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Review

Current status on behavioral and biological markers of PTSD: A search for clarity in a conflicting literature

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ABSTRACT

Extensive research has identified stereotypic behavioral and biological abnormalities in post-traumatic stress disorder (PTSD), such as heightened autonomic activity, an exaggerated startle response, reduced basal cortisol levels and cognitive impairments. We have reviewed primary research in this area, noting that factors involved in the susceptibility and expression of PTSD symptoms are more complex and heterogeneous than is commonly stated, with extensive findings which are inconsistent with the stereotypic behavioral and biological profile of the PTSD patient. A thorough assessment of the literature indicates that interactions among myriad susceptibility factors, including social support, early life stress, sex, age, peri- and post-traumatic dissociation, cognitive appraisal of trauma, neuroendocrine abnormalities and gene polymorphisms, in conjunction with the inconsistent expression of the disorder across studies, confounds attempts to characterize PTSD as a monolithic disorder. Overall, our assessment of the literature addresses the great challenge in developing a behavioral and biomarker-based diagnosis of PTSD.

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1. Introduction

Individuals exposed to intense trauma that threatens physical injury or death are at significant risk for developing post-traumatic stress disorder (PTSD). People who develop PTSD respond to a traumatic experience with intense fear, helplessness or horror (American Psychiatric Association, 1994) and subsequently endure chronic psychological distress by repeatedly reliving their trauma through intrusive, flashback memories (Reynolds and Brewin, 1999, 1998; Ehlers et al., 2002; Hackmann et al., 2004; Holmes et al., 2005; Speckens et al., 2007). These intrusions are frequently precipitated by the presence of cues associated with the traumatic event. The re-experiencing and avoidance symptoms of the disorder are commonly comorbid with the development of additional debilitating symptoms, such as depression and substance abuse (Stam, 2007; Nemeroff et al., 2006; Elzinga and Bremner, 2002; Bremner, 2006).

Research over the last several decades has documented numerous physiological and behavioral abnormalities associated with PTSD, including heightened autonomic arousal, exaggerated startle, abnormally low baseline levels of cortisol, smaller hippocampal volume and cognitive impairments based on impaired hippocampal and prefrontal cortical functioning (Moore, 2009; Nemeroff et al., 2006; Vieweg et al., 2006; Yehuda, 2006; McNally, 2006; Johnsen and Asbjornsen, 2008; Golier et al., 2006; Yehuda et al., 2005, 1995c). The primary purpose of this review is to assess this research, with an emphasis on determining whether the empirical work is consistent with a stereotypic profile of the PTSD patient. It is particularly important that we have an understanding of patterns of abnormalities that accurately define PTSD, as compared to less reliable measures, as we work toward developing strategies for identifying behavioral and biological markers of PTSD. Moreover, a thorough analysis of the PTSD literature may reveal why only a subset of traumatized people exhibit persistent physiological and behavioral abnormalities. We have also explored the likelihood of a differential expression of bio-behavioral markers of PTSD in different subpopulations, e.g., men, women and children. Overall, our goal is to provide a thorough assessment of the complexity of factors that contribute toward differences in the susceptibility and expression of PTSD in subsets of individuals. This work may facilitate the development of more targeted treatment options and biologically-based diagnoses for PTSD patients, as well as to enhance clinical and preclinical research into the etiology of this disorder.

2. An assessment of risk factors for PTSD

In the aftermath of trauma, most people display symptoms common to PTSD patients, including re-experiencing, emotional numbing, dissociation, impaired sleep, avoidance and hypervigilance. However, only about 10–25% of these individuals continue to exhibit post-trauma symptoms for at least 1 month and then ultimately meet the criteria for a diagnosis of PTSD (McFarlane, 2000; Ozer and Weiss, 2004). For most traumatized individuals, the cluster of symptoms evoked by the trauma subsides within 3 months (Kessler et al., 1995). Thus, the acute response to trauma can be characterized by an intense and exaggerated stress response, which is followed by recovery and resilience, with only a subset of traumatized individuals who ultimately develop a chronic form of PTSD.

According to Duke and Vasterling (2005), risk factors that influence whether or not a traumatized individual will develop chronic forms of PTSD can be divided into three general categories: (1) factors pertaining to the trauma (e.g., type of trauma, intensity of trauma); (2) individual characteristics (e.g., age, sex, IQ, socioeconomic status, pre-existing psychiatric history, personality, medical history); and, (3) peri- and post-trauma variables (e.g., perceived threat to one's life, peri-traumatic dissociation, biological response to the trauma, emotional response to the trauma). Depending on the interactions among all of these factors, the traumatized individual will eventually (a) develop PTSD, (b) develop lasting symptoms that do not meet the diagnostic criteria for PTSD, or (c) fully recover and maintain satisfactory physical and mental health.

There has been extensive study of biological, environmental, behavioral and social factors which are associated with the susceptibility of a subset of traumatized individuals to develop chronic forms of PTSD. This topic has been addressed in recent reviews (Mehta and Binder, 2012; Toyokawa et al., 2012; Uddin et al., 2010; Shin et al., 2006; Amstadter et al., 2009; Shalev and Segman, 2008; Johnson and Thompson, 2008; Ursano et al., 2008; Liberzon and Sripada, 2008; Yehuda and Bierer, 2008; Pitman et al., 2012; Yehuda et al., 2011; Baker et al., 2012) and therefore a comprehensive discussion of PTSD vulnerability factors will not be addressed here. Instead, we have focused on the complexity of PTSD, which is manifested as inconsistent and controversial findings, such as hormonal (e.g., cortisol) factors and PTSD susceptibility and expression. Our discussion and review of the literature on these issues may enhance our understanding of why only a subset of traumatized individuals develops chronic PTSD, as well to advance current efforts to develop a biomarker-based assessment of risk and diagnosis of PTSD (Baker et al., 2012; Jovanovic et al., 2012, 2010; Miller, 2011; Su et al., 2009; Zhang et al., 2009).

2.1. Dose–response model of PTSD susceptibility

The dose–response model of PTSD contends that the incidence, as well as the magnitude of PTSD symptoms, intensify as the severity of the trauma increases (March, 1993), and studies have provided support for this hypothesis (Mollica et al., 1998a; Pynoos et al., 1993; Shore et al., 1986; Snow et al., 1988; Sutker et al., 1993). For instance, combat veterans who were prisoners of war (POWs) and tortured by the enemy displayed a significantly greater incidence of PTSD (roughly 75–80% developed PTSD) than combat veterans who were not POWs (Sutker et al., 1993). In another study, investigators examined the severity of PTSD symptoms as a function of individuals' distance from the epicenter of the 1988 Armenian earthquake (Pynoos et al., 1993). The results revealed a