in both DID and PTSD. Of course, fight, flight and freeze are not mutually exclusive, and any one can be the primary adaptive strategy under certain conditions, therefore one would predict the existence of mixed and intermediate adaptations.

Our study has a number of limitations in addition to the small sample size, which is nevertheless larger than the Vermetten *et al.* [16] study, which included 15 patients. It is possible that measuring sub-regions of the hippocampus, rather than the overall volume of the structure, might have led to significant differences between groups. Also, the sample may not have been representative of the population of traumatized inpatients, although this is doubtful because the participants resembled prior larger samples of individuals with high levels of dissociation on the DES and DDIS [41]. It would have been desirable to include a comparison group with PTSD and low levels of dissociation, and this should be done in future research. In their study of hippocampal volumes in DID, Vermetten *et al.* [16] reported average hippocampal volumes for controls of 2,380.30 mm³ for the left and 2,244.46 mm³ for the right. Our average hippocampal volumes for the controls were 2,352.255 mm³ for the left and 2,460.365 mm³ for the right. It is possible that our software also captured surrounding tissue and therefore obscured potentially significant findings, but this seems unlikely given the similarity of the findings for the control groups in the two studies. It would have been desirable to administer the clinical measures to the comparison group as well to ensure that they did not have trauma histories, and this should be done in future studies. Our results and our hypothesis that dissociation may have a neuro-protective function, should be considered preliminary and further investigation is warranted.

CONCLUSION

Future research should consider the hypothesis that dissociation has a neuro-protective function. In PTSD, for example, individuals with high trauma exposure and high levels of dissociation might have normal hippocampal volumes, while reduced hippocampal volume occurs in individuals with comparable trauma exposure but low levels of dissociation.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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