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### PTSD Precipitating from Sexual Abuse and Combat War Exposure and Co-Morbid Disorders of Chronic Pain, Substance Abuse and Immune Systems

Jessica Anzalone  
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**PTSD Precipitating from Sexual Abuse and Combat War Exposure and  
Co-Morbid Disorders of Chronic Pain, Substance Abuse and Immune  
Systems**

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Submitted in Partial Completion of the Requirements for  
Commonwealth Interdisciplinary Honors in Biology and Psychology

Bridgewater State University

May 8, 2019

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## **Abstract**

Posttraumatic stress disorder (PTSD) is a trauma and stress related disorder that some people develop after exposure to a traumatic life altering event. The person must witness the traumatic event, have the traumatic event occur to a loved one, or experience a traumatic event first hand. According to the publication of the American Psychiatric Association, the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), the diagnostic criteria for the identity of PTSD must include behavioral symptoms that accompany PTSD in four diagnostic clusters; re-experiencing, avoidance, negative cognitions and mood, and arousal (American Psychological Association, 2018). Two of the most common demographics affected by PTSD are survivors of sexual assault and combat war veterans and these are typically cached together. Yet, preliminary investigation suggests while there is overlap in manifestation of the disease, there may be important differences depending on the context in which the events took place: military versus sexual assault. Scientific literature will be used to create an in-depth comparison of the similarities and differences in symptoms and physiological impacts of PTSD between sexual assault survivors and combat war veterans. Specifically, this study will focus on differences and also the identification of biomarkers of chronic pain, addiction and assessment of immune function.

The desired outcome is to develop a better comprehension of PTSD and work towards public awareness of the differences between sexual and war combat PTSD. This will result in facilitating a more accurate and successful understanding of treatment for individuals who are experiencing symptoms of PTSD.

## Introduction

Individuals who have survived sexual violence or were involved in wartime combat experience rates of Posttraumatic stress disorder (PTSD) estimated to be between 10-40 percent higher compared to the general population (Brunet & Sareen, 2015). According to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, (DSM-5), PTSD is a trauma and stress related disorder that some people develop after exposure to a traumatic life altering event. To be diagnosed with the disorder, an individual must witness a traumatic event, have the traumatic event occur to a loved one, or experience a traumatic event first hand. The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), states that the diagnostic criteria for the identification of PTSD must include behavioral symptoms that accompany PTSD in four diagnostic clusters; re-experiencing, avoidance, negative cognitions and mood, and arousal (American Psychological Association, 2018).

Chronic pain is often reported in patients who have PTSD (Noel et al., 2016). Additionally, PTSD and substance abuse are prevalent and often co-occur (McCauley et al., 2012). Furthermore, individuals afflicted with PTSD have biological alterations in their primary pathways of neuroendocrine and immune function (Neigh & Ali, 2016). Therefore, this review will first focus on the neurobiological and anatomical characteristics of PTSD and then

identify the two primary demographics, combat war veterans and survivors of sexual abuse, that have been investigated in this study. The three conditions that are often co-morbid with PTSD and each other: chronic pain, addiction, and immune disorders, will then be discussed in relation to PTSD. Furthermore, this review will discuss the extent to which these co-morbidities differentially impact sexual assault survivors with PTSD and combat war veterans with PTSD. Finally, data will be presented describing the discrepancy in PTSD related research for these populations. Comparison of the similarities and differences between these two groups provides intrinsic benefits in forming a holistic understanding of PTSD.

### **Clinical Definition of PTSD**

The newest edition of the American Psychiatric Association's (APA) Diagnostic and Statistical Manual of Mental Disorders (DSM-5) has recently altered the criteria for the positive diagnosis of PTSD. Diagnostic criteria for the identity of PTSD must include behavioral symptoms that accompany PTSD in four diagnostic clusters; re-experiencing, avoidance, negative cognitions and mood and arousal. The precipitating event must be identified as an exposure to sexual violation, serious injury, or threatened death. The exposure to the precipitating event must result from a direct experience to a traumatic event; first hand repeated or extensive exposure to extreme details

of a traumatic event (not through movies unless work-related, television, pictures, or through media); witness a traumatic event in person; or learning of a traumatic effect that has affected a close friend or family member. The traumatic event must be persistently experienced in one of the following ways; flashbacks of the event, nightmares, unwanted upsetting memories, or emotional distress or physical reactivity after exposure to a traumatic reminder. In addition, the person must have an avoidance tendency of trauma related stimuli after the event such as trauma related external reminders or trauma related thoughts or feelings. The negative thoughts or feelings the person has towards the event must have begun or become exacerbated after the trauma in at least two of the following ways; exaggerated blame of one's self or others for causing the trauma, the inability to recall key features of the trauma, a pessimistic view about oneself or the world, feeling of isolation, negative affect, struggling to experience positive effect, and a reduced interest in activities.

PTSD has been correlated with both situations involving a single specific brief traumatic event, and also with situations involving long term patterns of regular abuse or trauma and chronic victimization. While studies have correlated age at the precipitating trauma with the resulting PTSD phenotype, it has still not been definitively determined what affect if any that this time frame for trauma has.

In addition, the individual must have at least two of the following alterations in arousal and reactivity that started or increased after the trauma: (1) difficulty falling or staying asleep, problems concentrating, impulsive, risky or destructive behaviors, aggression or irritability, heightened startle responses, or (2) a sensation of hypervigilance believing danger is constantly present. These symptoms must last for more than one month and must also create a functional impairment or clinically significant distress in the person's social interactions, their ability to work, or other crucial areas of functioning. PTSD is a trauma and stress-related disorder that frequently co-occurs alongside other disabling psychiatric and physical conditions (Shipherd et al., 2007). Due to these frequent co-morbidities, it is important to note that these symptoms cannot be a physiological result of substance use, medication, or other illness (American Psychiatric Association., 2013).

## **Neurobiology of PTSD**

One of the factors that has been the source of confusion and controversy in the understanding of PTSD, is the complex nature of the neuroendocrine, neuroanatomical, and neurochemical effects it has on the human brain and body. The underlying neurobiology of PTSD involves the neuroendocrine stress response and the sympathetic nervous system and

impacts several brain areas. The hormone, cortisol, which is a glucocorticoid is the primary driving component of neuroendocrine system hypothalamic-pituitary-adrenal axis (HPA axis), while adrenaline (also called “epinephrine”) is the driver of the sympathetic nervous system (Rege, 2017).

### **The Sympathetic and Parasympathetic Nervous Systems:**

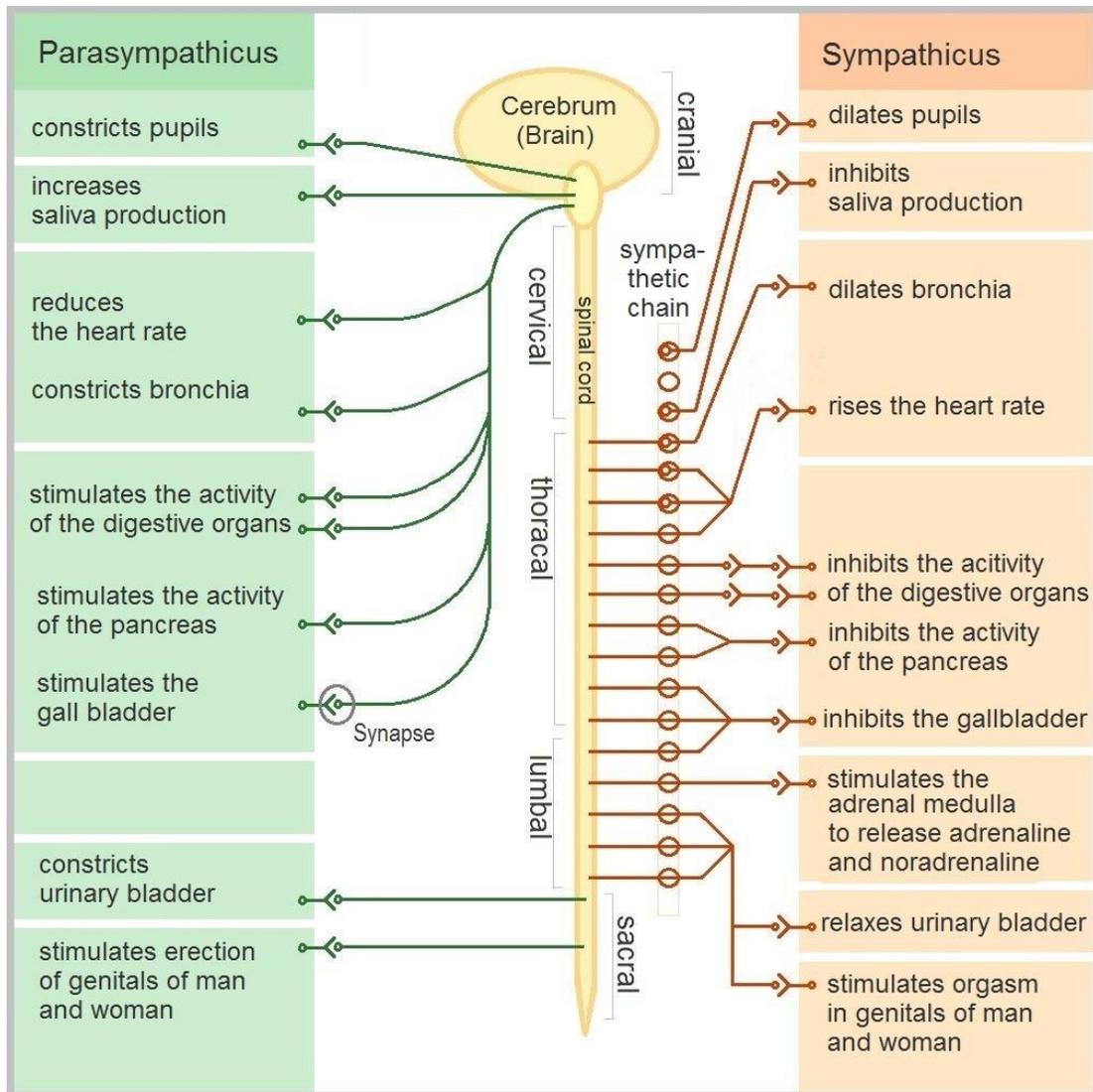
The sympathetic nervous system is responsible for the “fight or flight” response that the body has developed to respond to acute stresses. Respectively the parasympathetic nervous system is responsible for returning the body to a state of “rest and digest”. These systems typically balance each other out allowing intense sudden responses to stress while also allowing long term physiological stability (Figure 1). These involuntarily controlled systems are also responsible for the regulation of the catecholamine neurotransmitters: norepinephrine and epinephrine. The release of these chemical messengers increases oxygen consumption, heart rate, blood pressure, pupillary dilation, stimulates sweat secretion, and causes blood flow to facilitate glucose and oxygen coming together to form ATP (Sapolsky, 2004). Furthermore, this “fight or flight” response has a biphasic effect on the immune system. In general, it initiates aspects of innate immunity such as reducing inflammation to destroy antigens, pathogens and foreign

invaders whereas it tends to divert resources from long-term adaptive immunity (Hannibal & Bishop, 2014).

Concurrent with the activation of the sympathetic nervous system is often activation of the HPA which promotes the release of cortisol, a glucocorticoid which has receptors expressed in nearly every cell type. Cortisol is a lipophilic hormone responsible for the regulation of glucose levels (hence the label “glucocorticoid”) that is capable of crossing the blood brain barrier thus directly affecting the brain. In times of stress, the body has an increase in its need of the cell’s energy molecule, adenosine triphosphate (ATP) (Bremner et al., 1995), within areas specifically but not limited to those involved in the control of fear and aggression such as the amygdala, those related to learning and memory especially the hippocampus, and in voluntary muscle functions which may be necessary for “flight” or movement in order to avoid danger.

In typical reactions to acute stress, about 15 minutes after the stressful event, the levels of cortisol diminish, and the parasympathetic system takes over promoting the process of “rest and digest”—a neuroendocrine response to restore homeostasis. This system promotes energy storage, growth, rest, adaptive immunity and processes that slow the body down (Sapolsky, 2004). Individuals with PTSD however, do not transition from a state of “fight or

flight” to “rest and digest” in a typical manner due to inhibition of the normalization in cortisol levels.



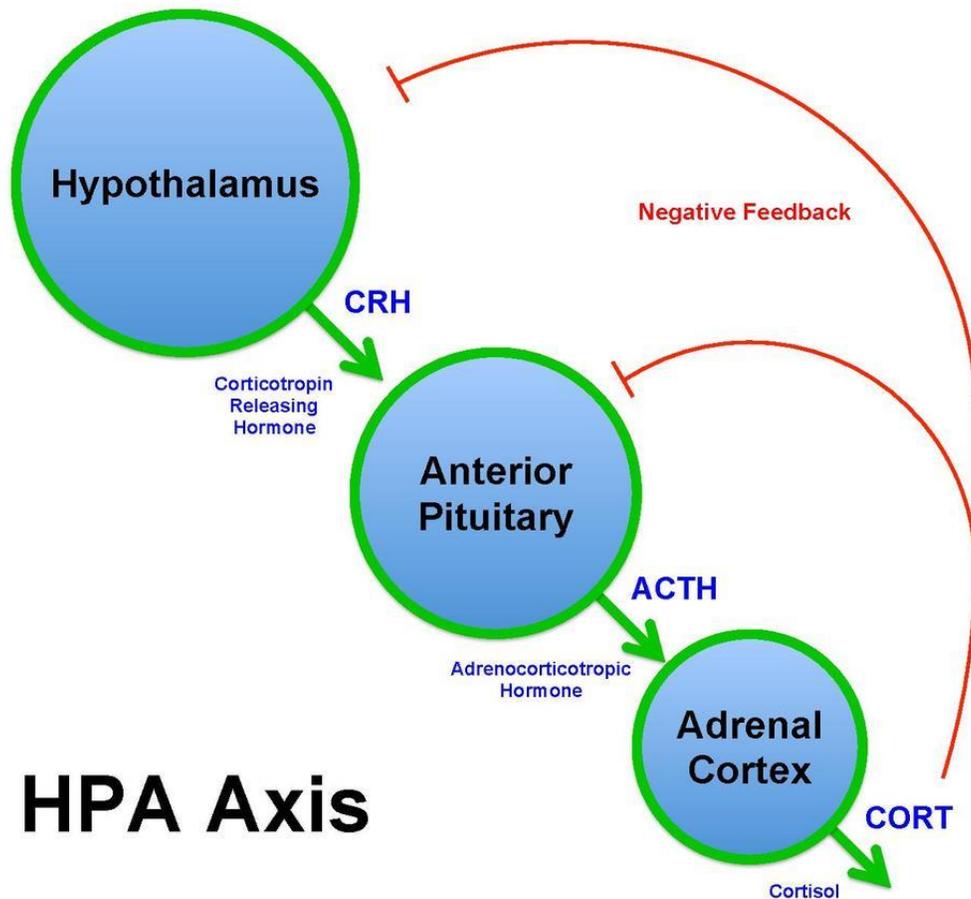
*Figure 1. Overview of the sympathetic and parasympathetic nervous systems.*

*In individuals with PTSD, activation of the sympathetic nervous system is not appropriately balanced by the parasympathetic nervous system due to sustained elevations in cortisol levels due to the HPA axis. This prevents the*

*individual from transitioning typically from a “fight or flight” state to a “rest and digest” state (Geo-Science-International, 2016).*

### **Hypothalamic-Pituitary-Adrenal Axis:**

The hypothalamic-pituitary-adrenal (HPA) axis, is largely responsible for the physiological responses to heightened levels of stress. In times of increased levels of stress, the hypothalamus initiates a chain of neurological and chemical events. Within the hypothalamus, the periventricular nucleus (PVN) secretes corticotrophin-releasing hormones (CRH), which causes the anterior pituitary to release adrenocorticotrophic hormone (ACTH). This then travels to the adrenal cortex and in response causes the release of corticosteroids (Cortisol) (Figure 2).



*Figure 2. Hypothalamic-Pituitary-Adrenal Axis Pathway. The hypothalamus releases corticotropin releasing hormone (CRH), which leads to the anterior pituitary to release adrenocorticotropic hormone (ACTH), followed by the adrenal cortex releasing cortisol. In individuals with PTSD, long-term activation of this pathway either dampens responses or downregulates glucocorticoid receptors (BrianMSweis, 2012).*

In individuals with PTSD, the typical balance of this hormonal cascade is altered. The HPA axis prevents the parasympathetic nervous system response from initiating in a typical manner resulting in sustained release of cortisol perpetuating the stress response. These individuals have a heightened resting level of CRH which causes a reduced ACTH response that ultimately leads to a reduction in overall glucocorticoid signaling (Rege, 2017).

Prolonged increased levels of cortisol can result in a compensation of down-regulation or resistance of the glucocorticoid receptor that blocks the binding of cortisol. The overall effect of this is the reduction in signaling leading to the failure of cortisol to function properly. This will also prevent negative feedback resulting in sustained higher levels of CRH.

### **Neuroanatomical structures involved in fear and memory**

In addition to the neurochemical changes identified in individuals with PTSD, several neuroanatomical changes are prevalent. Brain imaging has shown fundamental alterations in structures associated with stress and fear conditioning in individuals suffering from PTSD. Some of the most notably altered structures include the hippocampus, amygdala, and the prefrontal cortex (Yehuda et al., 2015).

**Hippocampus:**

The hippocampus is the primary site of learning and memory within the brain, wherein the neurotransmitter glutamate assists in the formation of short-term and long-term memories through long-term potentiation. This is affected by multiple factors one of which being the cortisol level present. Cortisol increases the release of glutamate and has been shown to be responsible for “flash-bulb” memories that take place in response to increased levels of stress (Popoli, Yan, McEwen, & Sanacora, 2011). Like many situations in which the brain will attempt to correct a perceived imbalance, studies have shown that stress increases the level of baseline glucocorticoids and that the release of cortisol specifically can increase the time required to process and learn new skills or information. In animal studies, elderly mice learned a maze more slowly when they possessed elevated blood levels of glucocorticoids compared to those who possessed average levels of glucocorticoids. The long-term exposure of glucocorticoids was proven to destroy hippocampal neurons (Yau & Seckl, 2012). Similar to what takes place in the victim of a stroke, an abnormal elevation of glutamate can cause over excitation of the post synaptic cells which may result in the death of the neuron. The hippocampus also is a key factor in the conditioning of stress responses, declarative memory, and fear extinction. There has been

a strong correlation between a reduction in hippocampal volume and the incidence of PTSD in an individual. This correlation has recently come under scrutiny bringing debate to whether the decrease in hippocampal volume is a result of PTSD or a trait increasing the risk of the development of PTSD (Rege, 2017).

**Amygdala:**

The processing of stressful stimuli, emotional processing and association of fear responses is most directly affected by the amygdala. Glutamate transmission is increased in times of stress. Due to this increase in glutamate transmission, any future exposure to traumatic events or associations connected to the initial event initiate a fear-based response. Individuals with PTSD can display both hypo-activity and hyper-activity within the amygdala sub-nuclei. Studies have shown that even in episodes of prenatal stress, fetuses that grow to adulthood develop similar physiological responses to those who suffer trauma at later stages of their lives. In studies with rats, such fetuses that were subjected to regular stress over the last week of their mother's pregnancy, displayed an approximately 30 percent increase in amygdala volume when compared to fetuses of rats that had not been subject to routine stress (Harmon, et al, 2009). Structurally, MRI analysis and a study focused on the brains of monkeys under continuous

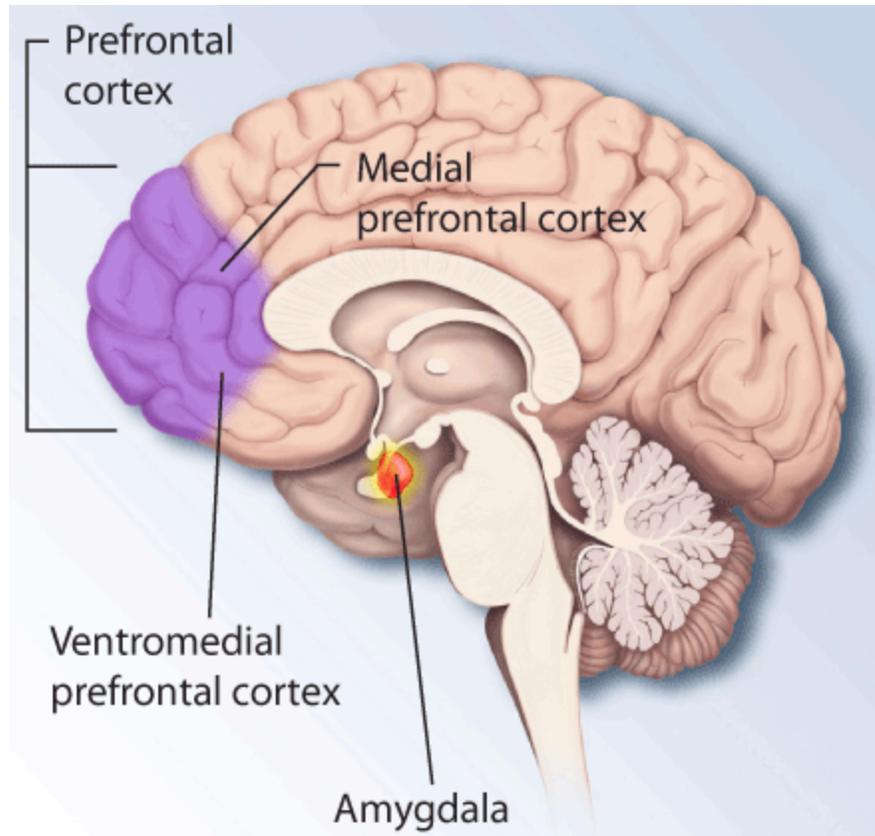
stress, have displayed both an overall general increase in the amygdala size, and pathological damage caused by hyper-responsiveness to perceive threatening stimuli (Uno, Tarara, Else, Suleman, & Sapolsky, 1989). These results indicate a long-term neurological alteration of an individual's ability to consistently and accurately interpret stimuli in stressful situations.

### **Prefrontal Cortex:**

The prefrontal cortex is responsible for the modulation of behaviors potentially via its role in working memory. An individual's ability to distinguish appropriate behavior within a given context is highly regulated through the prefrontal cortex. As shown in Figure 3, the prefrontal cortex is adjacent to the amygdala and both areas of the brain have a bilateral ability to directly affect each other. The prefrontal cortex is responsible for the inhibition of acquired fear responses allowing fear extinction to be possible. Along with displaying a general reduction in prefrontal cortex volume, the ability to inhibit the control of the amygdala's stress response system is shown to be decreased in individuals experiencing PTSD. Children who had experienced emotional maltreatment had a 7.2% reduction of the volume of their prefrontal cortex on average (van Harmelen et al. 2010).

This reduction in inhibitory function often results in a lesser degree of control over responses to traumatic associations leading to the individuals re-

experiencing of precipitating traumatic events in various forms from increased anxiety to “flash backs”. It was found in a functional imaging study that when individuals with PTSD were shown faces with fearful expressions, they displayed increased activation in the amygdala and a decreased activation in their prefrontal cortex when in comparison to individuals not experiencing PTSD (Shin et al., 2005). One group of researchers concluded that the prefrontal cortex is considered to be the structure responsible for controlling an individual’s behavior and reactions, and in individuals with PTSD, the prefrontal cortex can have such a diminished level of function that often, rather than being responsible for emotional reactions, the amygdala alone is considered as the overall controlling body for such responses (Rauch, Shin, & Phelps, 2006).



*Figure 3. Brain areas affected in PTSD. In PTSD the relationship between the amygdala and the prefrontal cortex is altered manifesting in either overmodulation of the amygdala emotional processing by the prefrontal cortex, or an inability to regulate emotional processing or fear responses from the amygdala (National Institutes of Health (NIH), 2007).*

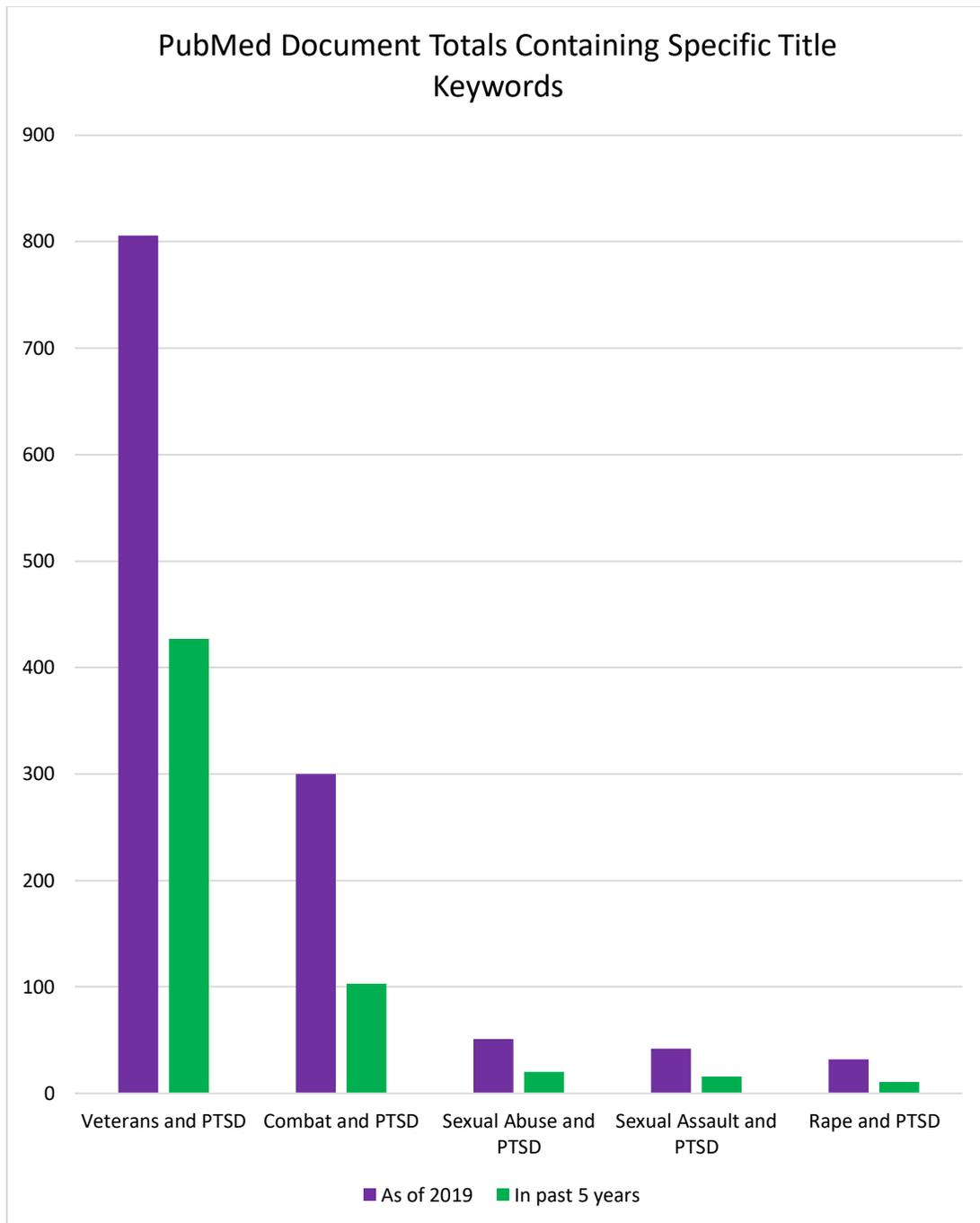
## **Prefrontal Cortex-Amygdala: Emotional Overmodulation and Undermodulation:**

One factor that has caused much controversy in the diagnosis of PTSD is its ability to manifest itself in seemingly opposite response types. The two primary phenotypes of PTSD are emotional undermodulation and emotional overmodulation. Emotional undermodulation is represented by a reduced prefrontal cortex inhibition, increased emotional autonomic responses, and an increased level of amygdala activity. Alternately, individuals experiencing emotional overmodulation tend to have an increased level of prefrontal cortex (PFC) inhibitory function, an emotional detachment, numbing or depersonalization, and an increase in prefrontal cortex activity coupled with a reduction in amygdala responses. The seemingly paradoxical nature of these two primary phenotypes has been the source of much confusion when diagnosing and treating PTSD. While both are displayed in seemingly opposite ways, they both are consistent in their areas of neuro-anatomic and neurochemical areas of modification (Yehuda et al., 2015).

### **PTSD Precipitating from Sexual Abuse**

Sexual abuse PTSD can be acquired from several different situations. According to [rainn.org](http://rainn.org), every 98 seconds an American is sexually assaulted.

The three main forms of sexual abuse that have a tendency to precipitate PTSD include, Child sexual abuse and assault, Sexual Assault (SA), and Intimate Partner Violence (IPV). Unlike the recently, widely publicized and accepted attribution of PTSD in combat war veterans, PTSD in survivors of sexual abuse, is often either undiagnosed or an individual's symptoms are considered to be predominantly psychological rather than deeply rooted in physiological changes resulting from psychological and trauma-based precipitating incidences. This discrepancy in demographic-based association of PTSD can be shown by the disproportional representation of title keywords within published studies from the scientific community as shown in (Figure. 4). Additionally, the association with shame and embarrassment weighs heavily on the statistical representations of individuals who have been victims of sexual abuse. In 1993, it had been believed that the percentage of women with a history of rape in the United States could be as high as 12.9% (Moser, Hajcak, Simons, & Foa, 2007) while a population of young adults studied in Detroit yielded a 1.6% prevalence of rape reported (Breslau, Davis, Andreski, & Peterson, 1991).



*Figure. 4 Graph comparing articles published and cited in PubMed with titles containing relevant keywords in total and over the past five years. All searches were run requiring the presence of both PTSD and the relevant keywords in the publication title as of May 4, 2019.*

Sexual assault (SA), including and not limited to rape, is any act of sexual contact or behavior that is not expressly permitted by the victim and is estimated to impact 17.6% of women and 3.0% of men in the United States (Tjaden & Thoennes, 2000). Intimate partner violence (IPV) is a sub classification of sexual assault wherein the transgressing individual is someone the victim is personally familiar with and may or may not have had a previous or current sexual or emotional connection with. It is estimated that IPV is experienced by 21.7% of women and 7.3% of men in the United States.

A sub classification of IPV that can cause PTSD is known as military sexual trauma (MST). Military sexual trauma is a form of high betrayal trauma because the social agreement of trust is broken for the violated victim due to their dependency on the perpetrator for survival. The victim is unable to leave, confront, or break ties with the perpetrator due to their military connection. This connection and betrayal damage the victim's wellbeing and their overall view of the world leading to PTSD. The victim is subjected to trauma by someone who was meant to help them develop as individuals and soldiers. Escaping the perpetrator may be difficult and lead to more violations, interpersonal violence, rape, and continued exposure and involvement with the perpetrator leading to long term consequences. Women who experience military sexual assault have higher rates of PTSD than

women who have been subjected to other types of trauma. MST has been reported to affect 40% of female veterans. The number is uncertain due to many veterans not reporting incidences (Lutwak & Dill, 2013).

While both forms of sexual violence, IPV and SA, are concerning adult men and women, SA has shown to be significantly more likely to increase symptom severity across multiple symptom clusters (Dworkin, Mota, Schumacher, Vinci, & Coffey, 2017). An individual's experiencing of IPV however, has been shown to be a less consistent indicator in the development of PTSD symptom clusters when regarding other forms of sexual violence. SA and IPV also display differences in their tendencies of phenotype manifestation.

Individuals suffering from PTSD due to an IPV-based precipitating event have shown a tendency to behave in manner consistent with chronic victimization. These individuals tend to behave in active avoidance subscribing more typically to the PTSD phenotype of Emotional Undermodulation. SA survivors on the other hand have a greater tendency to display tendencies of passive avoidance and emotional numbing depicting a greater predisposition to fall within the classification of Emotional Overmodulation PTSD (Matlow & DePrince, 2013).

Military sexual trauma has many similar components to the arguably most consistent form of sexual violence related PTSD precipitating events,

child sexual assault. Every year 63,000 children are sexually abused. Sixty-six percent of sexual assault and rape victims are children ages 12-17 (Morgan, 2017). Classification of an act of sexual assault of a child is considered to be when the child is involved in sexual activity in order to provide sexual gratification to the perpetrator. This includes exposure to pornography, use of the child for prostitution, sexual based touching, and acts of sexual non-touching such as exhibitionism, photography of the child for sexual gratification, and communication in a sexual way face to face, by internet, or by phone. Children's sexual abuse can involve molestation, incest, prostitution, statutory rape, pornography, or other sexual activities (Murray, Nguyen, & Cohen, 2014).

A study conducted in an Israeli out-patient ambulatory center found that of individuals who had experienced sexual abuse under the age of 16, 61.4% experienced a prolonged effect that had persisted until the time of study. When comparing the prevalence of continuing or prolonged effects as a result of childhood sexual abuse to that of Holocaust survivors (33.3%), victims of car accidents (34.8%), and veterans of the Gulf War (8.9%), the impact of sexual abuse during childhood is staggering (Gaon, Kaplan, Dwolatzky, Perry, & Witztum, 2013). Furthermore, this study powerfully highlights the potential lack of proper diagnosis in the area of PTSD in victims of sexual abuse. While nearly 11% of the 456 individuals who

reported a moderate to severe effect of traumatic events displayed a prolonged and current debilitating effect from the initial trauma, only 3.3% of the individuals who had been diagnosed with PTSD had been victims of sexual abuse. Respectively, in the same study, some of the most largely represented groups of individuals with PTSD reported sexual abuse to have occurred much more significantly. The presence of sexual abuse was reported to be 21.5% in individuals with major depression, 18.8% in those with bipolar disorder, 20.8% in respondents with personality disorder, and 19.4% in those suffering from psychotic disorder (Gaon, Kaplan, Dwolatzky, Perry, & Witztum, 2013).

It is also notable that it has been shown that individuals suffering from PTSD resulting from traumas such as chronic childhood abuse or other long term precipitating traumatic events more often display symptoms of emotional overmodulation resulting in symptoms of dissociation when compared to individuals suffering more acute precipitating traumas (Lanius et al., 2010). Studies have linked PTSD symptoms to childhood sexual abuse particularly those of posttraumatic fear, anxiety, and concentration. Research assessing sexually abused children has found up to a 48% increase in a diagnosis of PTSD when compared to children who had not been sexually abused (Briere, & Elliott, 1994). Despite the fact that the majority of child sexual abuse victims do not meet full PTSD diagnostic criteria, over 80% of

individuals experiencing such abuse have reported PTSD symptoms. Adults who were childhood sexual abuse victims have been shown to consistently show increases in avoidant, arousal, and intrusive symptoms of PTSD when compared to individuals who did not experience abuse as a child. Adult survivors of childhood sexual abuse have shown a prominent tendency to experience various forms of flashbacks. Sudden intrusive visual, auditory, tactile or olfactory sensory experiences reminiscent of the PTSD precipitating trauma often lead to vivid and intense flashbacks strongly leaving those suffering with the feeling that the events were actually presently occurring rather than just a recalled memory (Briere, & Elliott, 1994).

### **PTSD Precipitating from Combat War Exposure in Veterans**

The prevalence of PTSD in combat war veterans has been highly publicized and the focus of intense discussion and study in the recent past (Figure 4). This increase in public attention has been a driving force for further identification and treatment of PTSD in combat war veterans. While studies have varied significantly on concrete statistics of PTSD prevalence percentages, the rate of lifetime PTSD within combat war veterans is approximately two to four times higher than the general population (Gros, Szafranski, Brady, & Back, 2015). The National Vietnam Veterans Readjustment Study states that 30 percent of veterans have had PTSD at some

point during their lifetime which can persist many decades after the initial combat exposure (Shipherd et al., 2007). In the past 13 years, there have been as many as half a million U.S. troops who served in Iraq or Afghanistan that have been diagnosed with PTSD.

Intrinsically, combat war is a source of countless potential sources of trauma that could become precipitating incidences for the formation of PTSD in those exposed. Modern warfare and its tendency to trend more in favor of complex guerilla tactics, has posed several new areas of potentially heightened trauma exposure levels that could result in PTSD of the individuals experiencing them. Some sources of trauma that could precipitate the development of PTSD include but are not limited to; fear and trauma resulting from improvised explosive devices, a lack of clearly defined areas of conflict and safety, unpredictable urban-style guerrilla attacks and an increase in overall average exposure to a consistently traumatic environment (Reisman, 2016).

Specifically, study has been focused on a dissociative PTSD subtype now recognized as the emotional overmodulation phenotype of PTSD. While it was expected that PTSD symptoms would fall in line with the more common form of PTSD consisting of emotional undermodulation resulting in hyper arousal and re-experiencing symptoms, a 2014 study provided surprising results. A study was conducted of 63 U.S. soldiers four months after returning from

deployment in Iraq. This was the first study to demonstrate the interaction between attentional threat avoidance, behavior health symptoms during the post-deployment period and combat exposure. The resulting data posed the possibility that attentional avoidance (the directing of one's focus opposite the location of a threatening cue) of threat stimuli may be a robust phenomenon among symptomatic populations of individuals who are or have recently experienced highly stressful combat events. This display of attentional avoidance was a notable contradiction to the typical patterns of enhanced vigilance seen in patients diagnosed with PTSD (Sipos et al. 2014). A recent fMRI and script-driven imagery test conducted while individuals with PTSD were led to recall their traumatic experience showed that approximately 70% of patients displayed an increase in heart rate and had the subjective experience of reliving their traumatic experience. Respectively, the remaining 30% of the individuals with chronic PTSD tested displayed a dissociative response consisting of a subjective state of depersonalization and de-realization while showing no notable increase in heart rate (Lanius et al. 2010).

## Chronic Pain

Chronic pain is often comorbid with PTSD and as is generally the case, when looking at the two populations most affected by PTSD, most of the research on pain has been conducted with combat veterans (Figure 5).

Chronic pain is any form of pain lasting more than 12 weeks. Individuals with PTSD display consistently lower levels of cortisol. Cortisol is a potent anti-inflammatory and the desensitization promotes abnormal inflammation in response to pro-inflammatory stresses. In individuals with cortisol dysfunction, upon the activation of an acute inflammatory stress response, widespread inflammation often follows (Hannibal & Bishop, 2014).

Furthermore, the failure of cortisol to function properly limits the body's ability to reduce such inflammation which can lead to the production of free radical byproducts and stress damage to healthy tissues. Inflammation is also capable of widening the gap junctions in the blood brain barrier and intestinal lining. This widening can allow large foreign bodies or toxins to breach protective barriers and may result in illness (Sorrells, Caso, Munhoz, & Sapolsky, 2009).

One definitive aspect of the body's inflammatory response is the sensation of pain. Patients suffering from chronic pain tend to process pain in emotion-related circuits, also responsible for the reward processing, more actively than those with acute pain preceding recovery (Hashmi et al. 2013).

This was inferred from the substantial increase to activation overlap of brain emotional processing areas such as the prefrontal cortex and amygdala with regions involved in acute pain when imaging chronic pain patients. This increased interconnection highlights a correlation between reorganization in the reward and motivational circuits when related to the emotional circuits of the brain, leading to the possibility of their interconnectivity and explaining co-morbid disorders such as PTSD in chronic pain patients (Navratilova et al., 2016).

The connection of the reward centers of the brain to the prefrontal cortex and amygdala, which is responsible for the balance dysfunction in individuals with PTSD, has been shown to decrease dopamine release in response to pain. Individuals with fibromyalgia did not release dopamine in response to noxious stimulation whereas individuals not suffering from reward pathway dysfunction showed dopamine release when self-reported pain was induced (Wood et al., 2007). This self-reported pain correlated with dopamine amounts released in the basal ganglia.

PTSD alongside chronic pain are often comorbid (Gros, Szafranski, Brady, & Back, 2015) in veterans. Almost 50% of veterans have reported experiencing some sort of frequent chronic pain regularly (Kerns, Otis, Rosenberg, & Reid, 2003). According to Morasco et al. (2013), in a sample of 205 military veterans, 32% had chronic pain with comorbid PTSD. Veterans

were divided into two groups, those with PTSD and those without PTSD. The group of veterans with PTSD reported a remarkably higher pain severity and pain interferences than those without PTSD. The most common types of chronic pain within veterans who suffer from PTSD is neck or joint pain, lower back pain and rheumatism/arthritis, in that order.

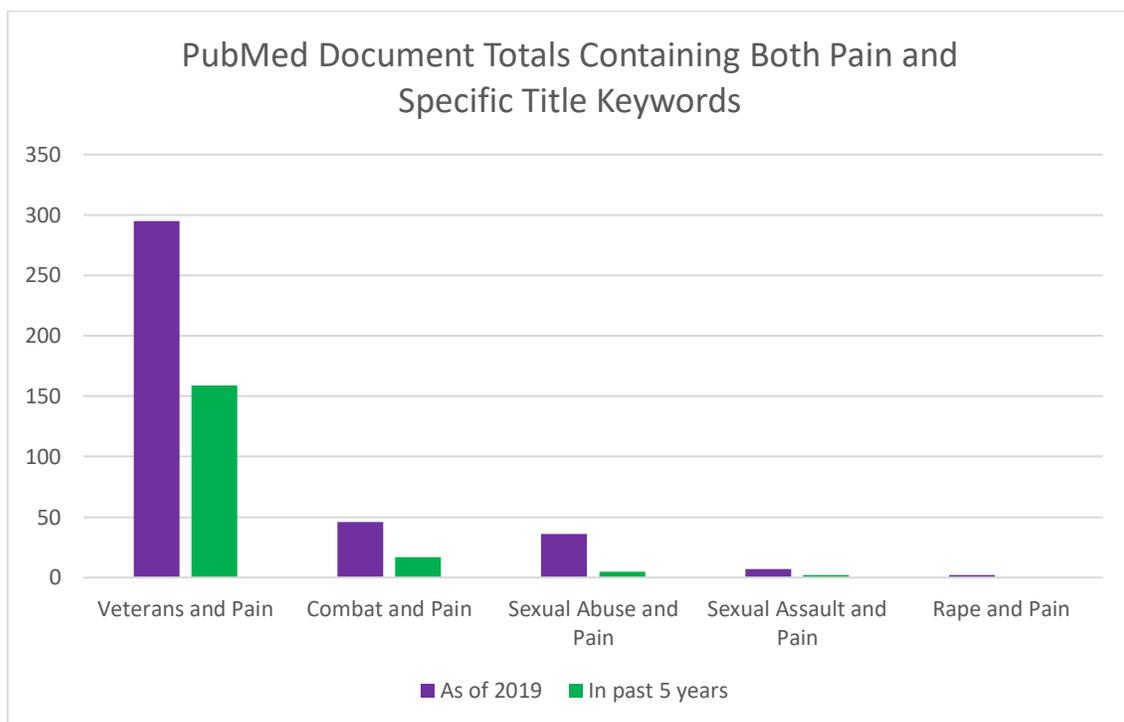
Additionally, in the study by Alschuler & Otis (2014), 198 veterans were surveyed for their pain levels. Veterans with comorbid pain and severe PTSD symptoms were found to have a lower differentiation between mild and moderate pain, whereas the cutoff between moderate and severe pain remained the same. Lower levels of pain intensity are connected to higher levels of pain-related interference in veterans with comorbid pain and severe PTSD symptoms when compared to veterans with pain without severe PTSD symptoms. Consequently, physicians should take into account PTSD symptoms when assessing a veteran's pain severity. Male veterans with combat- related PTSD have a decreased sensitivity to pain when compared to women who suffer from PTSD from intimate partner violence (Strigo et al., 2010).

In a study performed by Meltzer-Brody et al. (2007), 713 women were administered a questionnaire when they were seen for pelvic pain. Roughly 35% of participants who suffer from chronic pelvic pain were sexually abused with one in three women having been diagnosed with PTSD. The

psychiatric comorbidity of chronic pain and PTSD may contribute to the woman's severity in pain levels. PTSD resulting in sexual assault has been shown to display increased levels and regularity of abdominal pain, chest pain, pelvic pain and genital pain (Yeh, Watanabe, Sulkes-Cuevas, & Johansen, 2018). A nationwide survey of female veterans found PTSD is associated with at least one medical condition often involving pain. Arthritis and chronic lower back pain were the most common (Price, McBride, Hyerle, & Kivlahan, 2007). Women with PTSD have a higher chance of reporting their pain as severe when compared to women who do not have PTSD. In turn, gynecologists can create specific treatment interventions for patients who have chronic pelvic pain and PTSD instead of treating them alongside patients without PTSD (Yeh, Watanabe, Sulkes-Cuevas, & Johansen, 2018).

Countless studies have been done on the comorbidity of chronic pain and PTSD however statistical estimates of the prevalence of this correlation vary widely. Studies have shown that; 50 to 75% of patients present for PTSD treatment also suffer from chronic pain, 80% of combat veterans with PTSD report chronic pain, 20-37% of individuals reporting chronic pain suffer from PTSD, and most recently that a sample of veterans serving in Operation Iraqi Freedom, Operation Enduring Freedom and Operation New Dawn displayed a 12.6% comorbidity of chronic pain and PTSD. Extensive and disproportionate study has been focused on pain and PTSD in the veteran

community (Figure. 5) which could lead to a greater understanding of forms of PTSD more frequently identified in veterans. Despite the clear positive correlation between PTSD and chronic pain in general, the actual pathways and mechanisms responsible for such atypical pain sensitivities and persistence remain obscure (Scioli-Salter et al., 2016). Additionally, individuals who have PTSD and comorbid chronic pain tend to have more severe pain than those with chronic pain alone (Morasco et al., 2013).



*Figure 5. Graph comparing articles published and cited in PubMed with titles containing both relevant keywords and pain in total and over the past five years. All searches were run requiring the presence of both pain and the relevant keywords in the publication title as of May 4, 2019.*

Research on the PTSD and chronic pain relationship has suggested that these alterations to frequency and perceived intensity of pain are the result of both biological and psychosocial factors including but not limited to: depression, anxiety, physical disability, and a negative outlook on life control. Unfortunately, despite the various biopsychosocial models proposed to explain the comorbidity of PTSD and chronic pain, there is minimal data on the actual neurobiological influences on the holistic physiological system. Recent studies have proposed the contribution of abnormal deficits of neuropeptide Y (NPY) and the neuroactive gamma-amino butyric acid (GABA)-ergic steroids allopregnanolone and its stereoisomer pregnanolone which when together are considered (ALLO). These hormones are known to play a role in control of stress responses, and individuals suffering from PTSD have lower levels of these stress-buffering molecules. Cortisol and the androgen, dehydroepiandrosterone (DHEA) also could be potential influences on the perceived intensity and frequency of chronic pain and PTSD symptoms. Cortisol and the HPA axis have been concretely linked to the neurobiological systems affecting pain and PTSD. DHEA is secreted simultaneously with cortisol secretion and negatively modulates (GABAA) receptor function, reducing the effectiveness of the previously mentioned benefits of increased ALLO levels. This DHEA response to cortisol displays a possible mechanism for balancing the pain inhibitory effects of ALLO with the typical pain reduction due to the release of cortisol in individuals without a cortisol

dysfunction. In individuals with PTSD however, the reduction in cortisol effectiveness creates an imbalance in overall pain reduction due to DHEA's reduction in pain inhibition resulting from increased levels of ALLO. This results in the need for individuals suffering from PTSD to have a means to inhibit DHEA's effect on ALLO in order to experience benefits due to their increased overall levels of cortisol (Scioli-Salter et al., 2016).

These complex and interconnected neurobiological mechanisms have the potential to serve as therapeutic targets in both the mitigation of PTSD and chronic pain symptoms. Studies conducted have correlated increases in ALLO to a reduction in activity of the amygdala thus potentially reducing the tendency for the amygdala to overcome the prefrontal cortex in individuals with emotional undermodulation type PTSD. Inversely, this reduction in amygdala activity could also have the potential to exacerbate symptoms of emotional overmodulation PTSD. There is also evidence that increased plasma levels of allopregnanolone leads to increased connectivity between the prefrontal cortex and the amygdala resulting in a reduction of anxiety. This reduction in anxiety displays significant potential for emotion regulation and thus potentially beneficial means to regulate pain tolerance (Sripada et al., 2013).

## **Addiction**

Addiction has proven to be extremely prevalent in individuals who suffer from PTSD. The development of coping mechanisms is a common response to stressful situations. Along with general methods of avoidance, those suffering from PTSD often attempt to escape the trauma-based stress through the use or abuse of mood-altering substances and behaviors. The reward centers stimulated through chemical or behavioral addiction-based action promote the release of dopamine which has shown to have atypical effects in individuals with emotional processing and reward processing center dysfunction (Wood et al., 2007). Furthermore, fear and anxiety conditioning, or the behavior in which individuals learn to predict adverse events, has been shown to be affected by changes in the metabolism of dopamine in individuals with PTSD (Maren, 2001). Abnormalities in PFC dopamine transmission have been shown to be prevalent in pathological memory processing psychiatric disorders such as PTSD and opioid addiction.

While substance use disorders (SUD) continue to be one of the most substantial coping methods used by PTSD survivors, coping mechanisms may include but are not limited to; sex, compulsive spending, gambling, exercise, eating, religion or anything else an individual finds the ability to immerse themselves in. There is often a fine margin separating constructive forms of coping mechanisms from destructive ones (Howard, 2007). The portion of

women who have suffered from sexual assault coupled with the co-morbidity of substance abuse is 30-59% (Najavits & Walsh, 2012).

Victims of sexual abuse have shown heightened predispositions to the development of sexually based addictions. In a study following the recovery of over 1000 sexual addicts for 5 years beginning in 1985, researchers noted that among the sample population, 81% of the individuals had suffered sexual abuse. Victims of sexual abuse, especially victims of childhood sexual assault, have a greater likelihood of developing sexual compulsions associated with the precipitating traumatic event (Howard, 2007). Behaviors such as trauma repetition are often developed in an attempt to bring resolution to a traumatic event. The individual will repeatedly attempt to seek a way to respond to a situation of past trauma through reenacting similar often painful behaviors in hopes of eliminating the fear associated with the precipitating event (Carnes, 1997).

While there is overlap in the area of military sexual trauma (MST), acts of MST still possess the characteristics of traumatic acts of betrayal. Symptoms of PTSD developed in individuals affected by MST often are representative of this (Gilmore et al., 2016). MST survivors have higher rates of PTSD than women who have experienced other types of trauma. Rape and Intimate Partner Violence (IPV) that precipitate PTSD, are made even worse

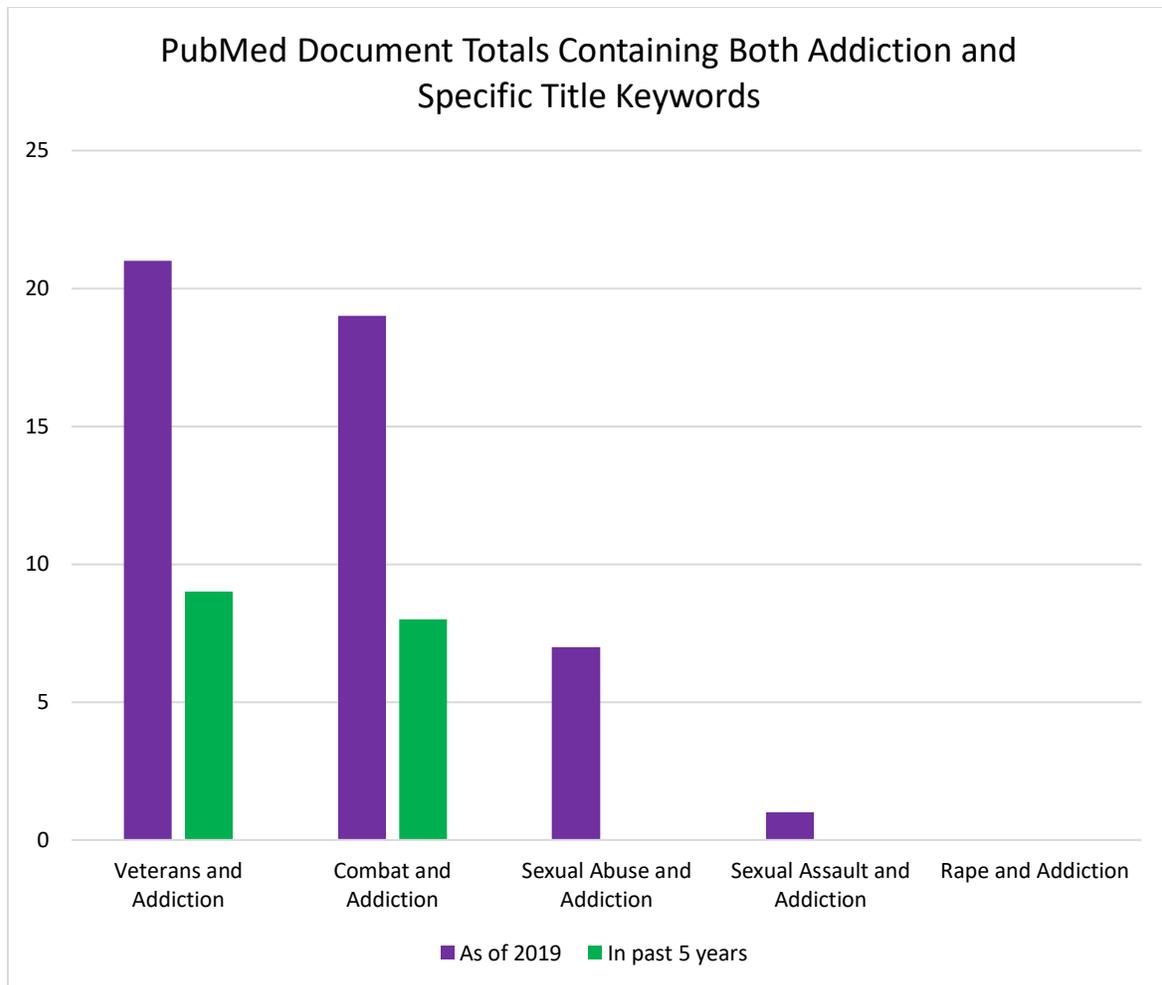
when it occurs in the military because of continued and unavoidable exposure and involvement with the perpetrator. The resulting PTSD may lead to greater risk of heart disease from change in health behaviors such as smoking, decreased physical activity and increased risk of SUDs (Lutwak & Dill 2013).

SUDs are by far the most prevalent form of addiction among individuals suffering from PTSD. The high frequency of comorbidity chronic pain and PTSD provides a setting that intrinsically is conducive for the development of SUDs. Apart from PTSD-related neurobiological influences on the susceptibility of an individual to develop a SUD, the increased likelihood to either self-medicate or seek prescription substances for chronic pain management provides a situation highly conducive for the initial use and continued abuse of drugs and alcohol (Morasco et al., 2013).

The increased access to pain management pharmaceuticals within the veteran population, has created controversially high levels of addiction to pharmaceuticals in particular those of an opiate nature. This system of symptom correlation has revealed a need for special considerations regarding the assessment and treatment of chronic pain in particular (Gros, Szafranski, Brady, & Back, 2015). While the seemingly sudden opiate addiction crisis in veterans has been the source of much public and media focus recently, the prevalence of self-medicating PTSD has been common much longer. The

comorbidity of alcohol disorders and PTSD in Vietnam era veterans had been shown to be approximately 70% (Carter, Capone, & Short, 2011).

While addiction and the veteran population has already been the focus of vast study and publication (Figure 6) and there is a history of SUD correlated with PTSD, the recent epidemic of opiate addiction may prove to be more complex than non-opiate based addictions. This may be due to the nature of the dopamine receptor transmission similar in prefrontal cortex-dependent memory processes such as PTSD and opiate related associative memories. A study in rats by Jing Li et al. (2018), showed an increase in sensitivity to normally non-rewarding morphine conditioning cues. This increased sensitivity indicates a potentially heightened vulnerability to addiction for opiate based substances in individuals with PTSD when compared to the general population.



*Figure 6. Graph comparing articles published and cited in PubMed with titles containing both relevant keywords and addiction in total and over the past five years. All searches were run requiring the presence of both addiction and the relevant keywords in the publication title as of May 4, 2019.*

## **Immune Function**

Neurochemically, psychological stress behaves very similarly to physical stress since both lead to the release of glucocorticoids due to

stimulation of the HPA axis. Cortisol binds to the intracellular glucocorticoid receptor in cells, thereby impacting the HPA axis causing negative feedback inhibition, which increases metabolic rate and alters immunosuppression (Neigh & Ali, 2016). PTSD is often comorbid with high rates of cardiovascular, respiratory, inflammatory, gastrointestinal, and autoimmune disease (Boscarino, 2004). PTSD's interconnected effects on the immune and endocrine system may increase risk or accelerate progression of inflammatory and autoimmune diseases.

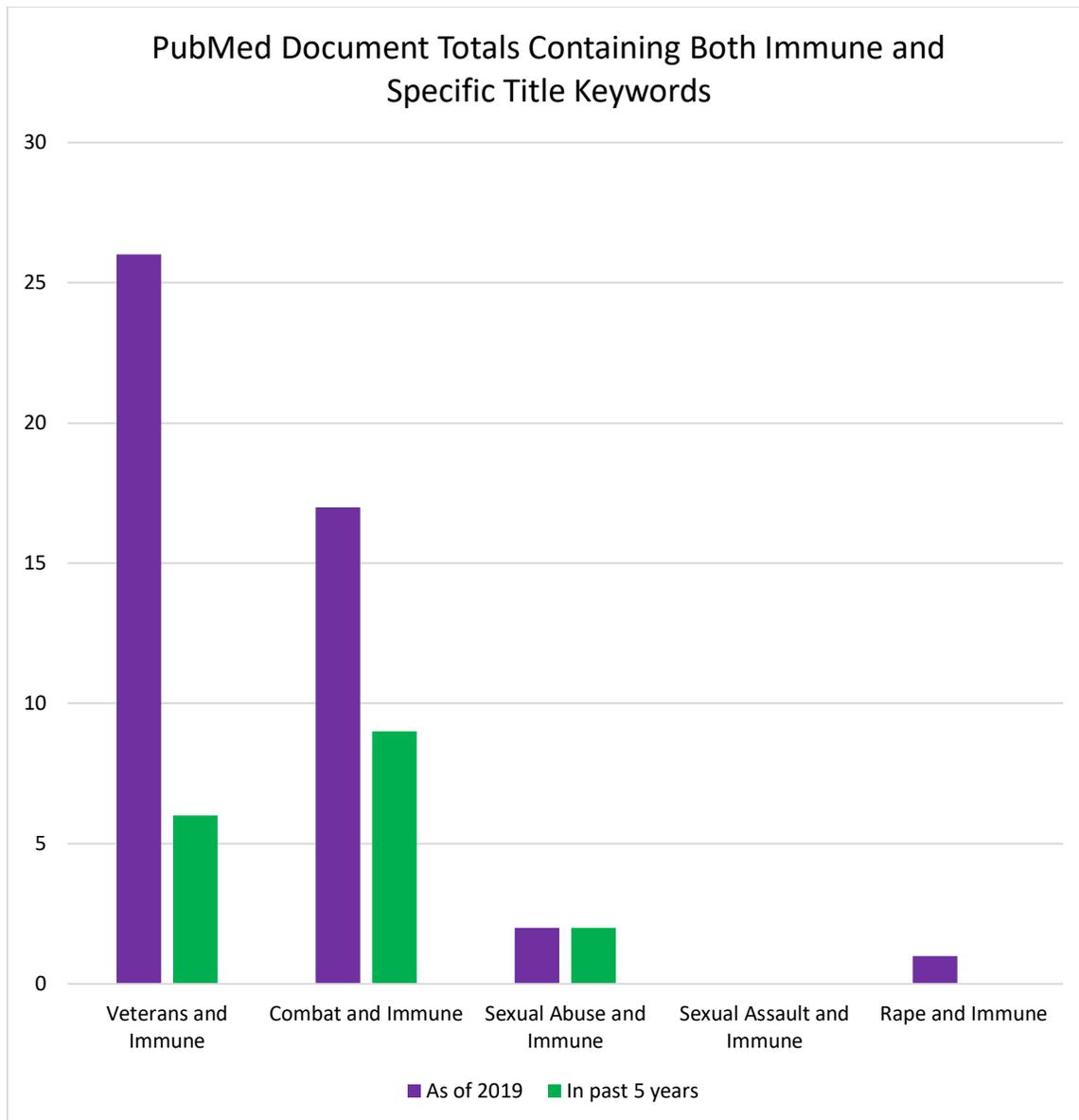
The effects of PTSD on the HPA axis and its increase in sympathetic activity stimulation can lead to an increase in cytokine production resulting in hyper-inflammatory states often co-morbid with PTSD. Chronic inflammation, as found in individuals with PTSD, often is found to be diagnosed alongside illnesses which include cardiovascular disease, asthma, fibromyalgia, chronic pain, hypothyroidism, rheumatoid arthritis, and psoriasis (Neigh & Ali, 2016). Cytokines have also been shown to directly affect the HPA axis and central nervous system and recently these effects have been proposed to present PTSD symptom development (Furtado & Katzman, 2015). Currently, there is debate on whether inflammation is a predictor or a symptom of PTSD and whether inflammation may be the biological basis or sensitization factor to stress that precipitates PTSD as a result of the exposure to trauma (Neigh & Ali, 2016).

A recent focus of study in the area of PTSD has been the relationship of PTSD and immune function. A study of 666,269 Iraq war veterans showed twice the autoimmune disease risk when comparing those with PTSD to those without any psychiatric illness. Furthermore, the same study showed that individuals with PTSD represented a 51% increase in autoimmune disease when compared to individuals with any other psychiatric illness (O'Donovan et al., 2015).

The role of cytokines could also be a potential source of the autoimmune function disorders often found co-morbid with PTSD due to their role in the differentiation of T cell subsets. T cells have also been proposed as a potential indicator of vulnerability to psychiatric disorders. A study conducted by Aiello et al. (2016), showed that prior to deployment, the responsiveness level of T cells to dexamethasone, a synthetic glucocorticoid, predicted PTSD and depression likelihood following deployment. Furthermore, decreases in functionality of regulatory T cells have been associated with auto immune disorders co-morbid with PTSD. Individuals with PTSD have been shown to have an approximate 50% decrease in regulatory T cells when compared to the general population (Jergović et al., 2014).

While immune function has been studied and shown to cause similar effects in both individuals with PTSD precipitating from sexual abuse and

combat related trauma, there are discrepancies between the two groups when related to the general population due to the general gender composition of both groups (Breslau, 2001). In fact, as in other areas of relative interest, there is significantly more information regarding veterans and immune dysfunction (Figure 7). Women are statistically far less likely to be combat veterans in the majority of world countries however, women are far more susceptible to being affected by PTSD, sexual abuse, and autoimmune diseases in their lifetimes. In a study by O'Donovan et al. (2015), it was shown that of individuals studied with PTSD, three out of four individuals that were diagnosed with autoimmune conditions were women. Due to the prior noted demographic discrepancies, there was not a statistically definitive change in magnitude of PTSD-related increased risk between Sexual Abuse survivors and combat war veterans with PTSD. Victims of Military Sexual Trauma however, displayed the highest risk of autoimmune diseases in both genders and was considered an independent risk factor when regarding the development of PTSD (Neigh & Ali, 2016). Veterans with MST-related PTSD additionally have displayed a higher rate of comorbid SUD than general combat war veterans suffering from PTSD (Gilmore et al., 2016).



*Figure 7. Graph comparing articles published and cited in PubMed with titles containing both relevant keywords and immune in total and over the past five years. All searches were run requiring the presence of both immune and the relevant keywords in the publication title as of May 4, 2019.*

## **Public Awareness and Understanding of PTSD**

One of the most powerful driving forces for the correct identification, research, understanding and treatment for a mental or physiological health issue is public awareness and understanding. There are many common misconceptions involved with PTSD ranging from the belief that PTSD is a psychological weakness, to the idea that one can get PTSD from watching a violent movie.

Issues plagued with negative preconceived stigmas or associations of shame have a long history of public avoidance or suppression. Behaviors ranging from homosexuality to racism have a history of being hidden or obscured within societal focus often based on value-based comfort of a given culture's norms. This cultural attitude towards complex issues also can be detrimental to the likelihood of individuals to seek treatment for negatively associated disorders or illnesses (Roman & Floyd, 1981). Both PTSD and sexual abuse have been greatly affected by historical societal views and stigmas which have led to confusion, misdiagnoses, and the debate of intrinsic definitions related to these areas of focus.

PTSD is a widespread biopsychosocial disorder that has been shown to affect approximately 5-10% of the population. Combat veterans of the Vietnam War showed rates of PTSD to be approximately 28% in those who were exposed to combat, and the disorder persisted in 11% of these

individuals 40 years after the conflict had concluded (Yehuda et al., 2015). While the combat veteran population is a significant and atypical demographic displaying a substantial elevation in likelihood to develop PTSD, there is frequently a misconception of PTSD's prevalence among civilians that can and has shown to be problematic. In fact, despite the fact that women are far less likely to be combat war veterans, they are twice as susceptible to developing PTSD. Public awareness of the combat veteran population of PTSD has shaped the general understanding of the disorder leading to the disassociation of symptoms and their potential underlying cause in a large percentage of those suffering (Harik, Matteo, Hermann, & Hamblen, 2017).

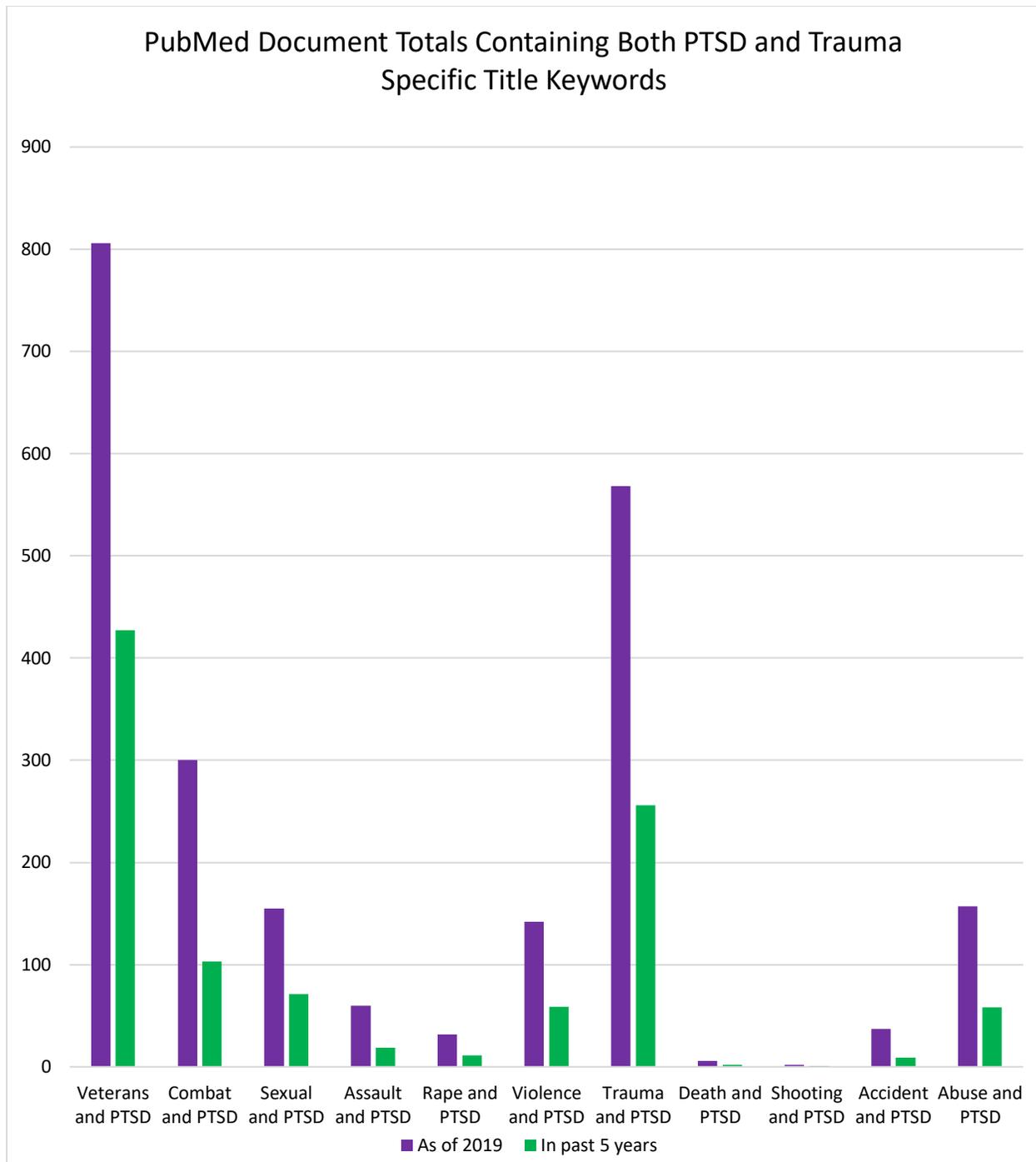
Another largely detrimental barrier to identifying and treating PTSD is the social stigma that this disorder is a mental illness. Research has shown that members of the combat war veteran population may feel embarrassed or ashamed to seek treatment resulting in a fear of being seen as weak. Couple this feeling of shame associated with PTSD with the shame and embarrassment often felt by victims of sexual abuse or even more so, childhood sexual abuse, and you have created a prison of socially-based fear that often can prevent survivors of PTSD from divulging sexual abuse experiences. Recently, there have efforts to attempt to change the societal and cultural views on PTSD such as the "About Face" awareness campaign created by the VA. Unfortunately, changing public opinion on issues of this

nature take time and in the transition, many individuals will slip through the cracks (Reisman, 2016).

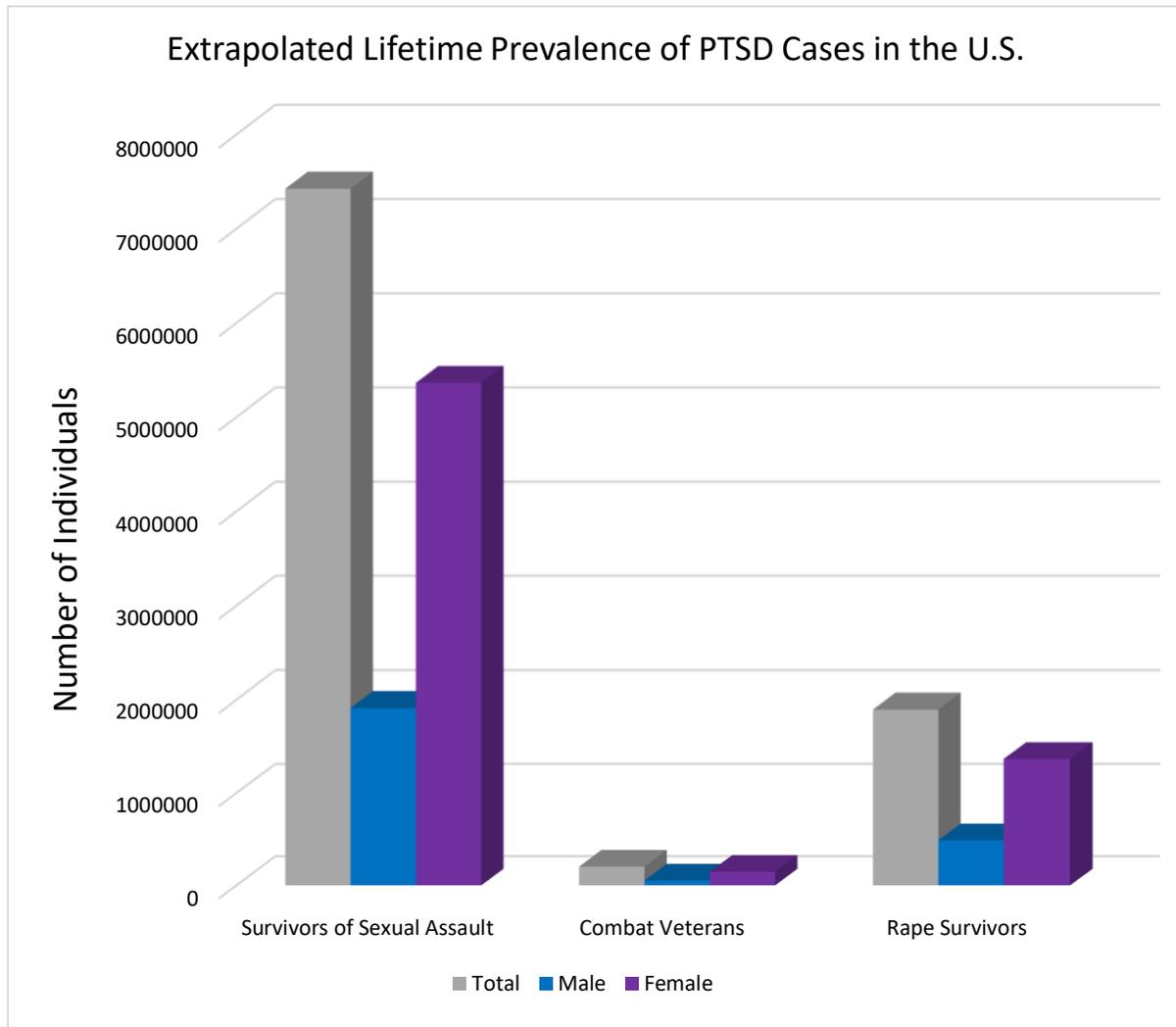
Another hindrance to ensuring the proper treatment of individuals is the constant historical fluctuation of both the name and understanding of this incredibly complex disorder. PTSD has likely been around since humans developed emotional modulation itself, and there are records describing trauma based psychological disorders as far back as 490B.C. with the account of Greek historian Herodotus of an Athenian warrior who went blind when the soldier next to him was killed despite no physical injury to himself (Reisman, 2016). The Civil War brought not only a new era of combat with rapid fire rifles and magnifying sights greatly magnifying the lethality of warfare, it also brought the first modern naming of “Da Costa’s syndrome” for what we now know as PTSD (Da Costa, 1951). Soon there was “shell shock”, “battle fatigue”, “post-Vietnam syndrome” and then finally in the 1970s, the diagnosis of PTSD was developed and made official in the 1980s (Reisman, 2016). The fact that a disorder affecting 5-10% of the population was rebranded five times in a period of only one hundred years certainly has not aided the holistic understanding of this condition for the general population.

When comparing statistics of individuals suffering from PTSD, there is a large discrepancy between the research focused on veterans and those who

have developed PTSD from sexual abuse related precipitating traumas. In an analysis of articles with titles containing keywords PTSD and some of the most common forms of precipitating trauma, there is an undeniable difference in total publications clearly distinguishing veteran related titles from other forms of trauma (Figure 8). When these publication numbers are compared to demographics representative of the relative frequency of precipitating trauma causes, the discrepancy is even greater. Despite the large number of publication titles containing PTSD and veteran, combat experiences in total are responsible for only 0.9% of cases of PTSD while 32.9% of cases can be attributed to sexual-relationship violence (“The World Mental Health (WMH) Survey Initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI) - Kessler - 2004 - International Journal of Methods in Psychiatric Research - Wiley Online Library,”). When relating these corresponding percentages to U.S. Population demographics, the lifetime prevalence totals of PTSD can be approximated for U.S. citizens as of March 2019 (Figure 9).

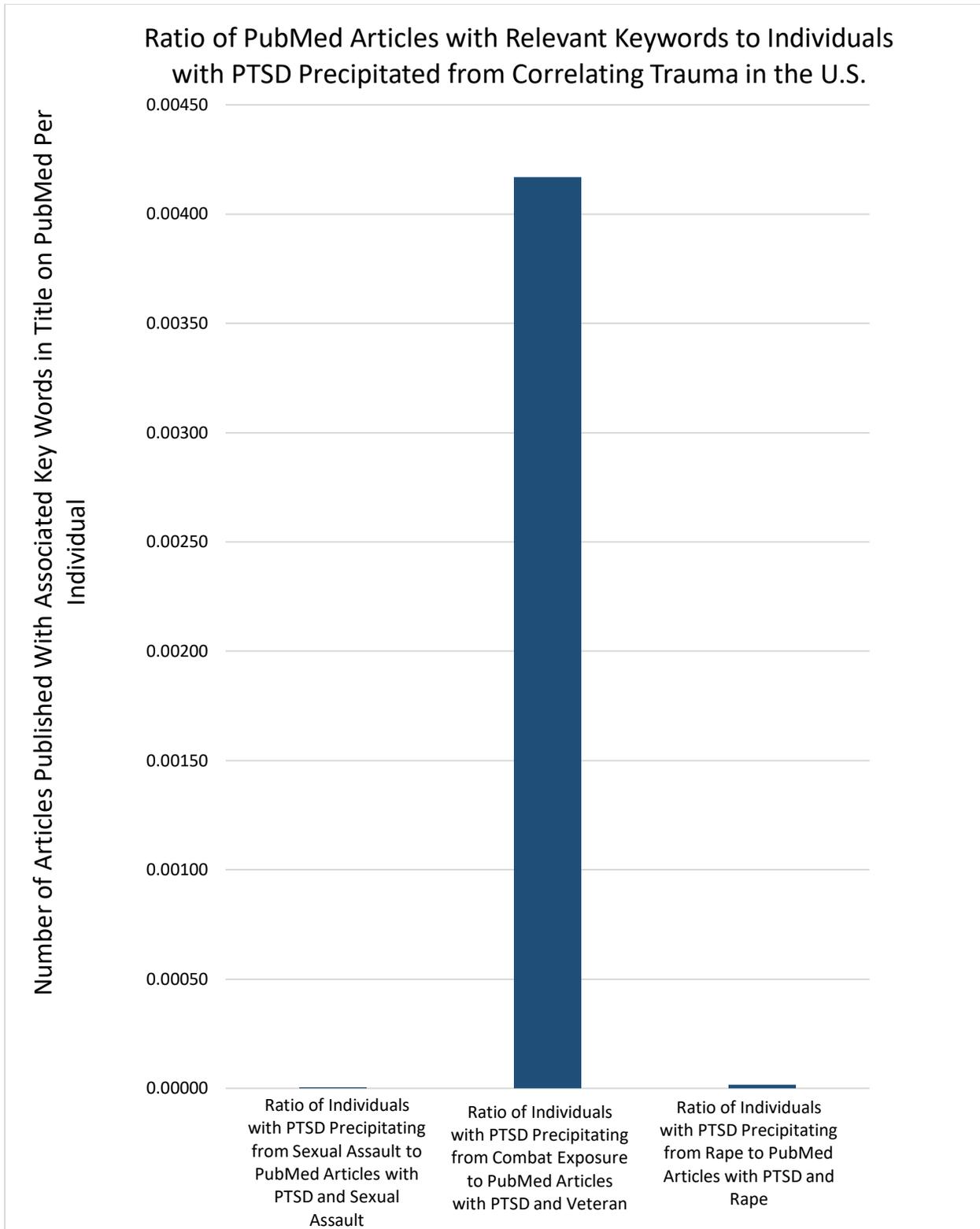


*Figure 8. Graph comparing articles published and cited in PubMed with titles containing simplified relevant keywords in total and over the past five years. All searches were run requiring the presence of both PTSD and the relevant keywords in the publication title as of May 4, 2019.*



*Figure.9 Lifetime prevalence totals of PTSD in U.S. citizens based on 2019 U.S. census, population demographics (“US population by gender 2010-2024 | Statistic,”) and distributions of conditional risk (“The World Mental Health (WMH) Survey Initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI) - Kessler - 2004 - International Journal of Methods in Psychiatric Research - Wiley Online Library,”) )*

The discrepancy between specific demographics and PTSD publications could be either considered a failure of the promotion of awareness for this debilitating disorder or a testament of the success of recent public awareness campaigns in advocacy of veterans. When the publication totals (Figure 8) are compared to the extrapolated lifetime prevalence totals of PTSD for specific forms of trauma in the U.S. (Figure 9), the exponentially greater focus on publication in the veteran population is undeniable (Figure 10). As of March 2019, the ratio of the number of U.S. veterans to every publication containing both words PTSD and veteran in the title is approximately 252:1. Respectively, the number of individuals per publication for survivors of sexual assault is approximately 176,700:1 when related to publications containing both sexual assault and PTSD in the title. Numbers are marginally better when concerning survivors of rape resulting in approximately 59,240:1 individuals to publications containing both the words rape and PTSD in the title.



*Figure.10 Lifetime prevalence totals of PTSD in U.S. citizens based on 2019 population demographics (“US population by gender 2010-2024 | Statistic,”) and distributions of conditional risk (“The World Mental Health (WMH) Survey Initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI) - Kessler - 2004 - International Journal of Methods in Psychiatric Research - Wiley Online Library,”) compared to total number of publications with respective title keywords on PubMed database as of March 2019. All searches were run requiring the presence of both addiction and the relevant keywords in the publication title as of May 4, 2019.*

## **Discussion and Perspectives**

The prevalence of misunderstanding regarding the actual nature, symptoms, and causes of PTSD has been greatly detrimental to the task of helping those suffering from this disorder. The cultural and societal stigmas associated with PTSD must be overcome in order to effectively progress. Without a more accurate and open understanding developed by the general public, not only will people suffer more deeply than they need, but the development of treatments and progress in combatting this disorder will be retarded. The inconsistent identification of individuals with PTSD will continue to lead to inaccurate sample groups for study and research creating

an increased challenge to the already incredibly difficult task of understanding and treating PTSD.

The vast discrepancy between publications concerning veterans and PTSD compared to PTSD and other precipitating trauma highlights room for tremendous improvement in drawing attention to PTSD in non-veteran demographics. Regardless of whether the large discrepancy of veteran related PTSD publications is due to praise worthy pro-veteran public awareness campaigns, or are indicative of a general societal failure to other demographic groups such as survivors of sexual abuse, it is apparent that an enormous population of U.S. citizens are not being identified properly. Even if the non-uniform distribution of publications is simply due to the study friendly controlled parameters and access intrinsic to military service, some of the successes in promoting PTSD awareness in veteran populations could undoubtedly be applied to the general public.

The proper diagnosis of those suffering of PTSD will require a more in-depth look at the various demographics affected and in particular, those who have suffered sexual abuse in both adolescence and adulthood. The staggering number of individuals who have come forward regarding their history of sexual abuse and still have not received proper diagnosis and treatment, highlights the failure of the medical and psychological treatment community in the treatment of this disorder in whole. Furthermore, an effort

to facilitate the comfort of the large suspected demographic of individuals with PTSD that have suffered sexual abuse and have been prevented from coming forward from fear, shame, or embarrassment, must be made. A systematic effort must be put forth in the proactive identification of sexual abuse related PTSD in a safe and non-threatening way to ensure that this population gets the help and treatment that they need and deserve.

The highly prevalent comorbid disorders of addiction, immune function and chronic pain must be consciously and comprehensively understood and integrated in future treatment plans to maximize their effect. The entanglement and overlap in the neurochemical characteristics and behavior of these four often comorbid disorders presents the potential for multiple disorders to be aided by a single treatment but also offers complications of maintaining overall neurochemical balance in these interconnected systems. Additionally, the high rates of addiction comorbidity with PTSD necessitates a strong need for the development of more successful non-narcotic treatments for chronic pain conditions that are prevalent among a high percentage of those affected. The biopsychosocial nature of this disorder requires a multifaceted and comprehensive approach to treatment that coordinates psychological, chemical and physiological treatments.

The presence of two seemingly opposite phenotypes of emotional undermodulation and emotional overmodulation manifestations of PTSD

necessitates a more holistic understanding in order to better help those affected. The tendency of one phenotype developing more frequently than the other under certain situations or due to certain forms of precipitating trauma, such as long-term childhood sexual abuse survivors tending to present emotional undermodulation behaviors, leads to the potential for more concrete and definitive correlations to be identified in various cases of PTSD. Further study of these similarities and the inferred correlations may provide opportunities for more productive study and treatment development.

Overall, the recent increase of societal understanding and the reduction in negative stigma coupled with the exponential development in the fields of medicine and psychology, has yielded progressive advancement in combatting this tremendously prevalent and debilitating disorder. There are however many opportunities to improve the effectiveness of future study and research through the more holistic and accurate understanding and communication of this incredibly prolific disorder.

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