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SYMPOSIUM – INTRODUCTION

Posttraumatic stress disorder: A neurocognitive perspective

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INTRODUCTION

Posttraumatic stress disorder (PTSD) is typically conceptualized as a fear-based disorder that develops following exposure to a life-threatening event. PTSD diagnostic symptoms cluster into groupings that relate to reexperience of the trauma (e.g., intrusive memories and nightmares), behavioral and cognitive avoidance of reminders of the trauma, emotional "numbing" (i.e., restricted range of emotional responsiveness), and heightened arousal (e.g., hypervigilance, exaggerated startle, irritability). In addition, it is increasingly clear that PTSD can be associated with a number of clinical features (e.g., grief, depression, and guilt) that are not central to the diagnostic criteria. Although the emotional relevance of PTSD is well understood, PTSD can also be viewed from a neurocognitive perspective. In fact, memory and attention abnormalities are sufficiently central to the clinical presentation of PTSD that they are incorporated into its diagnostic criteria (cf. American Psychiatric Association, 2000). Reexperiencing symptoms, for example, center on poorly regulated, intrusive memories of the trauma event, as well as psychological and physiological reactivity to associative cues that prompt recall of the trauma. Avoidance symptoms similarly involve behavioral and cognitive actions directed specifically at avoiding recall of trauma memories. Arousal symptoms include dysregulated attention, which manifests as inattentiveness (i.e., disturbed concentration) on one hand and over-attention to potential threat (i.e., hypervigilance) on the other.

Some cognitive conceptualizations of PTSD emphasize the role of fear learning. An associative fear network expands when stimuli that were previously emotionally neutral are interpreted as potentially threatening and elicit fear responses in their own right. In keeping with this conceptualization, a robust experimental psychopathology literature has demonstrated that trauma survivors with PTSD process potentially threatening environmental stimuli differently than non-fear-evoking stimuli (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoom, 2007; Buckley, Blanchard, & Neill, 2000; Constans, 1995). However, a rapidly expanding empirical base suggests that cognitive abnormalities are not limited to emotionally evocative or threatening contexts. Concurrently, there is now significant evidence of functional and structural neural abnormalities (Karl et al.,2006; Liberzon & Sripada, 2008; Rauch, Shin, & Phelps, 2006) and dysregulation of neurobiological systems associated with PTSD diagnosis (Heim & Nemeroff, 2009; Krystal & Neumeister, in press; Southwick, Rasmusson, Barron, & Arnsten, 2005).

On emotionally neutral tasks, the neurocognitive deficits associated with PTSD tend to be relatively subtle, with performances often falling within the normal range. Although this level of neurocognitive dysfunction may pale in comparison to that observed with more extensive neural insults or degenerative disorders, neurocognitive abnormalities associated with PTSD are of potential clinical relevance for several reasons. First, even when normatively unimpaired, if neurocognitive performance represents a change for the worse, the person experiencing the change may find it distressing and disruptive. Second, neurocognitive deficits existent before, during, and after the psychological trauma exposure may influence the development and course of PTSD. Some theorists, for example, suggest that the integrity and accessibility of the trauma memory are important to the emotional resolution of the trauma event (Brewin, 2007; Ehlers & Clark, 2000). Thus, impairment of executive functions or other cognitive skills integral to autobiographical memory retrieval (Conway, 2005; Conway & Pleydell-Pearce, 2000; Williams et al., 2007) would potentially thwart emotional recovery. Likewise, neurocognitive integrity may influence how individuals cope with PTSD, altering their ability to deploy environmental resources or internal coping mechanisms, such as adaptive reappraisal of the trauma event. Third, relative neurocognitive weaknesses (in encoding

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verbally acquired information) have been found in at least one study to hinder PTSD treatment efforts (Wild & Gur, 2008). It is likewise possible that neurocognitive deficits may affect exposure-based interventions that rely on the ability to reliably access the trauma memory, as well as cognitive behavioral interventions that require mental flexibility in shifting appraisals of the trauma event and related affective responses. Finally, the mild neurocognitive deficits associated with PTSD may cloud differential diagnosis. A contemporary example includes the diagnostic complexities clinicians face as increased numbers of military personnel return from war-zone deployments to Iraq and Afghanistan with mild traumatic brain injury and PTSD (Lew et al., 2008; Stein & McAllister, 2009).

Although well established as a diagnostic entity, there is still much that we do not know about PTSD, including how brain functioning affects its development, course, and response to psychosocial and psychopharmacological interventions. As a "window" into brain-behavior relationships, cognitive neuroscience and neuropsychological approaches may be particularly well suited to address these questions. This Symposium includes a group of articles that use cognitive neuroscience and neuropsychological methodologies to better understand the relationship between psychological trauma, PTSD, and brain functioning.

PTSD, the Brain, and Neuropsychological Functioning

Functional neuroanatomical models of PTSD have often focused on the vulnerability of the hippocampus to stress (e.g., Bremner, 2001). By logical extension, it has been reasoned that observed memory deficits associated with PTSD may reflect functional and structural hippocampal abnormalities. Woodward et al. (2009, this issue) document both smaller hippocampal volumes and verbal declarative memory deficits among military veterans with PTSD, but their study shows no significant associations between hippocampal volume and memory performances. These findings raise the question of whether other brain regions involved in memory (e.g., the prefrontal cortex) or the more general dysregulation of arousal may account in part for PTSD-related memory deficits. Work examining the nature of memory processes in PTSD, as well as error analyses of memory tests, have provided indirect support for the contribution of prefrontal dysfunction to PTSD-associated memory impairment (e.g., Vasterling, Brailey, Constans, & Sutker, 1998). Similarly, a growing body of work has documented both functional and structural abnormalities within the prefrontal cortex among trauma survivors diagnosed with PTSD (e.g., Geuze et al., 2008; Shin et al., 2004; Woodward et al., 2006). Finally, the lack of a significant relationship between memory performance and hippocampal volumes in the Woodward study may reflect varying temporal relationships between PTSD, the hippocampus, and neuropsychological functioning. Specifically, whereas some aspects of structural and functional brain abnormalities may precede development of PTSD, others may only arise after PTSD symptoms emerge or become chronic.

We still do not fully understand the extent to which cognitive abnormalities represent pre-trauma risk for PTSD development, are consequences of PTSD, or are a bit of both. Animal studies have provided compelling evidence that stress exposure leads to both neuronal damage and behavioral (e.g., learning and memory) changes (e.g., Arnsten, 2009; Conrad, 2008; Holmes & Wellman, 2009; Roozendaal, McEwen, & Chattarji, 2009). However, evidence coming primarily from human twin studies suggests that at least some aspects of neurocognitive functioning and neural integrity may be predisposing of, rather than consequential to, PTSD (Gilbertson et al., 2002, 2006). In these noteworthy studies, inferences about shared genetic vulnerabilities were made on the basis of similarities between PTSD-affected and nonaffected monozygotic co-twins. Using a prospective study designed around deployment to the Iraq war zone, Marx et al. (2009, this issue) report that visual memory performance assessed prior to war zone exposure confers additional risk of post-deployment PTSD symptoms beyond the variance contributed by combat experiences and pre-existing PTSD symptoms. Although the relationship between pre-trauma neurocognitive functions and post-trauma PTSD symptoms in that study is circumscribed to a single memory measure, the rigorous longitudinal methodology provides additional evidence that pre-exposure cognitive functioning may moderate the development of PTSD following stress exposure. Also using a longitudinal design, Samuelson and colleagues (2009, this issue) document subtle declines in visual recognition memory over a 34-month period among Vietnam combat veterans with chronic PTSD, but not among Vietnam veterans without PTSD, suggesting that the causal relationships between PTSD and memory deficits may be complex, reflecting bi-directional influences.

The study by Bryant et al. (2009, this issue) also provides insights into the temporal relationship between neural integrity and PTSD. Bryant et al. prospectively examined PTSD development in survivors of traumatic physical injury starting from the point of hospitalization. The results demonstrate that survivors of traumatic physical injury with mild traumatic brain injury are more likely to have developed PTSD three months following hospitalization than traumatically injured patients with no brain injury. Interestingly, the results also indicate that longer posttraumatic amnesia is associated with less severe intrusive memories at the acute assessment, but not at the 3-month assessment. Thus, duration of posttraumatic amnesia, as an index of injury severity, appears to have immediate protective effects against development of specific reexperiencing symptoms, but seems less influential with the passage of time. This is a particularly intriguing finding, which may reflect that attributes of the trauma memory, including its accessibility, change over time in a manner less protective against PTSD. It may also be that factors other than peri-traumatic recall become more important over time in determining outcome.

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In the only study in this issue to examine children with PTSD, DeBellis (2009, this issue) reports that children who had been neglected perform less proficiently than non-neglected children on a number of intellectual, cognitive, and achievement tasks, and that performance deficits are particularly pronounced among neglected children with PTSD, increasing in severity as PTSD symptoms increase. The DeBellis study has important public health implications at two levels. First, maltreated children, and especially those with PTSD, may be at increased risk of neurodevelopmental and academic problems. Second, the risk of unfavorable psychosocial outcomes may be additive over the life span. If childhood PTSD leads to neurocognitive deficits and, as Marx et al. (2009, this issue) demonstrate, neurocognitive deficits confer risk of increased PTSD symptom severity following trauma exposure in adults, residual neurocognitive deficits associated with childhood adversity may place individuals at additional risk for poorer outcomes following trauma exposure as adults.

Much of the literature examining PTSD and neurocognitive functioning, including the majority of the studies included in this issue, has used predominantly male military or military veteran samples. Thus, conclusions about how well findings generalize to the broader population have been less certain. Twamley et al. (2009, this issue) report that women with PTSD related to intimate partner violence demonstrate slower than normal processing speed, adding to a growing literature suggesting that neurocognitive findings relevant to PTSD are not limited to military populations.

Future Directions

The articles comprising this Symposium suggest that, in addition to the salient behavioral, emotional, and psychosocial correlates of PTSD, the neurocognitive context of PTSD provides a useful framework in which to view the disorder. Although the cognitive abnormalities associated with PTSD diagnosis are subtle and circumscribed, they nonetheless consistently represent a downward population shift as compared to the neurocognitive performance of trauma survivors without PTSD. That said, there are many intriguing question that remain regarding the relationships of brain structure and function to PTSD. For example, although radiological and neurocognitive indices of brain integrity each distinguish trauma survivors with PTSD from those without PTSD, imaging and neuropsychological findings are not uniformly correlated. Thus, the specific brain locus of PTSD-related neurocognitive abnormalities remains uncertain. It is also becoming increasingly apparent that PTSD, like many psychiatric disorders, may present heterogeneously, with some symptoms more or less prominent among different individuals. Several of the articles in this Symposium suggest that neurocognitive integrity is linearly related to PTSD symptom severity, with less proficient performances associated with higher overall symptom severity. It remains to be seen whether neurocognitive functioning is more relevant to certain types of symptoms or PTSD presentations than others.

Collectively, several of the articles contained within this issue also suggest that causal relationships between neurocognitive functioning and PTSD may be complex and potentially bi-directional. Neurocognitive performance appears both to moderate the impact of trauma exposure on PTSD and to change over time as a function of PTSD. Further longitudinal work will be particularly useful in better understanding the dynamic relationships between neurocognitive functioning, trauma exposure, and PTSD onset and course. A related possibility is that neurocognitive functioning may influence response to certain treatment interventions. If so, cognitive neuroscience approaches will be useful in helping match specific interventions to the individuals most likely to benefit from them.

Finally, the relationship between brain development and PTSD is poorly understood. DeBellis and his colleagues (2009, this issue) document neurocognitive deficits associated with early childhood adversity and PTSD. However, the relationship between age at exposure and long-term neurocognitive outcome remains unclear. Are younger brains more or less vulnerable to potential neurotoxic effects of stress? There may also be potential interactions between aging later in life and PTSD in regard to neuropsychological functioning (Yehuda et al., 2006). The extent to which such relationships are a function of the chronicity of the disorder, as suggested by Samuelson et al. (2009, this issue), or of age itself remains to be clarified. The neurocognitive approach illustrated in this collection of articles may be particularly useful as we seek to gain a fuller understanding of the impact of traumatic experiences on the development and maintenance of PTSD throughout the life span.

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