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The genetic and somatic expressions of trauma: A review of pathology and treatment

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Abstract
Traumatic experiences change one's orientation to self, others, and the environment. In the wake of trauma, survivors are besieged by powerful emotions, sensations, and memories as they adapt to a new and unwanted reality. Chronic recall of disorganized traumatic memory engenders a myriad of unpleasant psychological and somatic responses. Confrontation with an overwhelming experience from which escape is not possible will challenge and change the way the brain communicates- both with itself and other parts of the body. While quickly adapting to environment and experience, what the brain is designed to do, in the presence of trauma, the brain is concurrently trying to find a way to internally escape the external environment. The symptoms that present secondary to PTSD are compulsory and biological, making traditional psychotherapy practices limiting as they do not resolve neurological conflicts in brain synapses or brain communication. This work explores the implications of trauma, innovative treatment modalities, and the genetic expression of PTSD.

Keywords: Post Traumatic Stress Disorder, PTSD and the brain, dissociation, genetic expression, PTSD treatment, Neurotherapy, Brain spotting vs. EMDR, MDMA

Introduction

In accordance with The National Institute of Mental Health, approximately 12 million Americans suffer from Post-Traumatic Stress Disorder (PTSD), giving one cause to recognize its standing as a public health crisis (National Institute of Mental Health, 2019). With only 20% of those suffering from PTSD reporting interventions such as medication and psychotherapy to be effective in providing moderate relief, status quo treatment approaches must be reassessed (Kleber, 2019; Norrholm *et al*., 2021) [30]. Within a fiscal year, a considerable number of resources are allocated to address PTSD. The Department of Veterans Affairs alone spends an estimation of three billion dollars annually, yet many continue to suffer in isolation; without access to comprehensive treatment, and at high risk for suicide completion (Koven, 2021; Vermetten & Rakesh, 2018) [22]. Once called "soldier's disease" and later "shellshock" the endemic crisis plaguing veterans could no longer be ignored and was the impetus to facilitate research, develop treatment, and give it a clinical name. Whereas combat veterans have been the population most often associated with PTSD, it is a pervasive affliction impacting an expansive range of groups and contemporary literature validates a genetic constituent to its pathology (Loughran, 2012; Maamar *et al*., 2019) [24].

Human experience is individual and impacted by a multitude of intersecting systems that affect biological development. Despite advances in technology, research, and neuroscience, the brain remains the most elusive of biological systems (Sasmita *et al*., 2018). However, there are concrete facts such as the brain being comprised of several parts, all of which are neuroplastic, that is, designed to change with experience, and gravely impacted by prolonged stress and trauma (Baldwin & Korn, 2021; Cloitre *et al*., 2021) [3, 10]. The brain's malleability combined with individualized genetic code creates unpredictability in discerning how one will respond to stimuli, environment, or acute prolonged stress. When treating PTSD, it is important to look at the brain comprehensively to understand how it becomes disordered by trauma, and how it maladapts and begins to function. The consequence is often a spectrum of secondary psychological and somatic disorders (Nicholson *et al*., 2016; Van der Kolk, 2015) [29, 38].

When an experience feels intolerable, to cope, the more conscious brain repudiates traumatic memory while the deeper recesses of the brain hold onto it; such being vestiges of evolution (Bagheri-Mohammadi, 2021). Although surviving acts of violence, military combat, traumatic accidents, and natural disasters are familiar examples of traumatic events sometimes resulting in PTSD, what constitutes a traumatic experience is subjective. Following such events, the brain looks for physiological ways to express what cannot be tolerated to articulate making somatic symptoms and conversion disorders common byproducts of PTSD (Kienle *et al*., 2017) [20]. The body finds a way to express repudiated mental health needs through alternate pathologies, and although not a rule, conversion disorders often present as neuropathic and/or autoimmune. For example, autoimmune deficiencies, chronic pain, sleep dysfunction, and other chronic health issues without distinction of cause or source (Boggs & Bookwalter *et al*., 2020) [7]. The complexities make diagnosing and effectively treating PTSD a challenging feat, compounded by a lack of access to treatment.

Trauma impacts the brain's neurobiological responses or otherwise manufacturing processes- how it communicates with the rest of the body. Conversion disorders are expressions of trauma- the body's expression of repressed traumatic memories (Nicholson *et al*., 2016; Van der Kolk, 2015) [29, 38]. The impairment of neurobiological responses creates a disturbance in neurotransmission. Trauma and traumatic stress interrupt how neurotransmitters, the brain chemicals that carry critical information to nerve cells, communicate with each other. Irregular neurotransmission contributes to the development of conversion disorders and general somatic symptoms (Kienle *et al*., 2017) [20]. Attempts at restoring irregularities in neurotransmission have been made with the use of psychotropic medications such as cyclical antidepressants, beta-blockers, and Benzodiazepines (Taylor & Elwy, 2014) [36]. Medications such as antidepressants and beta-blockers are of poor to moderate effect in providing symptom management and are not prescribed based on cause- they manage symptoms (Bowers & Ressler, 2015; Shrader & Ross, 2021) [8, 34]. Benzodiazepines, although briefly helpful, come with a high risk of dependency and are not ideal for long-term management (Guina *et al*., 2015; Steckler & Risbrough, 2012) [17, 35]. Furthermore, medications commonly prescribed for individuals suffering from PTSD inhibit the dopamine system (the brain's reward system) which can impair one's ability to fully experience positive events and emotions- a frequently reported side effect. A higher dosage is often necessary to treat PTSD, consequently, a greater likeliness of side effects and a leading reason why PTSD sufferers do not manage medication well long-term. It should be noted that the nature of side effects reported greatly impact life quality, short and long-term, not simply mild discomfort during adjustment periods. Medications are often effective adjuncts to treatment; however, they are most efficacious when integrated into comprehensive treatment plans (Bernardy & Friedman, 2015; Shrader & Ross, 2021; Steckler & Risbrough, 2012) [34, 35]. Their application and efficacy will be expanded further.

Like medications, traditional talk-oriented modalities are also limiting and can even be retraumatizing for individuals suffering from PTSD. They too do not restore the disordered processing in the brain or cognitive functioning. Talk-oriented modalities can be successful adjuncts to treatment; however, they are of moderate effect without the presence of brain-based interventions as they can only access the part of the brain that processes language. Because of their limited ability to reach critical parts of the brain impaired by trauma, efficacy is limited (Bowers & Ressler, 2015) [8]. The primary dysregulation marked in the brain communication of an individual suffering from PTSD is frequently in the cortical brain. The cortical brain houses the right, mid, and hinds of the brain, i.e., the prefrontal cortex, amygdala, and hippocampus. Intuitive, emotional, and body awareness are mediated here as these are the thinking/conscious parts of the brain. The cortical brain becomes dysregulated by the more complex and often disorganized brain processes that present secondary to trauma (Corrigan & Grand, 2013) [12]. Functional organization is critical to the brain's primary role of managing all biological systems. When brain physiology is organized it can solve most problems independently. What clinicians might refer to as psychological symptoms such as flashbacks or acute anxiety are often secondary to the brain being unable to sufficiently solve a problem. In cases of PTSD, the problem it is trying to solve is the eradication of traumatic memory, and it cannot do so because those exact events have disorganized its managing processes. For example, either the brain is unable to identify the problem, or it can, but is overwhelmed by its complexity and does not know how to correct it. For the afflicted, the result is a chronic feedback loop of discomfort and intrusive thoughts, or in more acute cases, dissociation (Keinle *et al*., 2017).

Unabated, the impairments cause the amygdala to become stuck in a state of high alert, impairing how sensory information is carried to the rest of the brain and nervous system. The amygdala is the brain's emotional switchboard, discerning and carrying information from the senses (all of which are close to the brain to limit synapse time) to the brain for translation. Trauma often has the gravest impact on this specific part of the brain (Bagheri-Mohammadi, 2021). The lapse in amygdala function, i.e., the inability to carry information with accuracy is the cause of most symptoms one suffering from PTSD experiences, particularly dissociative experiences. Before exploring genetic expression and treatment interventions, it is essential to first highlight the effects of dissociation, a hallmark feature of PTSD (Kienle *et al*., 2017) [20].

Dissociation

Traumatic events are held by the brain with more complexity and enmeshment than benign or even positive ones (Corrigan & Grand, 2013) [12]. Dissociation first presents during traumatic events and is the first association of how that memory becomes held. It is the foremost coping skill the brain develops- it exacerbates other symptoms and creates great complexity in the treatment process. Colloquially known as shock, dissociation is a prolonged state of being during which one feels detached from their emotional state and physical self, a maladaptive attempt at self-preservation. In simplified terms, dissociation is a type of intermittent amnesia. Following stress exposure, dissociative symptoms such as depersonalization i.e., detachment from oneself, and derealization i.e., detachment from reality will frequently precipitate the development of PTSD as they are strong indicators of maladaptive stress responses and enduring features of PTSD (Van der Kolk, 2015; Boyd *et al*., 2018) [38, 9]. Trauma exposure, especially when complex and enduring, will make one's primary orientation rife with threat, fear, and

the need for survival. The chronic presence of intrusive thoughts and memories becomes taxing and creates acute dysfunction in how brain chemicals are released. Fear and lack of safety leave one in a state of hypervigilance- constantly assessing the environment for threats (Baldwin & Korn, 2021; Cloitre *et al*., 2021) [3, 10]. Perpetual hypervigilance creates a disturbance in psychological equilibrium and the brain begins to rely on more primitive biological responses such as behavioral detachment, and the rapid release of the type of brain chemicals necessary when one is in a state requiring the fight/flight response. Such synapses often happen at a volume and speed the brain is ill-equipped to manage long-term (Kienle *et al*., 2017) [20].

The addition of the dissociative subtype to the PTSD diagnosis is expected to further advance research examining the etiology, epidemiology, neurobiology, and treatment responses to PTSD (American Psychiatric Association, 2013). Advances in research surrounding the dissociative subtype are direly needed. Such research is likely to provide a more comprehensive understanding of dissociation when presenting concurrently with PTSD, perhaps identifying dissociative subtype biomarkers, hence contributing to early intervention and prophylactic care. Aggregated data would also highlight lapses in evaluation, diagnosis, and current treatment design, as effective treatment options remain narrow and inaccessible (Boyd *et al*., 2018) [9]. Paradoxically, research does support the lack of efficacy conventional interventions have in sustainable symptom reduction for those who suffer (Bernardy & Friedman, 2015; Steckler & Risbrough, 2012) [35]. Treatment resistance is pervasive across the spectrum of individuals suffering from PTSD when the dissociative subtype is present although the greatest level of resistance is among first responders, largely combat veterans (Boyd *et al*., 2018; Watkins *et al*., 2018) [9].

Stress stimulates the cortico-limbic release of glutamate- a chemical that greatly impacts behavior because of how it stimulates changes in neuroplasticity. Neuroplastic changes have lasting effects on brain communication, functioning, and behavior. The state of dissociation occurs as a response to an overproduction of glutamate and dissociative symptoms become a learned habit by the brain (American Psychiatric Association, 2013; Bagheri-Mohammadi, 2021). First articulated by neuropsychologist Donald Hebb (1949), and later expanded upon by Keysers & Gazzola (2014) [21], "Neurons that wire together fire together" describes how pathways in the brain are established and reinforced by repetition, much like the traditional premise of repetitive practice. As such neurons that begin to maladaptively wire together will maladaptively fire together. Like the moderate efficacy of psychotropic interventions, medications designed to quell glutamate release are frequently prescribed to sufferers of PTSD to insignificant effect, as they only attenuate one of many symptoms secondary to a greater problem (Bowers & Ressler, 2015; Boyd *et al*., 2018) [8, 9]. Medications nor standard practice talk-oriented interventions can teach the brain how to rewire and refire (Keysers & Gazzola, 2014) [21]. PTSD is too multifaceted. Furthermore, the impact of genetic code and genetic expression must be considered in understanding and treating the condition, as the genetic constituent of trauma is a mediating factor in an individual developing PTSD (Maamar *et al*., 2018) [25].

Epigenetic Gene Expression, Genetic Markers, and Generational Trauma

Genetic markers not expressed in tangible identifiers such as eye, skin, or hair color require environment and experience to express themselves (Radley *et al*., 2011) [31]. In its course of development, the brain works with meaning and emotions, not just raw data. Genes, environment, and experience intersect, making a fair amount of genetic expression dependent on input from experience and environment to develop. This makes one's experiences and exposure to stress critical, impacting how and which genetic markers express themselves, whether adaptively or maladaptively. PTSD is the result of vulnerable genetics and less-than-optimal events of fate. i.e., biography informs and impacts the response of biology (Morsy *et al*., 2021). The comprehensive study of stress and trauma has origins in the field of physics, with the earliest research being conducted by stress research pioneer Hans Seyle (1965). Seyle proposed that stress was a non-specific strain on the body caused by irregularities in traditional bodily functions and maintained that the strain secondary to stress and trauma mediated the release of stress hormones (Seyle, 1965). These early findings laid the bedrock for the field of genetic study known as epigenetics, which is modern research validates that, aside from biogenetic vulnerabilities, stress is the leading cause of biological disease due, in part, to the genetic expression it mediates (Johnson, 2012) [18]. For example, stress impacts hormones and irregulates hormonal balance and PH balance, making the body of a highly stressed person more acidic, as opposed to the more optimal alkaline. Such imbalances result in an optimal breeding environment for the types of chronic illness that present secondarily to a preexisting genetic vulnerability- the previously described somatic and psychological expressions of trauma (Boggs-Bookwalter *et al*., 2020) [7]. Whereas stress does not change genetic markers, it changes the way epigenetics are understood by the body and brain (Radley *et al*., 2011) [31].

Epigenetics analyzes genetic phenotype changes that do not include changes in DNA sequences (Maamar *et al*., 2018). As the prefix epi suggests they are genetics on top of or in addition to. Epigenetic expressions do not impact the DNA double helix, but rather how the information held in the double helix is read and understood by cells. They are not evolutionary, nor are the changes in epigenetics permanent, although can be, and this is when genetic markers for PTSD become inheritable (Johnson, 2012) [18]. Changes in epigenetics represent a biological response to an environmental factor, and pertinent to PTSD, how long one has endured trauma is what determines the permanence of epigenetic changes and expression i.e., its inheritability (Radley *et al*., 2011) [31]. Epigenetic changes are the consequence of affected genes being expressed in response to experience (Maamar *et al*., 2018) [25]. Positive lifestyle habits such as diet and exercise can result in positive expression, or simply no expression of epigenetic response, whereas trauma, high stress, and psyche-disrupting events can result in a negative epigenetic response, e.g., behavioral and mood changes, or personality and psychiatric disorders (Johnson, 2012) [18]. In lay terms, one's epigenetics and subsequent expression are turned on and off in response to disturbances in the environment and stress exposure.

They are the mediators between genes, environment, and behavior.

A single-event trauma in adulthood will often process through the brain quickly as it will usually be contained to one part of the brain. By comparison, childhood and complex trauma are likely to have a greater impact on neuroplasticity as they infiltrate more parts of the brain (Radley *et al*, 2011) [31]. This makes childhood and complex trauma more challenging to resolve and a longer process. Complex childhood trauma is more likely to impact one's genes such as the genes one will pass down to their child, i.e., the vulnerability of PTSD's genetic expression (Maamar *et al*; 2018) [25]. Neurological disparities and other maladaptive neuroplastic changes that present in the brain following a traumatic event or prolonged stress exposure are secondary to one's genetic endowment (Johnson, 2012) [18]. Although trauma has a dire impact on genetic expression and as a byproduct, the brain's manufacturing processes, restoration is possible (Bowers *et al*., 201; D'Antoni *et al*., 2022; Grand, 2013; Van der Kolk, 2015) [38, 8].

Brain-Based Treatment Theories

Brain spotting vs. Eye Movement Desensitization and Reprocessing (EMDR): An Overview

Brainspotting, an evolution of the protocol used within an Eye Movement Desensitization and Reprocessing (EMDR) session, engages focal points in the line of vision to stimulate parts of the brain holding onto fragmented trauma and trauma memories (Baldwin & Korn, 2021; Corrigan & Grand, 2013; Grand, 2013) [3, 12]. Both interventions function similarly in engaging the optical and brain systems. Whereas EMDR uses eye movements to stimulate the brain bilaterally, Brainspotting requires one's gaze to be held on a fixed position for a duration of time after identifying an eye position engendering a strong emotional response. EMDR was the first in using the eyes and bilateral stimulation exercises as mediators and follows a stringent protocol whereas Brainspotting is more adaptable. While hyper-arousing eye positions that correlate to a traumatic event with a strong emotional response attached to it are identified, the isolated focal points held during Brainspotting deeply stimulate the brain, thus, engendering positive neurogenesis (Bhagheri-Mohammadi, 2021). By holding the focal point, i.e., spot, within the visual field from which one feels the most arousal is elicited, traumatic memory is processed with greater understanding and organization. The practice has advanced to engage other sensory methods such as auditory stimulation, clinically termed bilateral sound (Corrigan & Grand, 2013; D'Antoni *et al*., 2022; Grand, 2013) [12]. With EMDR touch stimulation via finger tapping and counting is more commonplace and requires more work on the part of the treatment recipient. Consistent with EMDR Brainspotting requires little sharing, which can be an attractive feature for one in recovery from PTSD (Baldwin & Korn, 2021; Sack *et al*., 2016; Van der Kolk, 2015) [3, 38].

EMDR was one of the first treatments for PTSD to be evaluated in controlled research, although Brainspotting, a younger intervention often yields faster results because it is more individualizable and localized in identifying traumatic memory whereas EMDR follows a stringent protocol (Grand, 2013; Sack *et al*., 2016). Brainspotting engages the frontal lobe and limbic system with greater precision and requires minimal dialogue-oriented engagement between clinician and client, making it an ideal treatment intervention for those who become easily overwhelmed or carry the concern of re-traumatization (Corrigan & Grand, 2013) [12]. One does not have to tell their story or relive their trauma should they not want to. Moreover, individuals such as those in the higher-ranking military and government positions cannot disclose certain events or experiences because they contain highly classified content. The verbal exchanges of talk therapy can be incorporated into treatment protocol using Brainspotting, while EMDR protocol, because of its stringency, does not allow for as much individualization (Grand, 2013; Sack *et al*., 2016).

Both EMDR and Brainspotting are empirically driven and validated, with 75% of recent experimental groups showing significant decreases in their PTSD scores after only three sessions using a hybridized model of the two (Van der Kolk, 2015; D'Antoni *et al*., 2022) [38]. Findings from recent meta-analyses support seven of 10 participants suffering from PTSD found brain-based interventions to be more effective and faster acting than trauma-focused cognitive behavioral therapy in conjunction with cyclical antidepressants (Bernardy & Friedman, 2015; Shrader & Ross, 2021) [34]. Because of the brain's ambiguity and personal experience being individual, it is unclear how Brainspotting and EMDR correct the way the brain holds on to traumatic memory. Efficacy is often credited to their eliciting positive neuroplasticity and neurogenesis which consequently stimulates the brain to reorganize its communication with itself and other systems (Baldwin & Korn, 2021; Grand, 2013; Sack *et al*., 2016) [3]. As previously highlighted, neuroplasticity is the brain's evolutionary ability to adapt to meet the needs of the environment, experience, and habit, while neurogenesis is the brainstem's ability to produce new neurons and neurotransmitters; neurogenesis is an action of neuroplasticity (Bagheri-Mohammadi, 2021; Keysers & Gazzola, 2014) [21]. Though Brainspotting is credited to be faster acting and less stimulating, because EMDR has a longer history of use, it is a more familiar practice and more commonly employed (Baldwin & Korn, 2021; D'Antoni *et al*., 2022) [3].

The therapeutic process of Brainspotting is measured by the correlation between a focal point, i.e., the spot in the visual field, and felt sense, i.e., where in the body stimulation is felt most (Grand, 2013). It is theorized that while holding the focal point that prompted the greatest physical response, the vagus nerve becomes activated. The crux of the parasympathetic nervous system, the vagus nerve runs from the brain to the heart, respiratory, and digestive systems. Vagal activation mediates the response of safety and quells the perpetual state of fight-flight that is a common byproduct of PTSD (Van der Kolk, 2015) [38]. Although EMDR enables such a response, Brainspotting interventions appear to be able to do so with greater precision and at a faster pace (Corrigan & Grand, 2013) [12]. As theorized by Grand (2013) and Van der Kolk (2015) [38], an additional reason for effectiveness is their ability to stimulate and mimic the recording component of trauma. For example, traumatic events are apt to be recorded sequentially in the brain and become disorganized secondary to maladaptive neuroplasticity (Bagheri-Mohammadi, 2021; Keysers & Gazzola, 2014) [21]. Both Brainspotting and EMDR elicit sequential processing by using the visual field to elicit the brain's natural ability to regenerate, self-restore, and readapt, allowing traumatic memories attached to traumatic events to process with more efficiency and without the risk of re-traumatization (Grand,

2013; Van der Kolk, 2015) [38]. When integrated into treatment, Brainspotting and EMDR access parts of the brain such as the vagus nerve and brainstem, which mediates most autonomic functions in addition to neurogenesis, access that treatment interventions such as the singular use of medication or talk-oriented interventions cannot (Baldwin & Korn, 2021; Bernardy & Friedman, 2015; Sack *et al*., 2016; Van der Kolk, 2015) [3, 38].

Whereas both EMDR and Brainspotting prove highly effective in restoration and recovery from trauma, Brainspotting appears to be providing greater relief for individuals with a history of childhood trauma because the brain and memory bank of an individual with a history of childhood trauma will hold onto traumatic memory with greater complexity (D'Antoni *et al*., 2022; Grand, 2013). The rapid biological and emotional changes of childhood and adolescence cause the brain to interpret traumatic memories in fragments that often present with a host of triggers later in life that cannot be ignored, though cannot be sufficiently identified and thus correlated to traumatic events. For example, the previously expanded upon dissociation and somatic disorders (which can be delayed in their onset) without distinction of cause or source (Kienle *et al*., 2017; Nicholson *et al*., 2016) [20, 29]. It is common for those with a history of early childhood trauma to be unable to understand the events as experiences of the past that they can recover and move on from- the trauma has become an ingrained part of their biology and psyche. Additionally, individuals with histories of childhood trauma often lacked secure attachments with caregivers and did not securely cultivate feelings of competency or a secure internal locus of control (Van der Kolk, 2015) [38]. With the absence of such primitive skills in tandem with the biological changes that present in the brain and body after exposure to trauma, the brain and body hold such traumatic events in their deepest recesses. This phenomenon is often observed in those who do not have clear memories of the traumatic events they survived, only the vestiges of them (D'Antoni, 2022; Grand, 2013). Brainspotting with incorporated auditory stimulation is an ideal intervention in these cases, as isolated ocular focusing is held while both left and right sides of the brain are stimulated. Eye movement and touch stimulations dictated by EMDR protocol are not required, which is appearing to elicit a more comprehensive reprocessing response (Corrigan & Grand, 2013) [12].

3.4. Methylenedioxymethamphetamine (MDMA)

First synthesized in 1912**,** 3,4 Methylenedioxymethamphetamine (MDMA), was not adopted for clinical use until the latter part of the twentieth century (Sessa, 2017). Although found to have significant therapeutic benefits such as enabling greater insight and improved communication surrounding the therapeutic dialogue, the U.S. Drug Enforcement Administration (DEA) banned the compound due to its high level of recreational use and the implications of misuse and addiction (Doblin, 2011). Designated as a schedule 1 controlled substance, and commonly identified as a club drug, MDMA is encumbered by a great deal of stigma and inaccurate stereotyping (Barone, 2019). MDMA is both a neuroplastigen/psychoplastigen, i.e., a therapeutic able to quickly promote positive neuroplasticity, and an empathogen/entactogen, i.e., a therapeutic able to expand empathy towards self and others. Its chemical effects mediate the release of neurotransmitters such as norepinephrine, serotonin, and dopamine which are neuroplastigens/psychoplastigens, with a concurrent increase in the production of feel-good and attachment hormones such as prolactin, vasopressin, oxytocin, and cortisol, which are empathogens/entactogens (Doblin, 2011). In clinical settings, neuroplastigen/psychoplastigen is becoming the contemporary language used to refer to MDMA, replacing the term psychedelic, with the hope of increasing credibility, and removing stigma (Sessa, 2017; Varker *et al*., 2021). Flooding the brain with these hormones and neurotransmitters elicits feelings of trust and well-being, which allows patients to reexamine traumatic memory while building a stronger rapport with their treating clinicians due to the increased feelings of calm and safety, and the decreased feelings of paranoia and threat (Doblin, 2011). Individuals in controlled settings being clinically administered MDMA describe feelings of sensory pleasure, increased energy, well-being, and wholeness. Such responses lend to engendering empathy towards oneself and others, which benefits the therapeutic alliance and process, and provides an almost detached ability to engage in the recounting and reprocessing of traumatic memory. In this context, detachment is described as positive because the treatment recipient re-experiences traumatic events as an unbiased and in control witness as opposed to a victim (Feduccia *et al*., 2018).

MDMA is a highly effective intervention for resistant cases of PTSD (Doblin, 2011). Controlled clinical trials and meta-analyses found that over 65% of persons suffering from PTSD have a significant enough reduction in symptoms to no longer meet the clinical criteria for diagnosis (Barone *et al*., 2018). As postulated by Feduccia *et al*. (2018), MDMA allows for traumatic memory to be reprocessed because of its ability to allow one to detach from traumatic memory while holding a sustained sense of awareness and control. The treatment recipient witnesses their thoughts and memories without strong triggering attachments while maintaining an orientation to self and setting- a detachment style contrary to what is experienced while in a state of dissociation (Taylor & Elwy, 2014; Varker *et al*., 2021) [36]. Subsequently, the traumatic emotions and maladaptive coping defenses the brain attached to the traumatic memory are eradicated (Feduccia *et al*., 2018). Research is also supporting that when used clinically MDMA is restoring the amygdala by temporarily decreasing blood flow during critical windows of synaptic plasticity- when the brain is most malleable (Sessa, 2017). As noted, the amygdala is the most significant part of the brain in delivering sensory information and is gravely impacted by trauma. Restoration to optimal functioning is believed to be a consequence of MDMA's ability to considerably reduce activity, almost, but not quite, disconnecting the amygdala while the brain re-processes traumatic memory. As a byproduct, there is no longer a fear signal attached to the traumatic memory/memories after treatment terminates (Varker *et al*., 2021).

MDMA-assisted psychotherapy sessions are overseen by a treatment team in a controlled environment and are individualized to accommodate the recipient. Sessions last approximately six to eight hours depending on dosing, treatment objectives, and metabolic profile. After approximately two to three hours post-initial dose, a second, lower dosage is administered to create a sustained release effect, during which the recipient becomes capable of revisiting traumatic events without the presence of the paralyzing responses attached to them. Integration sessions

complement the gains made during the initial session, and a standard treatment cycle is approximated at 12 weeks, two to three times per week. Throughout the treatment cycle MDMA is administered three times in tandem with integration sessions. MDMA-oriented sessions are administered every four weeks, with the ratio of sessions with vs. without MDMA being 50/50, though that may vary marginally to accommodate individualization (Barone *et al*., 2019). MDMA-assisted psychotherapy is still pending approval from the FDA; therefore, treatment is only accessible within the context of a clinical trial. Recreational use will not mediate the same responses because the treatment is designed to be guided by an interdisciplinary medical team clinically trained in treating PTSD, i.e., it is a very specific skill set. Moreover, the chemical compounding of the MDMA used in clinical trial settings is far more precise in its biochemical profile. To assist in reprocessing two clinicians are bedside during treatment sequences. The recipient is guided through the process by their primary clinician, and a second ancillary clinician is present (Doblin, 2011).

A strong belief within the neuroscience community supporting MDMA's efficacy is its ability to cause a neural response called a critical period during which the brain becomes receptive to learning new feedback loops, for example, restoring context processing i.e., having neurotypical responses to stimuli in the environment as opposed to a fight/flight/flee response. Consequently, context processing restoration begets what is known as the extinction of fear memory (Sessa, 2017). By comparison to other interventions commonly used to treat PTSD, MDMA-assisted treatment demonstrates the greatest efficacy, and symptom reduction can often be measured after the first session (Doblin, 2011; Varker *et al*., 2021). Although used therapeutically for quite some time, credible research supporting MDMA's clinical use is still young (Barone, 2019). MDMA is not yet patentable and because of that does not stand to generate revenue for pharmaceutical companies. It can be argued that lack of monetary incentive is a primary reason many big pharma conglomerates do not fund research; most research involving MDMA has been funded by small non-profit entities (Doblin, 2011; Sessa, 2017)**.** This is further compounded by the illicitness attached to MDMA, and general mental health needs not being regarded as critically as somatic health needs (Kiebler, 2019; Taylor & Elwy, 2014) [36]. Although the illicitness attached to MDMA is beginning to dissipate, it is still colloquially known as a club drug or an otherwise recreationally used substance which deters larger pharmaceutical companies from supporting research efforts (Doblin, 2011; Sessa, 2017)**.** The expansion of strong and robust empirical data is on the horizon (Fiduccia *et al*., 2018; Taylor & Elwy, 2014) [36]. With time and increased data validating its efficacy, MDMA is likely to be embraced as a leading treatment modality for PTSD, regrettably, we are just not there yet.

Neurotherapy

Neurotherapy is effective in its use to treat a broad range of neurologically oriented mental illnesses and general mental health challenges. Its ability to stimulate neuromodulation, neuron healing, and neurostimulation by reorganizing disorganized firing and wiring patterns promotes optimal brain function (Van der Kolk, 2015) [38]. Known also as neurofeedback, electroencephalogram (EEG), and biofeedback, neurotherapy is a brain-based, narcotic-free intervention that restores brain communication within itself and the body. Applications can be used to treat brain injuries, stroke, and movement disorders among other neurological afflictions. Pertinent to this work, acute psychological disorders such as PTSD (Barnett *et al*., 2014; Taylor & Elwy, 2014) [4, 36]. Neuro feedback Therapy is a brain-body practice using auditory, visual, or both types of stimuli while consequent responses are monitored in live time (Barnett *et al*., 2014) [4]. The language of Biofeedback and Neuro feedback are commonly used interchangeably although they do differ. Biofeedback is more likely to be used in treating physiological impairment whereas neurofeedback is more brain-based and directly treats psychopathology (Thibault *et al*., 2015) [37]. Like Brainspotting and EMDR, Neurofeedback uses sensory and brain engagement but is more technologically advanced in its use of computer-oriented hardware and software programs (Baldwin & Korn, 2021; Grand, 2013) [3]. These technologies teach the brain and conscious individual how to respond to acute stress and its physiological symptoms such as muscle tension, rapid heart rate, increases or decreases in body temperature, and the management of intrusive thoughts. Both Biofeedback and Neurofeedback are rooted in the practice of correcting or enhancing the way the brain functions using live time displays of the brain's electrical activity, i.e., its brainwaves (Barnett *et al*., 2014; Taylor & Elwy, 2014) [4, 36].

Neurofeedback models employ computer-based hardware and software that when attached to sensory points, traditionally on the head and hands, restore damaged brainwave patterns thus restoring optimal functioning. Noninvasive software and hardware systems work in tandem to generate an award system to which the brain can respond (Thiabault *et al*., 2015). The restoration of functional communication within the more complex parts of the brain helps to dissipate both psychological and somatic symptoms. For those presenting with a high level of somatic symptoms a hybridized model of neurofeedback and biofeedback is employed (Taylor & Elwy, 2014) [36]. Certain software programs used in sessions mimic video games, while others allow for the treatment recipient to watch a movie during session time. Electroencephalogram (EEG) sensors quantify brain activity and communication while the treatment recipient engages in a sensory-oriented video game or simply watches a movie. When brain wave activity is poor, the exercise on the screen will cease; when optimal, the exercise continues (Barnett *et al*., 2014; Thibault *et al*., 2015) [4, 37]. The brain is rewarded in a Pavlovian-like way for producing optimal activity by being given something "it likes" for doing so, i.e., the continuation of the video game or movie. The treatment recipient's brain begins to intuitively use the reward system circuitry because it has learned that, in doing so, it receives positive reinforcement. Consequently, the brain learns to rewire itself (Bowers & Ressler, 2015) [8].

Traumatic experiences disorganize brain communication; they change the referenced wiring and firing. By restoring a baseline of functional communication among the brain's impaired parts the wiring and firing become better regulated, an example of positive neurogenesis (Keysers & Gazzola, 2014) [21]. Neurotherapeutic interventions are often successful in reducing more acute symptoms secondary to PTSD because of their ability to correct brainwave dysregulation (Thibault *et al*., 2015) [37]. Like Brainspotting and EMDR, neuro and biofeedback sessions require little

work on the part of the treatment recipient, minimizing the risk of re-traumatization, and offering a relaxing experience (Baldwin & Korn, 2021, Grand, 2013; Bagheri-Mohammadi, 2021; Keysers & Gazzola, 2014) [3, 21]. Such features make Neurotherapy interventions attractive options for children and adolescents or individuals that cannot talk to a psychotherapist because of the classification status of traumatic events, e.g., individuals in certain military and government positions (Boyd *et al*., 2018) [9].

Summary and Conclusion

PTSD has a multifaceted symptom profile. Although the causation of the disorder is understood, i.e., trauma exposure, the symptomology is individual and so much about the brain remains unknown. Research attention has been focused on the type of memory processes implicated in PTSD and their conjectured neurobiological processes, yet access to effective treatment remains narrow. Brain-based interventions such as those detailed offer both psychological and physical resolve while providing greater insight for those living with PTSD. Understanding what is happening within one's mind and body can restore a sense of control and safety- feelings that have been inhibited and may be unfamiliar to those afflicted by PTSD. For some, recovery from trauma can be a lifelong pursuit. The therapeutic relationship requires equal collaboration between the client and clinician. The symptoms secondary to unprocessed trauma are too complicated to treat and eradicate with only one intervention. The brain becomes incapable of processing verbal information about the events, making more common treatment modalities limiting at best, and retraumatizing at worst. By employing brain-based methods in treatment, the brain is restored and reorganized. The more disabling symptoms secondary to PTSD are substantially reduced, if not eradicated, without requiring the client to relive the events they were victimized by, and offering hope in recovery.

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