The Structural and Functional Changes in the Human Brain of Those With Post-Traumatic Stress Disorder

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Post-Traumatic Stress Disorder (PTSD) is a complex mental health condition as it affects multiple parts of the brain, causing different areas of the brain to expand in size and thus change the brain's way of functioning, and manifests differently in different individuals based on multiple factors. The consistent results of the literature review indicate that the amygdala and the hippocampus, the neural regions responsible for processing emotions and consolidating memories, undergo remarkable changes in the presence of PTSD. The main findings of the resources reviewed show that the brain volume in both the amygdala and the hippocampus reduce in size in individuals with PTSD, causing the brain to perform irregular actions and prevent the individual from conducting a normal life. The implications of the papers reviewed include that the changes in both the amygdala and the hippocampus, as a result of PTSD, completely alters the way in which the brain functions. It is certain that the repercussions of PTSD are far from uniform and that the symptoms of PTSD vary from individual to individual. Factors involved in the manifestation of PTSD in an individual include, but are not limited to: genetics, life experiences, individual neurobiology, and environmental influences. The dynamic interplay between the amygdala and hippocampus, coupled with an individual's unique constitution and life history, underscores the profound complexity of PTSD as a mental health condition.

Introduction

It is estimated that about 8% of men and 20% of women worldwide develop Post-Traumatic Stress Disorder (PTSD) following the experience of a traumatic event. There is an immense amount of change that occurs in the brains of those with PTSD[1]. The human brain is an incredibly intricate and complex organ, responsible for a wide range of cognitive, emotional, and physiological functions[1]. When it comes to conditions such as PTSD, the impact on the brain is multifaceted[1]. Notably, there are not only functional deficits within the brain, such as in various regions of the brain responsible for communication and processing of information[2], but also observable structural differences, involving changes in the size and morphology of several brain regions[2]. The functional deficits in the brain associated with PTSD manifest as disruptions in neural networks and communication pathways. These disruptions can lead to heightened reactivity in certain brain regions[2]. Post Traumatic Stress Disorder has been associated with the structural changes in the human brain: What are the specific structural changes and their impacts on those diagnosed with Post Traumatic Stress Disorder? With the review of eight previously performed experiments, from papers such as: Effects of Psychotherapy on Hippocampal Volume in Out-Patients With Post-Traumatic Stress Disorder[3], and research identified through a search on Google Scholar, the explanation of how the brain changes both structurally and functionally in PTSD can be understood.

Post-Traumatic Stress Disorder

PTSD is a mental health condition that arises in individuals who have encountered or witnessed a traumatic event[3]. Events most commonly contributing to PTSD development are life-threatening or seriously harmful situations such as physical or sexual assault, natural disasters, accidents, combat experiences, witnessing violence, or the sudden loss of a loved one[1,2]. These events can elicit a wide array of emotional and psychological responses. The severity and intensity of the traumatic event play a role in whether or not an individual will develop PTSD following a traumatic event. The intensity of the trauma refers to how impactful the traumatic event was in itself and determines how much an individual is impacted by PTSD. For example, an individual with PTSD who had previously fought in a war might have a worse case of PTSD than an individual whose traumatic event was a dog bite. Similarly, the severity of the traumatic event directly relates to the individual itself and is determined by how the individual's traumatic event specifically impacts them and how they react when faced with encountering certain stimuli. This causes individuals to have different levels of PTSD, ranking from severe to mild PTSD. For example, an individual who had been through a school shooting as a child might experience trouble with going back to school whereas an individual whose traumatic event was a dog bite might be comfortable with going on evening walks around a neighborhood. PTSD is affected by many factors, including genetics. Certain individuals may possess a genetic inclination that makes them more susceptible to developing PTSD. This predisposition can be shaped by the existence of specific genetic variations or alterations that impact the brain's response to stress and trauma. On the other hand, some people may have genetic factors that help them cope with stress more effectively, reducing their risk of developing PTSD even after exposure to traumatic events[4]. Polymorphisms are one of the most common types of genetic variation that causes individuals to be more susceptible to developing PTSD. Individuals with PTSD may experience a range of symptoms, such as intrusive memories, flashbacks, nightmares, avoidance of triggers related to the trauma, negative changes in mood and thoughts, and increased arousal and reactivity[1]. Intrusive memories are distressing or unwanted thoughts, images, or memories that enter a person's mind without their intentional control. These thoughts can be disturbing, repetitive, and challenging to manage. Nightmares are intense, distressing, and vividly disturbing dreams that can evoke strong feelings of fear, anxiety, sadness, or other negative emotions. They often wake a person from sleep and can leave them feeling shaken and anxious. An avoidant tendency causes an individual with PTSD to disrupt schedules and become unreliable both to others and themselves. Oftentimes, the avoidant tendency roots from the individual's dread of having to relive the stress of the traumatic event[1].

Several treatments have been found to be effective for treating PTSD. Few of which include cognitive behavioral therapy, medication, and group therapy[5]. Cognitive behavioral therapy (CBT) is a form of psychotherapy that focuses on helping individuals identify and change negative thought patterns and behaviors that contribute to their emotional distress and psychological issues, in this case PTSD. It is a therapeutic approach that aims to help people develop coping strategies. However, CBT is a commitment that sometimes does not work in the long run for individuals with PTSD[6]. Pharmaceutical treatment options can be used in severe cases of PTSD. These medications are prescribed by a psychiatrist and aim to target neurotransmitters that are altered in the brain, causing PTSD in the individual[2]. A major drawback of pharmaceutical treatment options is that oftentimes, they are difficult for people to afford when paying out of pocket[6]. Common medications prescribed to those with PTSD include Group therapy is another useful tool for those with PTSD. Group therapy allows individuals facing the same psychological issues to come together and share hardships and coping mechanisms. Sharing with others allows for those with PTSD to be able to relate and feel less alone in facing their challenges with PTSD[2].

Neural Regions Involved with Post-Traumatic Stress Disorder

There are many neural regions which are implicated in PTSD, however, most previous works have identified three main areas associated with PTSD - the amygdala, hippocampus, and prefrontal cortex[7]. Here we will focus on the changes in the amygdala and hippocampus. The amygdala is a structure located deep within the brain's temporal lobe and plays a crucial role in processing one's emotions and memory[7]. The amygdala is essential in triggering the body's physiological responses to stress, including the release of stress hormones like cortisol[8]. The amygdala's significance in PTSD is centered on its role in processing and storing traumatic memories and its influence over fear and stress reactions[8]. The dysregulation of the amygdala is often linked to PTSD[8] The amygdala's enhanced encoding of traumatic memories can lead to intrusive memories and flashbacks in PTSD[8]. These memories can be triggered by reminders of the traumatic event and cause distressing re-experiencing of the trauma. In PTSD, the heightened reactivity of the amygdala causes fear conditioning, in which an individual becomes excessively responsive to cues linked with the traumatic experience, resulting in an elevated state of alertness and an expectation of danger. We can be sure of the amygdala's function since the majority of research and experiments conducted all some to the same conclusion about the way the amygdala functions and serves the human body.

Additionally, the hippocampus, a region of the brain located in the medial temporal lobe, plays a crucial role in memory formation, learning, and spatial navigation[7]. Moreover, the hippocampus is essential for fear extinction, the process through which the brain learns to reduce fear responses to non-threatening stimuli over time[7]. In PTSD, fear extinction may be impaired, contributing to the persistence of fear and hyperarousal linked to trauma-related cues[7]. The hippocampus is slightly more complicated in the sense that it plays a larger role in sleep than the amygdala does. Since we do not know much about why humans need sleep, this makes the hippocampus comparatively harder to understand in the context of PTSD since a major symptom of PTSD is nightmares.

Neuro-Imagining Techniques Used to Assess Post-Traumatic Stress Disorder

Brain imaging plays a vital role in visualizing and studying the brain's structure, function, and activity. By providing valuable insights into the brain's workings, changes over time, and responses to different stimuli, these techniques have proven to be useful in studies regarding those with PTSD. A commonly used brain imaging technique in PTSD studies is the functional Magnetic Resonance Imaging, or fMRI. fMRI is a specialized form of MRI that measures changes in blood flow and oxygenation to infer brain activity. By detecting which areas of the brain are more active during specific tasks or while at rest, fMRI allows researchers to map brain function and connectivity. This allows researchers to analyze what parts of the brain are more or less active in response to various stimuli[7]. fMRI, however, must be performed in a timely manner[9]. In individuals with PTSD, an fMRI should be taken regularly starting after the individual's diagnosis to determine how the functionality of the individual's brain is changing[9]. The consistent fMRI can add up in cost and not many individuals can afford to pay for this process[9]. Another useful way to utilize MRI, is structural MRI or sMRI. In sMRI the non-invasive radio waves and powerful magnets create detailed images of the brain's internal structures. It can visualize the brain's anatomy, including the size and shape of different brain regions, making it easier to identify structural differences in brains of those with PTSD[7]. sMRI can reveal structural changes in the brain, such as alterations in gray matter volume or connectivity between brain regions as well help explore how traumatic memories are encoded, consolidated, and retrieved in individuals with the disorder[7]. sMRI also shows the different regions and structures of the brain, such as the amygdala and hippocampus, allowing researchers to determine the size and shape of certain structures in the brain. Understanding these processes may offer insights into the intrusive memories and flashbacks experienced by individuals with PTSD. However, the process of getting an sMRI done is rather uncomfortable for the individual and requires them to be still in a very tight space for a certain amount of time[10]. In individuals with PTSD, this would not be ideal as it may trigger the individual[10]. Other neuroimaging techniques such as Electroencephalogram (EEG) and Positron Emission Tomography (PET) scanning can also be utilized to understand aspects of PTSD in the brain. Here we will focus on MRI research.

Results

With the use of Google Scholar, 13 sources were found. 5 sources directly explained the changes in the amygdala that occur in individuals with PTSD, 4 sources explained the changes in the hippocampus, and 4 sources gave specific information regarding the specifics of PTSD itself. To avoid bias in the selection of these sources, we limited our selections to sources that were published in the last 25 years and appeared on the first page of Google Scholar. This allowed for the findings to be consistent across all sources while also bringing up ideas for further studies in order to completely solidify the findings being analyzed.

Aims and Hypotheses

Here a literature review was conducted which aimed to examine the following research questions:

- What are the specific structural changes occurring in the brain of individuals of PTSD?
- What are the functional changes that result from PTSD?
- How do these structural and functional neural changes respond to commonly used methods of treatment for those with PTSD?

The initial hypothesis is that the amygdala and the hippocampus have reduced brain volume in individuals with PTSD. Additionally, the symptoms of PTSD directly connect to these changes in the brain.

Discussion

Structural Changes in PTSD

One of the sources found through Google Scholar directly explains how the structural changes in the brain occur when an individual has PTSD. A study conducted in 2005 measured the mean structural volume in cubic centimeters (cc) of the hippocampus, amygdala, and parahippocampal gyrus of two different groups. In one group, the control group, 14 individuals with controlled trauma were studied. In the other group, the independent group, 35 individuals with PTSD were studied. Almost 50% of the PTSD patients had a history of previous therapy treatments for trauma. The individuals in the control group were found through an advertisement for traumatized police officers in a local newspaper. The individuals in the PTSD group were diagnosed following the structure of the DSM-IV. MRI's were taken for all individuals in both groups to confirm the results shown in Table 1.

The control group had a mean hippocampal volume of 4.71cc whereas the group with PTSD had a mean hippocampal volume of 4.06cc. The group with the PTSD had a lower average hippocampal volume by about 0.65cc. This is a significant reduction since the brain should not randomly reduce in size, especially the hippocampus. Additionally, the average volume of the amygdala of those in the control group was 2.55cc whereas the group with the PTSD had a slightly higher amygdala volume of 2.60cc. The difference in the size of the average amygdala when comparing those with controlled trauma versus PTSD, was about 0.50cc[3]. This confirms our initial hypothesis stating that both the hippocampus and the amygdala would reduce in size in individuals with PTSD.

The decrease in hippocampal volume plays a critical role in the symptoms of PTSD. The symptoms impacted by hippocampal volume reduction include , the inability to focus,

Table 1: Brain Volumes of a PTSD Group vs a Controlled Trauma Group (Directly from Nutt et al., 2004)

Variables	PTSD ($n=18$) Mean	PTSD ($n=18$) S.D.	Controls ($n=14$) Mean	Controls ($n=14$) S.D.	F (df = 1)	p^a
Hippocampus (cc)						
Total	4·06	0·52	4·71	0·50	10·71	0·003
Right	2·05	0·27	2·37	0·30	8·47	0·007
Left	2·01	0·27	2·34	0·22	11·78	0·002
Amygdala (cc)						
Total	2·60	0·45	2·55	0·39	0·84	0·37
Right	1·37	0·26	1·26	0·23	3·17	0·09
Left	1·24	0·23	1·29	0·20	0·04	0·85
Parahippocampal gyrus (cc)						
Total	2·28	0·39	2·05	0·22	4·60	0·04
Right	1·12	0·18	1·02	0·12	2·80	0·11
Left	1·17	0·22	1·03	0·14	5·34	0·03
Grey matter (cc)	568 262	62 143	601 778	41 042	0·61	0·44
White matter (cc)	590 672	69 652	623 210	91 545	0·61	0·44
Cerebrospinal fluid (cc)	180 942	25 528	175 270	21 871	1·11	0·30
Total brain volume (cc)	1 158 934	118 182	1 224 988	123 809	1·54	0·14

[a] Statistical differences between the PTSD and control group computed by multivariate analysis of covariance with total brain volume as covariate.

avoidant tendencies, as well as the constant recollection of the traumatic event. A smaller hippocampus can lead to an increased stress response, potentially resulting in heightened levels of stress hormones and a reduced ability to downregulate stress reactions[3]. Additionally, this can also prohibit individuals with PTSD from being able to differentiate between past events and current experiences, leading to difficulties in distinguishing between past trauma and present situations[3]. This can contribute to flashbacks, intrusive memories, and a heightened state of alertness since the brain is preoccupied in determining the "threat" at hand and causes the individual to question one's state of mind. This also decreases the individual's ability to navigate and orient themselves in physical spaces. Moreover, this can lead to challenges in spatial memory, getting lost easily, and difficulties in recognizing familiar places since the brian is preoccupied in attempting to avoid the perceived threat at hand[3]. This is mainly due to the fact that the brain experiences a heightened level of adrenaline, causing a flight or fight response within an individual[3]. A criticism of this experiment is that although the decrease in hippocampal and amygdala volume is found, the study fails to connect these decreases in volume with the symptoms the specific individuals were experiencing.

Although the difference in the average volume of the amygdala between both the control group and the group with the individuals with diagnosed PTSD is seemingly small, its impact causes a lot of difficulties for an individual with PTSD. A smaller amygdala may lead to reduced fear responses and potentially result in blunted reactions to threatening situations. Conversely, a smaller amygdala could also result in an inability to appropriately regulate fear and anxiety, contributing to heightened anxiety levels. This is because a decrease in the size of the amygdala causes the brain to be hyperactive[11]. Furthermore, a smaller amygdala, especially in those with PTSD, impacts an individual's ability to modulate emotional reactions and exert cognitive control over emotional impulses since the neurotransmitters in the brain are altered, increased in sensitivity, causing an increase in chemical reactions causing the flight or fight response within the brain[3].

Although PTSD is a direct link to the decrease in the size of the amygdala and hippocampus, aging can also be a contributing factor[12]. In order to solidify these claims and be confident in the findings that PTSD is the sole reason for the reduction in amygdala and hippocampus size, further studies should be done focusing around the change in amygdala and hippocampus size within individuals with PTSD of all ages.

Functional Changes in PTSD

A study was conducted with two groups by Nutt and colleagues to identify the activity in the left amygdala when triggered by stimuli. The control group consisted of randomly selected individuals with no known prior trauma. The second group consisted of individuals with PTSD. When played white noise and combat sounds were played, the relative activity in the left amygdala was recorded using fMRI, PET, and SPECT. The data is measured in regional cerebral blood flow (rCBF).

When Combat Veterans with PTSD are played the white noise, the relative activity in the left amygdala rests in between those of the combat controls and the normal controls. However, when playing the combat sounds, the relative activity amount in the left amygdala in those with PTSD, is well above the control group. When played white noise, the relative activity in the left amygdala of those with PTSD rests at around 1475 rCBF. Alternatively, when playing the combat sounds, the relative activity in the left amygdala of those with PTSD rises to around 1550. Heightened amygdala activity, such as the increased level of neural activation, can significantly impact the ability to allocate cognitive resources, namely the awareness of an individual's surroundings and the ability for an individual to stay present around others[13]. Attention becomes acutely focused on the emotional stimuli at hand, sometimes at the expense of other ongoing cognitive processes[13]. This occurs mainly because the brain is working overtime in order to fight the stress response signal given off in the brain. Emotions become more vivid and immediate, often colored by a sense of urgency or intensity when the amygdala's activity is heightened[13]. The intricate network of connections between the amygdala and other brain regions facilitates the rapid transmission of information, allowing us to swiftly process the emotional import of what we perceive[13]. This causes those with PTSD to be hyper fixated on their triggering stimuli, causing them to change their day to day life in an attempt to avoid any reminders of their initial traumatic event[7]. For example, an individual with PTSD stemming from serving in the war may refuse to go outside during the Fourth of July to avoid the loud bomb-like sounds and flashing lights.

These functional changes can contribute to the structural differences in the brains of individuals with PTSD[13]. For example as the amygdala decreases in size, causes an individual to be under a more constant state of stress. This feeling of stress can also trigger the fight or flight response, which is one of the biggest symptoms of PTSD[13].

Similarly to the alternate reasoning behind the changes in the amygdala and hippocampus volumes, aging can be another explanation for the change in functionality of the amygdala and hippocampus[12]. As individuals age, the neural connections in the brain weaken. This can be a possible theory as to how the amygdala and hippocampus act differently in individuals of different ages[12]. A way to consolidate these claims is by conducting more research on the impacts of aging on the amygdala and hippocampus.

Methods

To identify research articles examining the structural and functional changes in the human brain in those with PTSD, a literature review was conducted using Google Scholar. The search terms used were "Functional brain changes with PTSD", "Structural brain changes with PTSD", "Brain imaging techniques", "PTSD and the amygdala", "PTSD and the hippocampus", and "Stress and PTSD". By using sources only created in the past 25 years and found on the first page of Google Scholar, we were able to ensure that our search was relevant and unbiased.

Limitations

The results of this paper need to be considered in the context of its limitations. Notably this is not a systematic, comprehensive literature review. Therefore, not all available sources on the topic of structural and functional changes in the brian due to PTSD were reviewed. Due to this fact, we have not taken into account any sources that may contradict the findings we have analyzed due to those sources not falling under our search guidelines. The studies we have reviewed include experiments involving individuals that may fall under a specific category such as: age, gender, and profession. In order to make these findings more universal to all individuals with PTSD, a broader analysis of more studies involving changes in the brain within those with PTSD should be done.

Future Directions

PTSD can manifest itself in any individual regardless of age. Although the studies previously analyzed focus mainly on adults, children are also susceptible to PTSD. In order to fully understand the impacts of PTSD, more studies should be done with individuals of varying ages, race, and gender. Additionally, more research should be done on individuals suffering from non combat related PTSD. This would offer a more holistic review on the effects of PTSD originating from various types of trauma. This should be done in an organized manner, starting with identifying specific elements that current research on PTSD are lacking. Taking different variables into consideration when performing experiments is important as it determines whether or not a study can be generalized to a certain population. Thorough experiments that take all the patients' individuals into consideration can help establish treatment options for all individuals with PTSD.

Conclusion

In conclusion, the brains of individuals with PTSD undergo a series of complex and interconnected changes that contribute to the characteristic symptoms and experiences associated with the condition. While the exact mechanisms are not fully

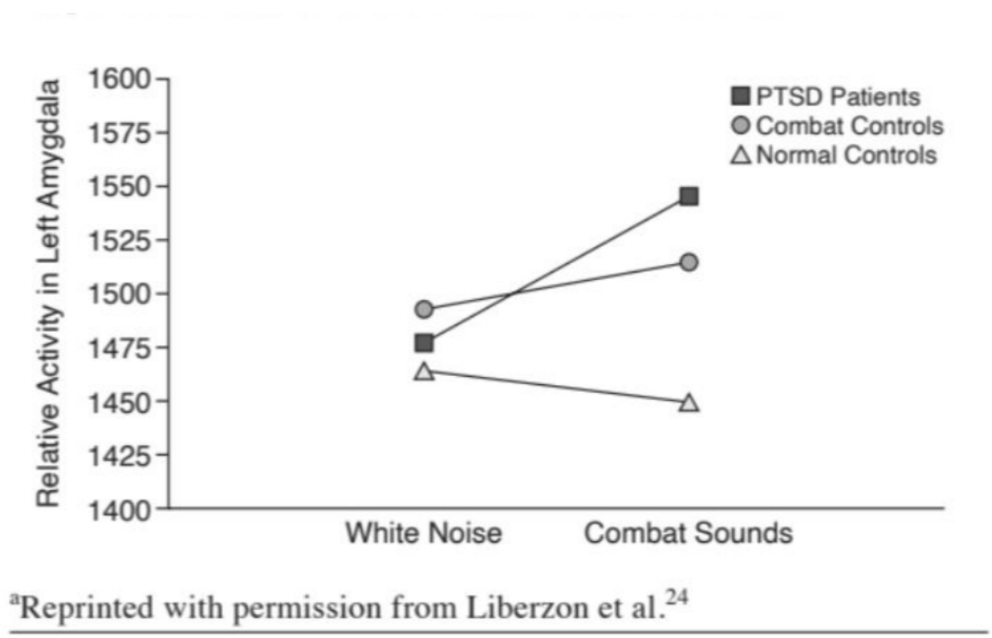

Fig. 1 Brain Volumes of a PTSD Group vs a Controlled Trauma Group (Directly from Nutt et al., 2004)

understood, research has provided insights into how PTSD affects various brain regions and neural pathways. A smaller hippocampus affects stress response by increasing stress hormones and reducing stress regulation[13]. This hampers differentiating between past trauma and current situations, leading to flashbacks, intrusive memories, and heightened alertness[11]. The inability to differentiate between past trauma and current situations also impairs spatial orientation and recognition[11]. A smaller amygdala, especially in PTSD, diminishes fear responses, hinders fear regulation, and affects emotional control[11]. Heightened amygdala activity narrows attention on emotional stimuli, intensifying emotions[11]. This hyper-focus disrupts cognitive processing, influencing those with PTSD to alter daily life to avoid triggers[13]. Although there are treatment options for those with PTSD, it is crucial to remember that medications and therapies do not have the same impact on all individuals (Morey et al., 2013), adding to the difficulty of creating a universal treatment for PTSD. This is precisely why it is important to take into consideration the varying factors such as age, genetic variations, and professions of all individuals with PTSD when determining the type of medication they should take. Being able to understand the precise changes in the structure and functionality of the brain can assist with determining the best plan of action to help those with PTSD.

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