The Lasting Effects of Psychological Trauma on Memory and the Hippocampus

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Educational Objectives

Upon completion of this Cyberounds®, the participant should be able to:

- Discuss how extreme stressors, including childhood abuse and combat, can have lasting effects on hippocampal-based verbal declarative memory and what the relevance of this to education, public policy, rehabilitation and psychiatric treatment
- Describe research findings showing reduction in volume of the hippocampus in posttraumatic stress disorder related to abuse or combat and theoretical explanations for findings
- Describe how dysfunction of medial prefrontal cortex may contribute to symptoms of stress-related disorders like PTSD.

The invisible epidemic

The invisible epidemic of childhood abuse and other psychological traumas and stressors represents a major public health problem in our society today. Childhood sexual abuse alone affects 16% of women (about 40 million) in the U.S.A. (including rape, attempted rape, or molestation) at some time before their 18th birthday.¹

Childhood abuse is the most common cause of posttraumatic stress disorder (PTSD) in women, which affects 8% of the population at some time in their lives,² although there are a range of other types of psychological trauma that can also lead to symptoms of chronic PTSD, including car accidents, combat, rape and assault. Some of the symptoms of PTSD, which include intrusive memories, nightmares, flashbacks, increased startle and vigilance, social impairment and problems with memory and
concentration, may be related to the effects of extreme stress on the brain.$^3,^4$

Individuals with a history of exposure to childhood abuse or combat had a reduction in volume of a brain area involved in learning and memory called the hippocampus, which is felt to be related to stress, with associated deficits in hippocampal-based learning and memory.$^5$ Children under stress develop impairments in academic achievement that are specifically related to the development of PTSD. Other symptoms, including fragmentation of memory, intrusive memories, flashbacks, dissociation and pathological emotions, may also be related to hippocampal dysfunction$^6$ and may explain delayed recall of childhood abuse.$^7$ The hippocampus has important links to the medial prefrontal cortex, another brain area that mediates emotion and the stress response, dysfunction of which has also been implicated in PTSD.

A disease of memory

Alterations in memory form an important part of the clinical presentation of patients with PTSD. PTSD patients report deficits in declarative memory (remembering facts or lists, as reviewed below), fragmentation of memories (both autobiographical and trauma-related) and dissociative amnesia (gaps in memory that can occur for minutes to days and are not due to ordinary forgetting).

Psychiatric Symptoms Associated with Childhood Abuse

**PTSD**

- Nightmares
- Flashbacks
- Memory & Concentration problems
- Hyperarousal
- Hypervigilance
- Intrusive memories
- Avoidance
- Startle responses
- Feeling worse with traumatic reminders

**Dissociative**

- Out of body experiences
- Derealization
- Amnesia
- Fragmented sense of self & identity

**Anxiety**

- Panic attacks

http://www.lawandpsychiatry.com/html/hippocampus.htm

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- Claustrophobia

Substance Abuse

- Alcoholism
- Opiate addiction

Many abuse victims claim to remember only certain aspects of the abuse event. For instance, a patient who was locked in the closet had an isolated memory of the smell of old clothes and the sound of a clock ticking. Later, she connected that with feelings of intense fear and, then, the entire circumstances relating to the abusive events. PTSD is also associated with alterations in non-declarative memory (i.e., types of memory that cannot be willfully brought up into the conscious mind, including motor memory, such as how to ride a bicycle). These types of non-declarative memories include conditioned responses and abnormal reliving of traumatic memories following exposure to situationally appropriate cues. Many of these memory disturbances may be related to dysfunction of the hippocampus and related brain areas such as medial prefrontal cortex.

Effects of psychological trauma on the hippocampus and memory

Childhood abuse and other extreme stressors can have lasting effects on brain areas involved in memory and emotion. The hippocampus is a brain area involved in learning and memory that is particularly sensitive to stress. As reviewed in greater detail by Bruce McEwen in other Cyberounds high levels of glucocorticoids (cortisol in the human) released during stress were associated with damage to neurons in the CA3 region of the hippocampus, and a loss of neurons and dendritic branching. Glucocorticoids disrupt cellular metabolism and increase the vulnerability of hippocampal neurons to excitatory amino acids like glutamate. Other neurochemical systems interact with glucocorticoids to mediate the effects of stress on memory and the hippocampus, including serotonin and brain-derived neurotrophic factor (BDNF). Stress also results in deficits in new learning that are secondary to damage to the hippocampus. Exciting recent research has shown that the hippocampus has the capacity to regenerate neurons and that stress inhibits neurogenesis in the hippocampus.

Studies in animals showing glucocorticoid-mediated hippocampal toxicity and memory dysfunction with stress raised the question: Does early stress, such as childhood abuse, result in similar deficits in human subjects? With this in mind, we used neuropsychological testing to measure declarative memory function in PTSD. We selected measures that were validated in studies of patients with epilepsy to be specific probes of hippocampal function. These neuropsychological measures (including delayed paragraph recall and word list learning) were correlated with a loss of neurons in the hippocampus in patients who underwent surgical resection of the hippocampus for the treatment of epilepsy. We initially found verbal declarative memory deficits using similar measures in Vietnam combat veterans with PTSD.

In the first report to use brain imaging in PTSD, combat veterans were found to have an 8% reduction in
right hippocampal volume, measured with magnetic resonance imaging (MRI), with no difference in comparison regions including caudate, amygdala and temporal lobe (Figure 1).

![Normal vs PTSD brains](image)

Decreases in right hippocampal volume in the PTSD patients were associated with deficits in short-term memory (r=0.64; p<0.05). This initial report was replicated in survivors of childhood physical and/or sexual abuse with PTSD. We found similar deficits in short-term memory as in the combat veterans, which were correlated with level of abuse as quantitated with the Early Trauma Inventory (Figure 2) and a 12% reduction in left hippocampal volume.

**Sexual Abuse Severity and Memory Deficits in Childhood Abuse-related PTSD**

![Severity vs Memory Deficits](image)

Two other replications of the original study have now been reported showing hippocampal volume reduction in PTSD. Our preliminary data show a failure of hippocampal activation measured with PET during memory retrieval in PTSD. We also showed that hippocampal volume reduction is specific to PTSD and not other anxiety disorders (panic disorder).

Studies are ongoing to assess the effects of treatments on hippocampal volume in PTSD using medications, including fluoxetine and phenytoin, that were shown in animal studies to increase dendritic branching or block the effects of stress on the hippocampus. We are also comparing monozygotic twins with and without PTSD to rule out the possibility that smaller hippocampal volume at birth can explain findings of hippocampal volume reduction in PTSD, acting as a type of risk factor.

The hippocampus has an inhibitory effect release of corticotropin releasing factor (CRF) from the pituitary. CRF plays a critical role in the stress response, both mediating peripheral HPA axis activation...
in stress and acting centrally to mediate fear-related behaviors and chronic stress in animals was shown to lead to chronic increases in CRF release. Again consistent with hippocampal dysfunction, we found elevations of concentrations of CRF in the cerebrospinal fluid (CSF) in PTSD.  

Empirical studies on memory and the hippocampus may shed some light on the controversy surrounding delayed recall of memories of childhood abuse. The hippocampus plays an important role in integrating or binding together different aspects of a memory at the time of recollection and is felt to be responsible for locating the memory of an event in time, place and context. We have hypothesized that atrophy and dysfunction of the hippocampus, following exposure to childhood abuse, may lead to distortion and fragmentation of memories. For instance, in an abused patient who was locked in the closet, there is a memory of the smell of old clothes but no visual memory of being in the closet and no affective memory of the feeling of fear. Perhaps, with psychotherapy, there is a facilitation of associations to related events that may bring all of the aspects of the memory together. Or, if the patient has an event such as being trapped in a dark elevator, the feeling of fear with darkness and the enclosed space may be enough to trigger a recollection of the entire memory.

The effects of childhood trauma on memory and the brain also have important implications for public health policy. This is especially pertinent for inner-city children who often witness violent crimes in their neighborhoods and families, in addition to trauma, such as childhood abuse. If abused children have damage to brain areas involved in learning and memory, this may put them at a serious disadvantage that programs such as Head Start will not be able to overcome. Consistent with this, traumatized Beirut adolescents with PTSD had deficits in academic achievement, compared to non-traumatized adolescents and traumatized adolescents without PTSD.  

Dysfunction of the medial prefrontal cortex in PTSD

Abnormalities of other brain areas (Figure 3), including medial prefrontal cortex, are also associated with PTSD.

Medial prefrontal cortical areas modulate emotional responsiveness and mediate conditioned fear responses to fear-inducing stimuli through inhibition of amygdala function. We have hypothesized that dysfunction in these regions may underlie pathological emotional responses in patients with PTSD. This area also has important functional connections with the hippocampus. In several studies
using positron emission tomography (PET) imaging of brain function in PTSD, we have found dysfunction of the medial prefrontal cortex and hippocampus during provocation of PTSD symptoms and presentation of traumatic cues. We stimulated PTSD symptoms with the noradrenergic agent, yohimbine. We found a relative failure of activation in metabolism in parts of medial prefrontal cortex (orbitofrontal), decreased function in hippocampus, in comparison to placebo and in comparison to responses in healthy subjects.\textsuperscript{31}

In a study using combat-related slides and sounds to provoke PTSD symptoms, combat veterans with PTSD (but not combat veterans without PTSD) demonstrated a decrease in blood flow in the medial prefrontal cortex (Brodmann's area 25 or subcallosal gyrus) (Figure 4), with a failure of activation in anterior cingulate (area 32 and 24) and increased activation in posterior cingulate, motor cortex and lingual gyrus.\textsuperscript{32}

Women with childhood sexual abuse and PTSD, compared to sexually abused women without PTSD, exposed to personalized scripts of childhood sexual abuse, again showed decreased blood flow in medial prefrontal cortex (area 25) and failure of activation in anterior cingulate, with increased blood flow in posterior cingulate and motor cortex. PTSD women also had decreased blood flow in right hippocampus. These imaging findings are consistent with dysfunction of medial prefrontal cortex and hippocampus in PTSD that may underlie pathological emotions in these patients.

Summary

This review has covered the broad impact of childhood abuse and other traumas on memory and the hippocampus. The hippocampus, a brain area involved in verbal declarative memory, is particularly sensitive to stress. Patients with combat and abuse-related PTSD were shown to have smaller hippocampal volume and deficits in hippocampal-based verbal declarative memory functions. Hippocampal dysfunction may underlie many symptoms of PTSD and may explain elevations in concentrations of CRF in PTSD. Another brain area affected by stress is the medial prefrontal cortex. Functional imaging studies show dysfunction in this area (as well as hippocampus) during provocation of PTSD symptoms and presentation of traumatic reminders. Medial prefrontal cortical inhibition of amygdala responsiveness is felt to underlie extinction to fear responding. Dysfunction of this area in abuse-related PTSD may lead to problems modulating emotion in PTSD.

CME Questions

References


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