Application of Neuroscience Research to the Understanding and Treatment of Posttraumatic Stress Disorder (PTSD)

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Abstract

The following article outlines the possible application of the technologies of neuroscience to improve medical and mental health professionals' understanding of the sequelae and maintenance of symptoms of posttraumatic stress disorder (PTSD). A neurocognitive model of PTSD is presented, incorporating findings of frontal and subcortical dysregulation after exposure to trauma. Suggestions for incorporating more neurologically-based techniques into PTSD treatment, including cognitive rehabilitation and neurofeedback, and speculations regarding the utility of transcranial magnetic stimulation (TMS) and deep brain stimulation (DBS) in the treatment of PTSD are also presented.

Keywords: neuroimagery, amygdala, hippocampus, frontal-subcortical circuits, post-traumatic stress disorder, transcranial magnetic stimulation (TMS), deep brain stimulation (DBS), neurofeedback, cognitive rehabilitation

1.1 Introduction

The last two decades have seen a tremendous growth in neuroscience research. Similarly, the investigation of causal, maintenance, and intervention efforts for trauma and trauma related disorders has recently begun growing since the increase in posttraumatic stress disorder (PTSD) diagnoses as a result of foreign wars (Richardson, Frueh, & Acierno, 2010). Moreover, there has been a significant overlap in findings from neuroscience research focused on trauma symptoms and more traditional correlational studies focusing on the type, frequency, impairment due to, and cognitive processes related to having experienced a trauma (Lohman & Royeen, 2002). Following suit, the treatment literature regarding PTSD has changed drastically from the previous focus on more traditional cognitive and exposure therapies to the point where even genetic testing to determine the appropriate psychopharmacological intervention has been recommended (Bowirrat, et al., 2010).

Given the increased emphasis on neurologically-focused and neurologically-supported treatments in the field of clinical psychology and clinical neuropsychology for issues such as traumatic brain-injury (TBI; Schoenberg & Scott, 2011), attachment issues (Siegel, 2012), attention-deficit hyperactivity disorder (ADHD; Sergeant, Geurts, Scheres, & Oosterlaan, 2003), it seems fitting to apply the same technologically-sophisticated and ground-breaking methods of assessing and treating impairing medically-grounded mental conditions to PTSD. Neuropsychological theorizing about the symptoms of PTSD, such as dissociation (Wilkinson, 2005), has already begun to spread throughout academic circles (Edlow, Kahn, Laufer, Nunan, & Simon, 2011; Liberzon & Sripada, 2007). Therefore, the following will explore the current understandings of PTSD, neuroscience technology, research on the symptoms and processes of trauma and trauma symptoms, and treatment from a neuroscientific perspective focusing on as less explored methods in PTSD treatment such as transcranial magnetic stimulation (TMS) and deep brain stimulation (DBS).

1.2 Trauma Background

The introduction of a diagnostic nomenclature specifically devoted to having been exposed to a traumatic stressor (i.e., PTSD) only entered into modern psychology in the Diagnostic and Statistical Manual, Third Edition, of the American Psychiatric Association (DSM-III, APA) in 1980. Similar reactions during the first and second world wars ("shell shock") and in the aftermath of sexual assault, and extreme grief associated with loss went unstudied in a scientifically validated manner since the beginning of psychological research in the late 1800s and early 1900s.

Since PTSD's introduction in 1980 there have been many revisions and clarifications due to better understandings of the varied presentations of symptoms associated with experiencing a traumatic stressor (Friedman, et al., 2011).

The importance of traumatic stress, and the resultant pathology after experiencing a trauma, has reached the point where the APA's newest version of the DSM, the DSM-5 (APA, 2013), has an entire chapter devoted to trauma-related disorders. There may be trauma diagnoses such as Complex PTSD (Herman, 1992) and Developmental Trauma Disorder (van der Kolk, 2005) that have not been added to the DSM-5 due to ongoing debate regarding these syndromes (Schmidt, Petermann, &Fegert, 2013; van der Kolk, Roth, Pelcovitz, Sunday, & Spinazzola, 2005; van der Kolk, et al., 2009).

Given the importance of trauma and traumatic stress disorders it seems as if a comprehensive understanding of the development and maintenance of traumatic stress disorders would serve clinicians and physicians in providing the best treatments for persons suffering from the symptoms of traumatic stress syndromes. Since PTSD is the most studied trauma related disorder it will remain the focus of this work. Recently, the trend in the research and treatment institutions for PTSD have been looking for models and treatment strategies that are founded in neuroscience

1.3 Neuroscience Background

There are multiple non-invasive neuroscientific techniques that have been created since the advent of the first magnetic resonance imaging (MRI). Common exploratory neuroscience processes include scans with MRIs, functional MRIs (fMRIs), positron emission tomography (PET), computerized axial tomography (CT), quantitative electroencephalograms (QEEG), and transcranial magnetic stimulation (TMS) combined with one of the aforementioned scanning processes. Other methods, such as track density imaging, or TDI (Calamante, et al., 2011), utilize fMRI technology and change the mathematical process and rate/intensity of scanning to arrive at a more accurate picture of brain tissue densities. Though some methods have limitations that make their data more circumspect (Assaf & Pasternak, 2008), the general consensus in fields related to neuroscience and mental health is that the ubiquitous nature of the numerous scanning and assessing technologies cannot be understated (Diamond & Amso, 2008).The professional drive for neuroscience-informed research is growing, with multiple projects across institutions like the TWIN-E project (GATT, et al., 2012) which focuses on the use of methods such as Diffusion Tensor Imaging (DTI) and MRI protocols to explore emotions. Imagery of brain structures, metabolic and neurotransmitter pathways and functions are yielding models of neurological and psychiatric pathology, and windows into more effective neurologically-informed interventions.

2.1 Neurological Model of PTSD

The symptoms of PTSD have traditionally been clustered into three main categories: arousal, re-experiencing, and avoidance (American Psychological Association (APA), 2000, 2013). Symptoms of arousal include difficulties with sleep, trouble concentrating, increased startle response, and a constant sense of anxiety or tension with no precipitant immediately present (APA, 2013). Symptoms of re-experiencing include nightmares, persistent intrusive thoughts & sensory imagery or frank "flashbacks" of the traumatic event. Symptoms of avoidance associated with PTSD include agoraphobia, avoiding sounds, activities, places, or objects associated with the original traumatic stressor, and over-engagement in activities with the stated purpose of not thinking about a traumatic stressor or feeling anxiety following a traumatic stressor (APA, 2013). Given the aversive nature of trauma-related over-arousal and re-experiencing, avoidance seems, at least initially to be an appropriate response.

Recently there has also been recognition of various cognitive aspects of PTSD, including attentional biasing, (Bar-Hainewt al., 133; Olatunji, Armstrong, McHugo, &Zald, 2013), reduced recall of both traumatic and non-traumatic material (APA, 2013; Elzinga & Bremner, 2002), and impaired executive skills (Kanagaratnam&Asbjørnsen, 2007; Leskin& White, 2007; Walter, K. H., Palmieri, P. A. &Gunstad, J, 2010). Neurological models of PTSD focus on the cognitive, arousal and re-experiencing aspects of PTSD. Decades of neuroimagery of patients with PTSD present a diagnostically specific and consistent profileimplicating dysfunction in medial prefrontal circuits (dorsomedial, ventromedial, rostromedial. and anterior cingulate cortices) and limbic system (amygdala, and hippocampus) circuits.

2.2 Subcortical/Limbic System Changes

2.2.1 Over-activation of the amygdala.

Hyper-reactivity of the amygdala is a robust finding in PTSD research (Ledoux, 2000; Milad, Rauch, Pitman & Quirk, 2006; Shin, Rauch & Pitman, 2006). In PTSD the amygdala also have exaggerated responses to non-trauma-related affective material, such as fearful facial expressions (Rauch et al., 2000; Shin et al., 2005; Williams et al., 2006), as well as on attentional tasks (Bryant et al., 2005; Semple et al., 2000). The degree of amygdala activation is also correlated with PTSD severity (Armony, Corbo, Clément, & Brunet, 2005; Protopescu et al., 2005; Rauch et al., 1996; Shin et al., 2004).

The functions of the amygdala are related to basic survival emotions. In particular, they specialize in threat detection and are involved in conscious and unconscious fear conditioning (Armony and Dolan, 2002; Cheng et al., 2003; Knight et al., 2004a,b; Davis & Whalen, 2001;LaBar et al., 1998; Ledoux, 2000; Morris, Ohman& Dolan, 1998; Orr et al., 2000; Otto et al., 2000). In PTSD, limbic biases towards survival-related stimuli are out of balance, and can prime attentional systems to be overly attuned to minor, often irrelevant signals of danger. The amygdala have numerous interconnections with medial orbit frontal and anterior cingulate circuits which provide top-down modulation/inhibition of fear and other basic emotions.

2.2.2 Underactivation and cell loss of the hippocampus.

Findings reciprocal to those of the amygdala are often reported for hippocampal structures. In PTSD, diminished activation of the hippocampus is often found (Bremnar, Narayan et al., 1999; Liberzon, I. &Sripada, 2002; Shin, McNally et al., 1999). Cell loss in the hippocampusis also a common finding, and can be severe enough to be detected at the gross anatomical level as hippocampal atrophy on MRI & CT scans of PTSD patients (Bremner, Vythilingam et al., 2003; Bremner Randall, Scott et al., 1995; Bremner, Randall Vermetten et al., 1997; Gilbertson et al., 2002; Stein, et al., 1997; Villareal et al., 2002; Wignall et al., 2004; Winter &Irle, 2004). Although some studies do not show hippocampal atrophy, a meta-analysis by Smith (2005) indicated that the pooled effects across MRI volumetric studies was significant, suggesting about 6% loss in hippocampal volume occurred in PTSD.

Cortisol neurotoxicity is a neuropathological correlate of these findings. Murine, primate and human models have shown that chronic stress result in sustained oversecretion of cortisol, which, in turn can destroy hippocampal neurons (Sapolsky, Uno, Rebert, & Finch, 1990; Swaab, Bao & Lucassen, 2005; Uno et al., 1994). Cortisol and its impact on neurological and affective processes has been a consistent focus in PTSD treatment studies as well (Gerardi, Rothbaum, Astin, & Kelly, 2010; Olff, de Vries, Guzelcan, Assies, &Gersons, 2007).

Alternatively, the general "neuronal integrity" (Shin, Rauch &Pitman, 2006) of the hippocampus is questioned, due to findings of decreased hippocampal levels of N-Acetylaspartate (NAA; an index of neuronal density) in PTSD patients (Brown et al., 2003: Freeman et al., 1998; MohanakrishnanMonen et al., 2003). This has been found even in the absence of statistically significant hippocampal atrophy (Schuff et al., 2001). It is often argued that hippocampal damage in PTSD may be due to underlying vulnerability, possibly genetic, or due to childhood trauma. Nonetheless, longitudinal studies following people from childhood through adulthood support idea that stress precedes PTSD, without any known predisposing factors, including smaller hippocampal volumes (Carrion, Weems, & Reiss, 2007).

It is well established that normal hippocampal functioning,is related to salience labelling crucial to encoding, memory consolidation, retrieval, and goal-directed behavior(Lisman, J. E. & Anthony A. Grace, A. A. 2005; Luo, Tahsili-Fahadan, Wise, Lupica, & Aston-Jones, 2011; Moore& Stickney, 1980). Under normal conditions, the hippocampus also provides some inhibitory influence on the amygdala (Ehrlich, Humeau, Grenier, Ciocchi, Herry&Lüthi, 2009; McGaugh, 2004). In PTSD, the amygdala-hippocampal circuits related to attentional biasing, encoding and memory processes are overactive, possibly due to increased innervation (Mahan &Ressler, 2012) from the original traumatic incident and a decrease in neuronal volume, a theoretical byproduct of stress related neurohormones (Morey, et al., 2011).

2.3 Cortical Changes

Impairments in the executive functioning of PTSD population are common. These may largely be due to underactivation of the medial PFC, which is often found in PTSD (Karl et al., 2006; Kasai et al., 2008; Matsuo et al., 2003).

2.3.1 Dysregulation of frontal-subcortical circuits (FSC).

Normal brain functioning requires complex feedback circuitry between subcortical and cortical systems. This is especially crucial for the self-regulatory and executive activities of the frontal lobes. The frontal lobes can only function as a cortical-subcortical network. All FSCs are closed loop “final effector mechanisms” which require the integration of external/sensory and internal/limbic information, and the formulation and initiation of appropriate responses.

Several frontal-subcortical circuits (FSCs) have beendescribed, the bulk of which involve motor planning and movement. Three large cognitive FSCs have been delineated: the dorsolateral, anterior cingulate and orbitofrontal FSCs (Cummings 1993; Lichter and Cummings, 2001). All of them have parallel but discrete circuits (similar to somatotropic organization). The architectonics of the prefontal cortex (PFC) are reflected in their PFC-striatal projections—functionally related cortical areas send converging projections to adjacent regions of the striate, so that within the striate, there are small functionally specialized domains. Frontal-subcortical circuits contain direct and indirect loops, but a "generic" FSC connects the frontal lobe to the striate (caudate and putamen), to the internal globuspallidum (GPi) and external globuspallidum (GPe)/substantianigra (SN) complex, on to the thalamus and back to the frontal lobe. The FSCs receive projections from non-circuit cortex, thalamus, and amygdala, and project to non-circuit inferior temporal, posterior parietal and pre-striate. Direct cortical-basal ganglia connections are only corticofugal, and the cortical output form these circuits, such as the thalamocortical projections, route almost exclusively back to the frontal lobes.

The extensive interconnectedness of these frontal subcortical systems permits readiness for action and flexibility of responsiveness. However, this also requires a dynamic balance between bottom-up survival-oriented activity and top-down directing of goal-oriented planning and behavior. This balance is often disrupted in PTSD. Of particular interest in the understanding of PTSD are the anterior cingulate FSC (ACFSC) and the medial division of the orbitofrontal systems (OFSC), which involve connections to the amygdala. The ACFSC is central to motivational functioning. Underfunctioning of this system results in apathy and diminished initiative. The orbitofrontal FSC has lateral and medial subdivisions, both of which are crucial for integrating emotional and motivational information into problem solving and planning. Underfunctioning of the OFSC results in disinhibited and inappropriate behavior, and affective lability. The medial OFSC is also considered to be the "limbic cortex" with extensive interconnections with the limbic system, especially the basal amygdala.

In PTSD research, many observations have been made of reduced medial frontal (mPFC) activity and impaired medial frontal modulation of the amygdala. This dysregulation is thought to account for a number ofproblematic neurocognitive processes in PTSD, such as fear conditioning, habituation, and extinction, cognitive–emotional interactions and emotionalprocessing. It is likely that the mPFC, in coordination with the limbic system, plays a role in the contextualization of stimuli, and dysregulation of contextualization might play a key role in the generation of PTSD symptoms, including disrupted memory and sense of reality (Elzinga&Bremner, 2002; Hamner, Lorberbaum& George, 1999; Liberzon&Sripada, 2007; Shin Rauch & Pitman, 2006).

To summarize, the reduction of top-down frontal lobe functioning, coupled with excessive or at least dysregulated bottom-up activity of limbic structures seems to account for a wide variety of PTSD symptoms. These include the disruptive, activating symptoms (affective and behavioral disinhibition, hypervigilance, heightened anxiety and startle reflex, attentional priming of potential threat,and flashbacks), as well as the de-activating aspects of PTSD (emotional numbing, depersonalization, derealization and unreliable/spotty retrieval from many aspects of memory) that are typical of PTSD and trauma-related disorders.Support for this neurological model of PTSD also comes from the mental health fields. Successful reduction of PTSD symptoms through medication, psychotherapy, or their combination, also results in improved neurological findings (e.g. Felmingham,2007; Fernandez et al., 2001; Walter, Palmieri & Gunstad, 2010).

3.1 Implications for Neurogically- and Neuropsychologically- Based Treatments of PTSD

The use of fMRI to analyze amygdala and anterior cingulate response to threat can predict successful response to cognitive-behavioral therapy, or CBT (Bryant et al., 2008), which, though it is the most empirically supported treatment for PTSD is effective in only about 50% of PTSD patients.No straightforward pharmacotherapy is effective in PTSD either. It is proposed that neuropsychological findings and methods might be used more directly in treating PTSD as an adjunct or primary technique.

3.1.1 Cognitive Rehabilitation.

Given the presence of executive skills deficits in many people with PTSD, cognitive rehabilitation of executive functions could be useful, as it has been shown to be effective for a wide range of executive dysfunctions (Cicerone, Levin, Malec, Stuss, & Whyte, 2006; Sohlberg & Mateer, 2001; Sohlber & Turkstra, 2011). Neuropsychological assessment can guide executive skills training directed in areas specific to PTSD, such as behavioral and affect regulation, automatic processing/inhibition (Stroop task), memory strategies (Kanagaratnam, & Asbjørnsen 2007), and nonverbal abstract reasoning (Craig, 2006). Similar impairments have been noted with memory, and complex attention and inhibition tasks, such as delayed response, delayed non-match to sample, and object alternation in PTSD patients (Koenen, et al., 2001), and executive control of attention(Lesking & White, 2007). In the latter study, participants with PTSD were specifically impaired in filtering irrelevant information or distracting flankers.

In addition, rehabilitation efforts aimed at other executive tasks such as organization and problem-solving, could reduce stressors and improve self-sufficiency. Compensatory strategies and environmental manipulations to optimize functioning are also common in cognitive rehabilitation, and would serve to augment functioning and reduce stress. Cognitive rehabilitation would be doubly indicated for the many veterans returning from combat with head injuries in addition to PTSD.

3.1.2Neurofeedback.

Biofeedback techniques provide information about otherwise non-conscious physiological processes, such as blood pressure, heart rate and skin conductance, rendering them amenable to conscious control, usually resulting in relaxation or other adaptive response. Neurofeedback provides EEG feedback about targeted brain wave activity, such as frequency or coherence, often in specific regions of the brain. Neurofeedback of slow wave (alpha and theta) frequency bands had been employed in the treatment of PTSD with reported success. Peniston & Kulkosky (1991) first showed reduced symptomology, when combined with psychotropic medication in 14 Vietnam-era veterans in comparison to medication alone (n=14), with continued positive effects at 30 month follow-up. As part of a NATO ebook series on security through science, Gruzelier (no date) described the role of brain's theta rhythm in synchronizing electrical activity in the hippocampus and over widely distributed brain regions implicated in PTSD. Frontal-subcortical circuitry is involved in survival behavior, navigation (including virtual reality tracking), memory retrieval, and the integration of emotion and cognition. Theta frequency activity in the hippocampus is associated with encoding, learning and re-learning or encoding new associations (e.g. Hasselmo, Bodelón, &Wyble, 2002)

Othmer & Othmer (2009) present a more refined version of the Peniston protocol in the successful treatment of PTSD, as illustrated in two case histories of combat veterans participating in a nation-wide neurofeedback treatment program. A major cite for the use of neurofeedback for PTSD is at Camp Pendleton (Othmer, 2012). Neurofeedback is often used in addiction recovery, but has not gained a foothold in the treatment of PTSD, in part because of small, often single-case studies. Validation studies also tend to be sparse, which is only recently beginning to be rectified (Gruzelier, Egner& Vernon, 2006; Wahbeh&Oken, 2013).

3.1.3 Transcortical magnetic stimulation (TMS).

TMS is a noninvasive method for directly stimulating cortical neurons. The application of brief bursts of electromagnetic energy depolarizes (excites) neurons with minimal discomfort, and without convulsions or cognitive impairment (Belmaker & Fleischmann, 1995). Possibly due to its influence on monoamines (Ben-Shachar, Belmaker, Grisaru, & Klein, 1997), TMS has been shown to have antidepressant and anxiolytic effects. Its use as a treatment in PTSD is also indicated by its apparent reduction in the activity of the hypothalamic-pituitary-adrenocortical system (Post & Keck, 2001).

TMS has been studied for use in the treatment of PTSD since the late 1990's, with some success. In a pilot study, Grisarua, Amir, Cohena, &Kaplana (1998), showed at least transient relief of PTSD symptoms with TMS. Repeated administration of TMS (rTMS) became more common, and was shown to be effective in double blind studies. Cohen, et al. (2004) demonstrated that repeated TMS (rTMS) at 80% motor threshold over the right dorsolateral prefrontal cortex of PTSD patients, reduced anxiety as well as some of the core PTSD symptoms related to re-experiencing and avoidance.

In a double blind study by Isserles et al. (2012), deep TMS of medial prefrontal cortex improved symptoms in treatment-resistant PTSD. Osuch et al., (2009) found incremental validity for the use of rTMS in addition to exposure therapy for refractory PTSD. Song &Chae (2005) reviewed the TMS literature, and suggested that the effect of rTMSmay be to normalize brain metabolism, and improve neuronal functional connectivity in patients with PTSD.

Across studies, the safety and effectiveness of TMS as a psychiatric treatment has been demonstrated, but its effect sizes vary, and the duration of some of its effects is short. As an adjunct therapy it can provide rapid relief from symptoms, and might be useful at initial or intractable phases of treatment. Repeated TMS has been found to effective as a single and adjunct therapy for refractory PTSD.

3.1.4 Deep brain stimulation (DBS).

While TMS stimulates cortical neurons, DBS stimulates deeper structures in the brain. It is an invasive procedure requiring stereotactic placement of electrodes in the brain, and a pacemaker-like device in the chest. Designed originally to reduce tremor in Parkinson's patients, it may have some utility for entrenched, treatment-resistant disorders. A three-cite collaborative study of DBS of the ventral capsule and striatum was effective in the treatment of refractory depression (Malone, Jr. et al., 2009). Recall that the striatum is a part of all of the frontal-subcortical circuits, which could be a target for PTSD therapy. For a variety of reasons, including the fact that DBS can sometimes impair cognitive skills or reduce the functionality of a brain region, possibly due to differential effects on ion-channel systems (Perlmutter& Mink, 2006) animal models of DBS in the treatment of PTSD are often employed. Langevin, De Sallesc, Kosoyand&Krahl, (2010) reduced the development of PTSD in rats with DBS of the amygdala during trauma-learning. Using a similar protocol Stid, Vogelslang, Krahl, Langevin, and Fellous (2013) found significant reduction in hyper-vigilance as compared to typical medication treatments in rats post-trauma.

In a human lesion study, based on discrete, penetrating wounds in Vietnam-era veterans (Koenigs et al., 2008), it was found that damage to either the amygdala or the ventromedial PFC (vmPFC), which is heavily interconnected with the amygdala, was associated with greatly reduced PTSD in unilateral lesions. Bilateral lesions were correlated with a total lack of PTSD, leaving the authors to suggest that therapies that selectively inhibit vmPFC and/or amygdala function would be effective in treating PTSD. Although DBS is currently an invasive procedure, deep brain stimulation is also possible with newer TMS protocols, and this might be a fruitful avenue to pursue in targeting amygdala and medial frontal regions

4.1 Summary

The neuroscience literature devoted to understanding trauma and PTSD is developing rapidly. However, neurologically sound treatment for PTSD is only in its early phases. Treatment protocols for emotional dysregulation, such as depression (Ramsubbu, Anderson, Chavda, & Kiss, 2013) and anxiety (Parsons & Rizzo, 2008; Rothbaum, Hodges, Anderson, Price, & Smith, 2002; Rothbaum, Hodges, Smith, Lee, & Price, 2002) have begun to utilize neurologically-guided treatment practices such as deep brain stimulation (DBS), transcranial magnetic stimulation (TMS), neurofeedback (NF), biofeedback, (BF), virtual reality exposure therapy (VRE) (see Anderson et al., 2013 for a review), medication regimens, and other somatic therapies (Andreas & Andreas, 1993).

The neurological correlates of PTSD symptoms also seem have a direct link to neuroscientifically informed treatment.Miniussi& Rossini (2011) discuss emerging non-invasive techniques, such as TMS, for stimulating neuroplasticity to modify more trenchant behaviors due to brain re-wiring after a physical trauma. Techniques related to TMS look promising for repairing the damage of neurological and neuropsychological conditions such as Alzheimer's dementia (Miniussi&Vallar, 2011). Lohman & Royeen (2002) have explored the possible implications of treating PTSD symptoms from the perspective of a cognitive rehabilitation model due to the similarity of symptom profiles seen in some traumatic brain injury patients. Peniston and Kulkosky (1991) showed the efficacy of neuropeedback in treating Vietnam veterans diagnosed with PTSD.

Given the far-reaching and potentially cost-saving implications of finding neurologically-sound and highly impactful treatments for cognitive issues, Miniussi & Vallar (2011), among others support the notion of expanding the neuroscience and neuropsychological literature focused on trauma and trauma related disorders such as PTSD.

The recent increased focus on neurologically-based treatments by mental health and medical organizations alike indicates support for further exploring interventions focused on emotional regulation. A review of success and dropout rates in PTSD treatment conducted by Schottenbauer, Glass, Arnkoff, Tendick, & Gray (2008), found that non-success rates were often as high as 50%.

In light of burgeoning treatment-resistant PTSD rates in multiply-deployed combat veterans, and the high human and financial costs of a chronic mental illness with high risk of self-harm, it behooves us to employ the knowledge base and techniques of neuroimagery and neurocognitive sciences to aid in the treatment of PTSD either as single modality or adjunctive therapies.

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