Anatomy of Fear. Literature Review of Neuroscience of Trauma

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ABSTRACT

The purpose of this literature review is to explore already existing research on emotional trauma, high stress exposure and their effect on the nervous system. The starting question is: Does, and if so, how the high stress levels and emotional trauma affect structures of the brain, nervous system and the whole body as a result.

PubMed electronic database was used for research of various studies documenting effect of stress/trauma on brain and its different structures. Spencer S. Eccles Health Sciences Library, University of Utah was used for video presentation of brain anatomy.

Initial research provided 27 abstracts, from which 15 were excluded as the studies were not fully published. A total of 4 studies were far two detailed in chemistry and pharmacology for the scope of this study, so 8 studies were used to document goal of this review — effect of fear and trauma on the nervous system.

The results showed that fear is not only emotion — it is a state of being with tangible anatomy and physiology. Trauma is one of the leading and most overlooked causes of physical and mental health issues. Somatic approach to treating emotional and physical trauma has shown solid results in trauma survivors. Further research is needed into these kinds of therapies so they can be established in mainstream health care system and made more available to population in general.

Keywords: limbic system, trauma, stress, nervous system, fear, brain, somatic.

"The only thing we have to fear is fear itself".

-Franklin D. Roosevelt

INTRODUCTION

For years, fear, anxiety and trauma have been observed mostly in the context of psychotherapy and psychology. Many times, patients that suffer from post-traumatic stress disorder and persistent symptoms of global stress are told "It is all in your head". But is it really so?

For the last few decades, neuroscience has been intensely researching the nervous system, brain and, in particular, the limbic system in order to discover what happens with human biology and physiology when a cascade of events is triggered on the cellular level.

This article will discuss four subjects: 1) anatomy and function of fear in relatively healthy humans, 2) stress/trauma effects on brain, hormones and the whole body, 3) anatomy of fear in individuals exposed to high stress levels/trauma and 4) integrative approach to trauma through therapy. The intention of this review is to highlight the physiological impact of stress/trauma, its existence in the neural circuitry and to suggest methods that incorporate body/mind connection in alleviating symptoms of post-traumatic stress disorder (PTSD).

METHODS

PubMed electronic database was used for research of various studies documenting the effect of stress/trauma on brain and its different structures. Spencer S. Eccles Health Sciences Library, University of Utah was used for video presentation of brain anatomy. The research covered four main areas: 1) anatomy of the brain, with an emphasis on the limbic system; and physiology of stress, 2) trauma and its biology, and consequences of trauma on the overall health, 3) studies performed using neuroimaging, questionaries and other scientific methods, 4) effect of alternative and somatic therapies on trauma resolution.

Inclusion criteria for this literature review study consisted of: published articles in PubMed database, studies related to the effect of trauma on anatomy and physiology of the brain and overall wellbeing, while language of publication/video was restricted to English and Spanish languages.

Exclusion criteria for this study included studies that did not provide full text, articles that did not provide methods and statistics of study, studies concentrating on brain trauma that was not caused by an emotional/psychological event/experience, articles that did not have a precise referencing of the study, and videos in other languages than English or Spanish that did not have subtitles in them.

Initial research provided 27 abstracts, from which 15 were excluded as the studies were not fully published. A total of 4 studies were far too detailed in chemistry and pharmacology for the scope of this study, so 8 studies were used to document the objectives of this review — the

effect of fear and trauma on the nervous system.

LITERATURE REVIEW

Anatomy of the Limbic System

Underneath the cerebral cortex and above the brainstem, laterally covered by temporal lobes, we encounter a set of structures related to our emotions and behaviors, a limbic system. Those emotions and behaviors are related mostly to survival: sense of hunger, fight or flight response, reproduction, feeding.

The main structures of the limbic system are: thalamus, hypothalamus, amygdala and hippocampus.

One of the functions of the thalamus is to act as a "relay station" (Moustafa et al, 2017). All sensory inputs, except olfactory, pass through the thalamus before they reach its final destination in the cortex. There are more than fifty nuclei identified in the thalamus. The following are just some of them: the anterior nucleus (extensively connected to the hippocampus and involved in memory formation); the dorsal medial nucleus, which is involved in emotional behavior and memory; the ventral anterior and ventrolateral nuclei, which are involved in motor functions; the ventral posterolateral nucleus (VPL) and the ventral posteromedial nucleus (VPM), which sends somatosensory information to the somatosensory cortex. The lateral posterior nucleus integrates sensory impulses with cognitive function, while the pulvinar nucleus processes visual stimuli. Medial and lateral geniculate nucleus are in charge of visual and auditory information. The thalamus also plays a role in attention, consciousness and sleep (Moustafa et al, 2017).

The hypothalamus is a small structure situated directly above the brainstem. It is made of numerous nuclei with many functions, but the main task of the hypothalamus is to maintain hemostasis and control hormones, primarily through the pituitary gland. It helps with the adaptation of the body to its environment with intention of survival. It controls sweating, blood pressure, stress reaction, metabolism, thirst, female sex hormones, balance of fluids and electrolytes, metabolism, circadian rhythm, thermostat, heartbeat. It is half gland, half nerve.

The amygdala is an almond shaped structure mostly involved in emotional responses like fear, pleasure, anger and anxiety. It is located next to the hippocampus on both sides of the brain. The amygdala also participates in memory formation, especially those that involve intense feelings, like fear. The main functions of the amygdala are, therefore: threat detection, trigger response (HPA axis activation), fear conditioning (association), positive emotions (intensity of emotion).

The hippocampus is a structure in the temporal lobe of each hemisphere of the brain. It is part of a larger structure in the brain known as hippocampal formation (dentate gyrus, subiculum, entorhinal cortex, parahippocampal gyrus). It is best known for its role in memory consolidation, transforming short term memory (STM) to long term memory (LTM).

Trauma

Individual trauma results from an event, series of events, or set of circumstances that is experienced by an individual as physically or emotionally harmful or life threatening and that has lasting adverse effects on the individual's functioning and mental, physical, social, emotional, or spiritual well-being (Substance Abuse and Mental Health Services

Administration, 2014). Besides being an event that has psychological and emotional consequences on the individual's health, trauma has a physiological impact on the body.

There are, by design of nature, three main survival responses to threat: freeze, flight and fight. Those responses are observed in both humans and animals. When the threat is perceived through the senses, there is a moment of immobility and orientation (neck, head, eyes). In case the fight or flight instinct (activation of sympathetic nervous system) is being performed, the high activation is released and one fights or runs away. If, however, this powerful impulse is thwarted, freezing is the last option left.

As it constricts, the energy that would have been discharged by executing the fight or flight strategies is amplified and bound up in the nervous system (Levine, 1997). If there is no second chance for the system to bounce back to active discharge, it will become immobile (freeze).

The intense, frozen energy, instead of discharging, gets bound up with the overwhelming, highly activated, emotional states of terror, rage, and helplessness. This further affects the nervous system and the whole body bringing it to a state of tonic immobility (uncontrollable paralysis to intense fear) and/or collapsed immobility (loss of muscle tone and sometimes consciousness).

During a trauma event, the brain activity and attention change as well. In ordinary life situations, the prefrontal cortex is in charge of our behavior and actions. It takes care of planning, inhibition of the impulses, it focuses and reasons, it draws on memory and it is able to regulate intensity of emotions. This is called Top-Down Attention. During a traumatic event, fear circuitry takes over, led by the amygdala (which regulates desire, fear, aggression, sex drive) and attention is driven by external factors and stimuli, fear, sensory input and survival-based impulses. This is known as Bottom-Up Attention, often characterized by tunnel vision and constriction of consciousness (Hopper, 2015).

Neurobiology of Trauma

The amygdala, or amygdaloid complex, consists of numerous nuclei (cluster of neuronal cell bodies). The following nucleus are important as inputs and outputs of information processed as potential threat: lateral, central and basal nucleus. The lateral nucleus receives information from: the thalamus via glutamate, sensory cortices, the ventral medial prefrontal cortex, the orbitofrontal cortex and the hippocampus, which has an important role in memory formation. The lateral nucleus sends information to basal and/or central nucleus, while the central nucleus has a main output role in the flight/fight response. It is not the only output channel, but it is highly connected to the hypothalamus and brainstem, which are involved in the autonomic response. The hypothalamus and brainstem will further activate sympathetic activation, stress response and behavioral changes in people or animals experiencing fear (Ingram, 2020).

The hypothalamus causes sympathetic activation by rising blood pressure, heart rate and dilation of the pupils. Corticotropin-releasing hormone is stimulated by the hypothalamus as part of a stress response and is further transported to the pituitary gland, that synthesizes the adrenocorticotropic hormone, which stimulates the secretion of cortisol and glucocorticoids. Thus, the hypothalamus-pituitary-adrenal (HPA) axis is established. Stress hormones are known to shut down the function of the prefrontal cortex. (Hopper, 2015).

The other output leads to the brainstem, which will cause changes in the behavior of animals and humans during threat response. The brainstem will stimulate the periaqueductal gray (involved in freeze response and stress induced analgesia) and the locus coeruleus (release of nor-epinephrine -NE and acetylcholine -ACh). Once in the blood stream, NE and ACh will cause more vigilance and arousal. The parabrachial nucleus, part of the brainstem will become stimulated. This stimulation of parabrachial nucleus will lead to change in respiratory rate. The dorsal motor nucleus of the vagus nerve induces a parasympathetic response (upset stomach, etc.). Cranial nerves V (trigeminal nerve) and VII (facial nerve) become activated showing fear expression on the face (Ingram, 2020).

Conditioned fear

Pavlov was a Russian scientist and physiologist who is known for his research of classical conditioning - a learning through association that he performed on dogs. In 1902. Pavlov started from the idea that there are things that dogs do not have to learn, such as salivation, that is already hard-wired into the dog. Food is an unconditioned stimulus and salivation is an unconditioned response. When a bell, that is a neutral stimulus, was introduced, dogs did not salivate, so they exhibited a neutral response. Pavlov then begun a conditioning procedure by ringing the bell just before food was given to dogs. After a number of these trials (repetitions), he introduced the bell on its own. Sure enough, dogs were salivating on the sound of the bell without food being offered. The sound of the bell had become a conditioned stimulus and salivation became a conditioned response. This experiment showed that even neutral stimuli initiate a response due to associative learning. In the year 1920. Watson and Ryner have shown that the same phenomenon is applicable to humans in the experiment known as “Little Albert”. Studies of Pavlovian fear conditioning in non-humans have highlighted the importance of the amygdala in the acquisition of fear conditioning (LeDoux, 2000; Pare et al., 2004; Sananes and Davis, 1992).

Neuroimaging studies

Neuroimaging studies have also confirmed activation of the amygdala during fear conditioning. Reexperiencing of trauma in post-traumatic stress disorder patients (PTSD) is often induced by external cues in the environment (Doronbekov et al., 2005). Doronbekov and his colleges measured the regional cerebral blood flow (rCBF) with positron emission tomography (PET) in PTSD patients before and after acquisition of fear conditioning.

In five out of ten subjects, the rCBF in the right amygdala and the left posterior cingulate gyrus after acquisition of fear conditioning significantly increased relative to the rCBF before conditioning.

In functional imaging studies by Alvarez et al. (2008), the activation of numerous structures of the limbic system and surrounding structures were recorded during cued conditioned fear in humans, such as: right anterior hippocampus and bilateral amygdala, activation in posterior orbitofrontal cortex, medial dorsal thalamus, anterior insula, anterior cingulate, and parahippocampal, inferior frontal, and parietal cortices.

Therefore, studies of fear conditioning and cues from the environment (emotional and facial expressions) have confirmed that response to stimuli that predicts threat and mediates that way fear/anxiety states. The amygdala is often hyper responsive in anxiety disorders that can

be the result of experience of extreme stress and trauma.

Post-Traumatic Stress Disorder (PTSD)

Post-traumatic stress disorder (PTSD) is characterized by recurrent trauma-related memories, increased fear responding and physiological reactivity to reminders of the trauma, coupled with sleep disturbances, nightmares, avoidance, increased startle, and other symptoms that can persist for many years after the original traumatic event (Pitman, 1989; Bremner et al., 1995). In PTSD patients, abnormal traumatic recall and fear response is present by provoking trauma related pictures and sounds or traumatic scripts. As a consequence, a PTSD patient experiences physiological symptoms like high blood pressure and increased heart rate (Blanchard et al., 1982; Malloy et al., 1983; Pitman et al., 1987).

Bremner et al. (1999) conducted a positron emission tomography (PET) study on ten Vietnam combat veterans with PTSD symptoms and ten comparison objects (Vietnam combat veterans without PTSD symptoms). When exposed to traumatic material, PTSD subjects had decreased blood flow in the medial prefrontal cortex, an area that plays a role in the emotion inhibition of the amygdala responsiveness. Meanwhile, non-PTSD subjects had anterior cingulate gyrus activated more than in PTSD subjects. The cerebral blood flow was also different, in both groups, in areas of memory and visuospatial processing, motor and inferior parietal cortex, and lingual gyrus. Diastolic blood pressure was significantly higher in PTSD subjects when exposed to combat images, which is indicating on automatic nervous system dysregulation.

Functional alterations in specific cortical and subcortical areas of the brain (memory, visuospatial processing and emotion) are existent in PTSD patients.

Brain Abnormalities in Trauma exposure

Not only are there existent pathways for chemical and biological stress conduction in the brain, but we can see, from numerous studies on animals and humans, that those high stress and traumatic events can cause actual physical changes of the brain structures. MRI studies have been used to document smaller hippocampal volume in PTSD, Borderline Personality Disorder (BPD), depression with early abuse, Dissociative Identity Disorder (DID) with early abuse. Smaller amygdala volume was found in patients in BPD with early abuse, and increased amygdala in depression. Patients with depression had smaller orbitofrontal cortex volume. Bremner et al. (1999), preformed the study on 31 women, dividing them in three groups: women with early childhood sexual abuse and PTSD, women with PTSD and no abuse, and a group of women with no abuse nor PTSD. MRI was used to measure the hippocampal volume, while PET was used to measure the hippocampal performance during verbal declarative memory tasks.

Results of the study showed that women with abuse and PTSD had failure of hippocampal activation and 16% smaller volume of the hippocampus compared to women with abuse and no PTSD. Women with abuse and PTSD had a 19% smaller hippocampal volume in comparison to women without abuse or PTSD, meaning no traumatized participants.

Many studies during the late 1960s indicated that prolonged exposure of the brain to stress or glucocorticoids can be extremely harmful. Forebrain and limbic structures contain a high level of specific receptors (McEwen and Schwartz, 1968) that can be damaged due to prolonged exposure to stressor chemicals. In

1969, Mühlen and Ockenfels did experiment with guinea pigs, injecting them daily for four weeks with glucocorticoids. The guinea pigs have all suffered from damage to hypothalamus and hippocampus. Harm to those two structures can further indicate on disturbance of HPA axis.

Comorbidities of emotional trauma and high stress

As we can see so far, emotional trauma, high stress levels and different disorders that can come out of them are real and have a physiological and biological impact on human body and psyche. Lives of affected individuals are changed on many levels, including lack of emotional inhibition and control, cognition and learning issues, memory failure, behavior and possible psychiatric diagnoses.

Shields and Cicchetti (1998) examined the complex interplay among emotion, attention, and aggression in a sample of 141 maltreated and 87 non-maltreated impoverished, inner-city children. Maltreated children were more likely than non-maltreated children to be aggressive, have attention deficits, while dissociation was more likely among children who experienced physical or sexual abuse.

A study by Althoff and colleagues (2010), that lasted 14 years, included 2076 Dutch children. Participants that had severe issues with emotional regulation were at increased risk for problems with regulating affect, behavior and cognition), Dvir at al (2016) have shown in the study that individuals with emotional regulation challenges in childhood as a consequence of trauma have multiple problems in many areas of life (psychological, sensory processing, emotional and cognitive fields) during adulthood.

In a retrospective cohort study done by Dube et al. (2006), on 8417 participants about adverse childhood experiences, (including abuse and neglect, household dysfunction of various forms, alcohol use), reported that 89% of participants were ever drinking. Among ever drinkers, initiating alcohol use by age 14 was increased two to threefold. The study concluded that adverse childhood experiences were strongly related to onset of alcohol use in early and mid-adolescence.

Approaches to Trauma treatment

An estimated 70% of adults in the United States have experienced a traumatic event at least once in their lives. Most of these individuals recover on their own, while 20% develop a post-traumatic stress disorder (Foa et al., 2007). Out of need to help those individuals integrate back in life and society as much as possible, many methods for treating trauma have developed over time. Those are psychoeducational and social work (Kafula, 2016), critical incident stress debriefing (Mitchell, 1996), exposure therapy (Foa et al., 2007), eye movement desensitization reprocessing (Shapiro, 2018), and somatic experiencing (Levine, 2010).

Somatic Experiencing is body focused therapy that integrates body awareness (interoception) and psychotherapeutic approach in treating trauma. Inner body sensations are used as a starting point in therapy. Extensive retelling of a traumatic event is not necessary, as it is in many other above mentioned modalities.

In Somatic Experiencing (SE), post-traumatic stress symptoms are considered an expression of stress activation and an incomplete defensive reaction to a traumatic event. From this theoretical perspective, the goal of therapy is to release the traumatic activation through an increased tolerance of bodily sensations and related emotions, inviting a discharge process to

let the activation dissipate (Levine, 2010). This is achieved through "felt sense", titration (keeping arousal at low level during processing of trauma), pendulation (balancing between regulated parts in the body and dysregulated ones) and discharge (dissipating arousal without re/traumatizing and overwhelming individual). Brom et al. (2017), did randomized control outcome study on effectiveness of SE in individuals experiencing symptoms of PTSD and found out that SE is effective (<4) method for treating PTSD, with large effect size (Cohen's *d* > 0.8) on both PTSD and depression, while clinical results should be considered moderate with 44.1% participants losing diagnoses of PTSD.

DISCUSSION

Fear and its pathway in the brain throughout different structures has biological and evolutionary importance to protect life and assures survival of the species. The limbic system and its structures have an important role in this process - from threat detection, response mechanisms to termination of stress reaction. If those steps are not able to unfold in its natural biological way, many complications can occur.

Due to prolonged exposure to stress, repeated traumatic experiences, violation of boundaries as it is the case in sexual abuse, the threat response is stuck in the nervous system and it never ends, causing long term damage to different brain structures as well as to general health. The HPA axis activation and longer then needed secretion of glucocorticoids and cortisol cause damage that is often irreversible. Changes in the volume and function of different structures of the brain, inhibition of reasoning of prefrontal cortex as a consequence of taking over of fear and limbic system are often run by survival impulse, memory failure, emotional dysregulation, as well as a chain of health issues like high blood pressure, cardiovascular disorders, anxiety, depression and insomnia more than often are a result of unresolved traumatic experience. Unfortunately, this cause is too often overlooked.

Since effects of trauma are so far reaching when it comes to mental and physical health and since so many individuals suffer from its consequences, the cost of treatment for different conditions caused by trauma is extremely high, for social services as well as for individual families (which creates even more stress). American Psychological Association provides us with staggering costs of treatments: $2.3 trillion in United States only, during 2013, of which depression weighs $71 billion (Winerman, 2017).

A lot of studies are already done on this subject of fear, trauma and brain, but more need to be done in the area of treatment that does not necessarily include pharmacology as the primary path. Although the pharmacological approach has its place in treatment of trauma and its symptoms, it more than often does not resolve the cause of it, which is physiological dysregulation of the autonomic nervous system (ANS). Body-mind psychotherapy approach and practice of mindfulness have a promising future in this field and more research is needed to document it.

CONCLUSION

Relevance between emotional/psychological trauma and its effect on the nervous system, and overall health and wellbeing, is not a new area of research. This review has summoned studies that indicate on long term effects of trauma on physical, emotional and cognitive behavior and performance. Survivors of this type of trauma often have difficulties integrating in the society, having stable relationships, being able to support themselves

financially, develop professionally and they often suffer from multiple physical issues like high blood pressure, heart disease, psychiatric conditions, insomnia, diabetes, etc. Considering that nervous system runs throughout the physical body and regulates function of inner organs (autonomic nervous system), the consequences can be dire. This all creates burden on the very individual who survived trauma, their families and communities.

Being alive is stressful and trauma seems to be unavoidable part of life. The real question is if this much trauma happening around the whole world is avoidable to much greater degree than it seems. Trauma is being handed down from one generation to the other, perpetuating problems in the family and society as a whole. Resolving trauma with mindfulness, emotional release, or a somatic psychotherapy approach that addresses body and mind can make a difference in the world. More studies in this area are needed in order to document measurable effectiveness of somatic therapies on PTSD and its symptoms. The presented review can contribute to stimulation of the interest of various health care providers for a more integrative approach to treating presenting alinements of their patients.

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