Clinical Psychology Review 72 (2019) 101747

Contents lists available at ScienceDirect

Clinical Psychology Review

journal homepage: www.elsevier.com/locate/clinpsychrev

Review

Posttraumatic stress disorder and neurocognition: A bidirectional relationship?

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HIGHLIGHTS

- Neurocognition may moderate risk of PTSD after trauma.
- PTSD symptoms and neurobiological alterations may influence neurocognition.
- Bidirectional influences may create a feedback loop that helps sustain PTSD PTSD.

ARTICLE INFO

Keywords:
PTSD
Cognitive functioning
Neuropsychology
Risk
Resilience

ABSTRACT

There are well-known associations between PTSD and neurocognition, however, the direction of causality between the two is not well-understood. Neurocognition may alter risk of the development and maintenance of PTSD. Conversely, PTSD may pose risk to neurocognitive integrity. With cognitive and neurobiological conceptualizations of PTSD as a backdrop, this review will summarize results from several lines of research including preclinical, human analogue, retrospective, longitudinal, and treatment studies to inform the directional relationships between PTSD and neurocognition. Based on the collective findings from these related literatures, we suggest that a negative feedback loop between PTSD and neurocognition exists but that PTSD treatment and cognitive enhancement strategies may break this loop.

1. Introduction

The estimated lifetime prevalence of posttraumatic stress disorder (PTSD) in the general adult U.S. population is approximately 6–7% (Alegria et al., 2013; Goldstein et al., 2016; Kessler, Chiu, Demler, & Walters, 2005; Pietrzak, Goldstein, Southwick, & Grant, 2011), with higher rates in at-risk populations such as military veterans and first responders (e.g., Berger et al., 2012; Fulton et al., 2015). Internationally, higher rates are found in countries with greater trauma exposure and low access to trained mental health professionals (e.g., Atwoli, Stein, Koenen, & McLaughlin, 2015). Neurocognitive abnormalities associated with PTSD have received much interest because of their potential impact on day-to-day functioning (Kalechstein, Newton, & van Gorp, 2003; Machamer, Temkin, Fraser, Doctor, & Dikmen, 2005; Papero, Howe, & Reiss, 1992) and their potential to inform neurobiological conceptualizations of PTSD.

Neurocognitive performance is typically conceptualized across common domains. Within the PTSD literature, the most commonly examined domains include basic attentional processes (e.g., orientation to stimuli, maintaining focus), working memory (i.e., the ability to temporarily hold information in an accessible "buffer"), speed of information processing (i.e., the rate at which responses to cognitive tasks are executed), higher order "executive" cognitive processes such as mental flexibility and cognitive control (e.g., attentional control, or the ability to selectively attend to certain information, cognitive inhibition, or the ability to resist interference from extraneous information, and response inhibition, or the ability to prevent automatic responses), and learning and memory (i.e., ability to learn new information and retain

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https://doi.org/10.1016/j.cpr.2019.101747
Received 29 August 2018; Received in revised form 25 April 2019
Available online 13 June 2019
0272-7358/

and recall the information after a delay). Previous cross-sectional studies in both military veterans and civilians have demonstrated links between PTSD and neuropsychological deficits with robust evidence that PTSD is associated with neurocognitive deficits in the domains of learning and memory, attention, working memory, and executive functioning (for meta-analytic reviews, see Brewin, Kleiner, Vasterling, & Field, 2007; Johnsen & Asbjørnsen, 2008; Polak, Witteveen, Reitsma, & Olff, 2012; Scott et al., 2015). The Scott et al. (2015) meta-analysis examined a broad range of cognitive domains and found small to medium effect sizes (range, Cohen's $d = -0.29$ to -0.62) for PTSD as an independent variable, with the largest effects sizes in the domains of verbal learning (Cohen's $d = -0.62$), information processing speed (Cohen's $d = -0.59$), and attention/working memory (Cohen's $d = -0.50$), and slightly smaller effects sizes for verbal memory (Cohen's $d = -0.46$) and executive functioning (Cohen's $d = -0.45$). Effect sizes in this meta-analysis were also larger among treatment-seeking samples, potentially reflecting more severe PTSD.

Although the literature addressing PTSD and neurocognitive performance has increased dramatically over the past several decades, much remains unknown about the direction of causality. The directionality of relationships between PTSD and neurocognitive performance is relevant to the development and course of PTSD (e.g., whether neurocognitive skills exert a protective effect against trauma), neurocognitive conceptualizations of PTSD (e.g., Dual Representation Theory; Brewin, Dalgleish, & Joseph, 1996), expectations regarding functional impairment associated with PTSD, and, finally, the potential use of neurocognitive measures as an ancillary indicator of treatment response. The goal of the current review was to synthesize literatures that are potentially informative to causal pathways between PTSD and neurocognitive integrity. Because trauma exposure cannot ethically be manipulated, causality must be inferred from varying methodological approaches balanced in their strengths and weaknesses. Therefore, this review includes a range of methodologies from human clinical PTSD populations (e.g., naturalistic longitudinal cohort studies), human analogue studies, and preclinical animal studies that collectively inform causal direction.

Studies incorporating clinical samples were included if PTSD was diagnosed using structured clinical interview and/or if PTSD symptom severity was assessed with a validated psychometric questionnaire. In regards to neurocognitive outcomes, studies were included only if they incorporated performance-based measures of neurocognition derived from standardized neuropsychological tests or, within the context of experimental paradigms, objectively-measured cognitive processes. Because subjective cognitive impairment has been shown to diverge from performance-based measures of neurocognitive functioning (Schwert, Stohrer, Aschenbrenner, Weisbrod, & Schroder, 2018), particularly under conditions of emotional distress (e.g., Donnelly, Donnelly, Warner, Kittleson, & King, 2018; French, Lange, & Brikkell, 2014), self-reported neurocognition would not be as informative to the causal pathways of interest in this review.

Human studies using experimental paradigms further required measurement of emotional responses to analogue trauma (e.g., viewing of a traumatic film) or self-report of an emotionally distressing event and measures of PTSD-like behavior (e.g., self-report of intrusive thoughts). Clinical and experimental studies that included both emotionally neutral and emotionally relevant stimuli were included for review. Observational research on clinical populations included twin studies, longitudinal studies, retrospective studies using archival data, and cross-sectional studies. Additionally, we briefly review select animal studies that included repeated measurement of cognitive behaviors (e.g., learning) and PTSD-like behavior (e.g., reduced exploring in a maze) prior to and/or following exposure to a threat. Databases searched included PubMed and MedLine; bibliographies of all located articles were reviewed. Search terms included combinations of the following: *posttraumatic stress disorder, PTSD, cognitive impairment, cognitive functioning, neuropsychology, neurocognitive, longitudinal, animal model, twin*.

We review separately evidence for neurocognitive integrity as a potential moderator of the expression of PTSD following trauma and evidence of neurocognitive deficits as a consequence of PTSD. Prior to each of these sections, we introduce representative examples of relevant theoretical conceptualizations. Within each of the two major sections on causal directionality, we begin by reviewing studies using methodologies that provide experimental control of potential confounds but are conducted on non-clinical samples in which PTSD can only be approximated (i.e., animal, human analogue studies). Complementing these tightly controlled experimental studies, we then review findings from studies conducted on samples in which some subset of the sample is characterized by clinically significant PTSD, thus providing more naturalistic evidence for causal relationships between PTSD and neurocognition, progressing from cross-sectional (e.g., twin studies) and retrospective designs to prospective, longitudinal designs. For studies providing sufficient information, we include effect sizes to illustrate the degree of the relationship between PTSD and neurocognition in human clinical samples. We conclude with an integration of these literatures and considerations for future research and clinical implications.

2. Neurocognition as a risk/resilience factor for the development and subsequent course of PTSD

2.1. Theoretical conceptualizations

Theoretical conceptualizations of PTSD aim to account for PTSD symptomatology, the course of the disorder, and response to treatment (Gillihan, Cahill, & Foa, 2014). Neurocognitive processes such as memory and cognitive control have been a central focus of some conceptualizations. For example, Ehlers and Clark's cognitive theory of PTSD (Ehlers & Clark, 2000) emphasizes two reciprocal processes as underlying the sense of current threat associated with PTSD. Specifically, biased appraisals (i.e., thoughts and beliefs) about the traumatic event and its consequences contribute to selective recall of information that is consistent with the appraisals. Conversely, disorganized and fragmented trauma memories that are poorly integrated into other autobiographical memories contribute to negative appraisals of self. Similarly, emotion processing theory (Foa & Cahill, 2001) posits that a fragmented and disorganized trauma narrative contributes to the development of emotional representations that are easily triggered and lead to pathological emotional, behavioral, and cognitive reactions. Dual representation theory (Brewin et al., 1996; Brewin, Gregory, Lipton, & Burgess, 2010) holds that trauma memories are comprised by both sensory/perceptual and verbally accessible representations. When sensory/perceptual images are not properly contextualized with verbal narratives of the trauma, they may be involuntarily triggered and experienced as happening in the present (i.e., re-experiencing symptoms).

Cognitive control deficits are also thought to underlie certain PTSD symptoms. For example, Aupperle, Melrose, Stein, and Paulus (2012) suggest that persistent re-experiencing and hyperarousal symptoms following trauma exposure may be related to deficits in inhibitory and attentional control that make it more difficult for individuals to disengage from both internal (e.g., memories) and external (e.g., reminders) threatening stimuli. They further suggest that this difficulty in regulating responses to threatening stimuli may perpetuate the use of avoidance coping strategies and lead to heightened arousal and sense of threat.

Neurocognition may also indirectly influence the course of PTSD via its impact on coping mechanisms and treatment response. For example, certain coping strategies (e.g., cognitive reappraisal, problem solving, seeking social support) and treatment interventions (e.g., cognitive-behavioral interventions) rely in part on the individual's ability to recall the trauma memory, think flexibly, problem solve, and/or inhibit automatic responses to trauma triggers and other emotionally-relevant information. Illustrating this point, research in other populations (e.g., traumatic brain injury [TBI], schizophrenia, multiple sclerosis) suggests that poorer executive functioning and memory is related to decreased use of active, problem focused coping strategies and increased use of less adaptive avoidant and passive coping strategies (e.g., Krpan, Levine, Stuss, & Dawson, 2007; Rabinowitz & Arnett, 2009; Wilder-Willis, Shear, Steffen, & Borkin, 2002). In regards to PTSD treatment, in theory, cognitive-behavioral interventions require the ability to inhibit maladaptive thoughts, the flexibility to reappraise more constructively, and the capacity to overwrite associations between the trauma memory and intense negative emotions.

In sum, a number of PTSD conceptualizations have neurocognitive implications, yet the literature assessing the role of neurocognitive processes in PTSD onset and maintenance is still developing. In the following section, we review empirical literature implicating neurocognitive abilities as causal influences on PTSD.

2.2. Animal studies

A challenge in studying causal relationships between PTSD and neurocognition is that ethical limitations in human studies preclude experimental manipulation of trauma. Animal research can only approximate human trauma exposure, higher order thinking, and psychiatric symptoms, but nonetheless affords the opportunity to manipulate stress. Although, most animal research has examined learning, memory, and other neurocognitive processes as a consequence of stress exposure, a few studies have examined the influences of pre-exposure learning and memory on post-exposure behaviors. For example, in a rodent study of recognition memory and stress exposure, rats were exposed to a predatory threat model of PTSD; one week later the rats were rated as resilient if they spent any time exploring open arms of an elevated plus maze (i.e., areas of the maze with no walls) or PTSD-like if they did not explore the open arms, instead remaining in the arms of the plus maze that were contained by walls. The rats categorized as PTSD-like (i.e., those that displayed compromised exploratory behavior in the maze) exhibited higher pre-threat hippocampal-dependent deficits on a recognition memory test (Goswami, Samuel, Sierra, Cascardi, & Paré, 2012), suggesting that poorer explicit memory may increase risk for a maladaptive response to threat.

Ritov and Richter-Levin (2017) used a novel pharmacologic approach of administering the cognitive enhancing agent, methylphenidate, to rodents prior to encoding and consolidation of a threatening experience (i.e., underwater stress). Relative to the rodents that received no intervention, those administered methylphenidate exhibited attenuated pathological fear responses (i.e., more exploration in open arms of a maze that included reminders of the threating experience) one month later. Generalizability of animal studies to humans with PTSD is limited, in part by the inability of an animal with a less developed brain than humans to capture the complex emotional symptomatology that characterizes PTSD, as well as the inability to measure the full range of higher order neurocognitive functions inherent to humans. Nonetheless, the findings described in this section suggest that the examination of neurocognition as a moderator of the development and course of PTSD in humans requires further attention.

2.3. Human analogue studies

As with animal studies, human studies that manipulate analogue trauma have provided evidence of a causal link between PTSD and neurocognition, especially in regards to cognitive inhibitory and control processes. Studies have varied in the specific paradigms used and cognitive processes assessed but have generally converged in finding relationships between pre-exposure cognitive processes and post-exposure emotional responses. Specifically, studies have examined pre-exposure working memory, proactive interference, and retrieval suppression.

High working memory capacity (i.e., the ability to hold information in mind and manipulate it, even in the face of irrelevant information) has been associated with success in intentionally suppressing both non-personally-relevant thoughts (i.e., of a white bear) (Brewin & Beaton, 2002) as well as personally relevant, distressing thoughts in healthy participants (Brewin & Smart, 2005). Also relevant to cognitive control processes, the ability to resist proactive interference (i.e., the interference of previously relevant information on the learning of new information) just prior to viewing a stressful film has been associated with lower self-reported frequency of film-related intrusions and fewer self-reported attempts to avoid film-related cognitions in the 48 h following viewing of the film (Wessel, Overwijk, Verwoerd, & de Vrieze, 2008). Similarly, Verwoerd, Wessel, and de Jong (2009) found that resistance to proactive interference, but not response inhibition (i.e., ability to prevent automatic responses), was associated with fewer self-reported intrusive memories related to emotionally distressing life events experienced by the individual. Of note, these stressful life events were not formally assessed for meeting criteria for a traumatic stressor (as would be required for a diagnosis of PTSD), and the intrusive memories were not of clinically significant levels. The events, however, were rated of at least moderate intensity.

Further evidence that cognitive control may influence the development of PTSD symptoms comes from a study investigating the relationship between retrieval suppression (i.e., the ability to control retrieval of memories even when presented with reminders of the memory) and the frequency of intrusions and level of associated distress following viewing of a traumatic analogue film (Streb, Mecklinger, Anderson, Lass-Hennemann, & Michael, 2016). Prior to viewing the film, retrieval suppression was measured using a think/no-think task consisting of neutrally valenced word pairs. During the task, participants were repeatedly prompted with memory cues and were instructed to either retrieve the memory (“think”) or stop retrieval of the memory (“no-think”). After viewing the “traumatic” film, participants recorded intrusive memories from the film (defined as spontaneous involuntary memories, including pictures, thoughts, emotions, and noises) for five days using an electronic diary. On the sixth day, they rated their distress related to the film. There was no relationship between pre-film retrieval suppression and frequency of intrusive memories following the film, which the authors suggested may have been related to a lack of engagement in suppression given that the participants were not explicitly told to suppress memories of the film. However, there was an association between poorer pre-film retrieval suppression and increased self-reported distress related to intrusive memories from the film (Streb et al., 2016). Overall, the findings from human analogue studies suggest that individuals with more proficient cognitive control may be better able to manage their emotional/behavioral responses in stressful contexts. However, there are several limitations in generalizing these findings to clinical populations. First, the level of distress evoked in response to the stressors in these human analogue studies is not comparable in severity to the emotional reactions experienced by individuals who develop PTSD. Additionally, the relatively brief onset and duration of the reported distress in these analogue studies and the isolated stress exposure are not representative of the prolonged time course and complex nature of the stressors experienced by individuals with PTSD.

2.4. Retrospective studies using archival data

One approach to the investigation of pre-trauma neurocognitive risk factors for PTSD development in clinical samples has relied on archival data to estimate general intelligence (e.g., Army entrance exams). Findings from these studies generally suggest that higher pre-trauma estimates of intellectual functioning are associated with lower risk of developing PTSD following trauma exposure (Gale et al., 2008; Macklin et al., 1998). Such retrospective research has been extended by studies examining interactions between trauma severity and estimated pre-trauma intelligence, which have shown that higher pre-trauma intelligence may be protective in military veterans with low trauma exposure (as measured by a self-report of frequency of exposure to different combat-related events), but not in veterans with higher trauma exposure (Sørensen, Anderson, Karstoft, & Madsen, 2016; Thompson & Gottesman, 2008). The authors suggest that high levels of trauma may exhaust intellectual resources for coping, even among those with higher intellectual resources.

In contrast to findings indicating an interaction between trauma severity and pre-trauma intelligence estimates, Nissen et al. (2017) found in a sample of 9695 Danish Army personnel that a negative association between pre-deployment intelligence estimates and PTSD symptoms at six to eight months post-deployment remained when level of perceived war-zone stress (as well as military rank and social support) was taken into account. The association between intelligence and PTSD symptoms, however, was no longer significant after adjustment for pre-deployment education level. Studies using data from military entrance examinations have not consistently included pre-deployment education level; however, the findings of Nissen et al. (2017) stand in contrast to those of Sørensen et al. (2016), which indicated that inclusion of pre-deployment education as a covariate did not significantly attenuate the association between pre-deployment intellectual functioning and PTSD. It is possible that the discrepancy is accounted for by methodological differences, including that Nissen et al. (2017) assessed post-deployment PTSD at a relatively earlier time point (i.e., months vs. years post-deployment), which may not capture differences in individuals whose PTSD symptoms developed later, persisted beyond several months, or increased in severity over time. Additionally, Nissen et al. (2017) stratified their sample by level of perceived war stress, whereas, Sørensen et al. (2016) included war-zone stress as a continuous co-variate. The aforementioned retrospective studies highlight potential associations between PTSD in cohorts studied across multiple time points. For the purposes of this review these studies should be considered in the context of their limitations, particularly the limited ability of the researchers to include potentially confounding variables and specific measures of neurocognitive functioning that were not part of the original data collection.

2.5. Twin studies

Twin studies also provide evidence that pre-trauma neurocognitive integrity influences risk of PTSD development. In a sample of 2386 male, identical and fraternal twin Vietnam era veterans, those with the highest intelligence estimates were at 48% lower risk of developing PTSD. In addition, intelligence estimates were lowest for twin pairs in which both twins met criteria for PTSD, highest for twin pairs in which neither twin experienced PTSD, and intermediate for PTSD-discordant pairs (i.e., one twin was diagnosed with PTSD and the other was not). In PTSD-discordant identical twin pairs, PTSD- and non-PTSD diagnosed brothers demonstrated pre-trauma intelligence estimates comparable to each other and to intelligence estimates in PTSD concordant twin pairs. In contrast, in discordant fraternal twin pairs, PTSD-diagnosed members of the twin pairs had lower intelligence estimates than their non-PTSD-diagnosed co-twins. The results are consistent with lower intelligence representing a potential preexisting familial vulnerability for PTSD (Kremen et al., 2007).

In a smaller sample of identical twin pairs in which one twin served in combat (exposed) and the other twin did not (unexposed), combat veterans with PTSD and their unexposed co-twins without PTSD did not differ significantly in performance on neuropsychological measures of attention, verbal memory, and executive functioning (Gilbertson et al., 2006). Furthermore, the performance of the 19 PTSD discordant twin pairs was less proficient than that of the 24 non-PTSD twin pairs, suggesting that attention, verbal memory, and executive functioning proficiency may represent a familial protective factor against the development of PTSD (Cohen's $d = 0.77–1.11$). A similar study from the same cohort revealed that both twins in the PTSD discordant pairs demonstrated poorer allocentric spatial processing (i.e., the mental manipulation of spatial cues among distal environmental features) than non-PTSD twin pairs (Cohen's $d = 0.89$) (Gilbertson et al., 2007). Poorer performance on the task was also associated with lower hippocampal volume and greater PTSD symptom severity. The authors hypothesized that less proficient allocentric spatial processing may increase risk of PTSD by way of diminished processing of contextual information to aid in discrimination between threatening and non-threatening stimuli (Gilbertson et al., 2007). In addition to neurocognitive findings, studies using this twin cohort have revealed other familial vulnerabilities that may be indirectly related to neurocognitive integrity, including smaller hippocampal volume (Gilbertson et al., 2002), abnormal cavum septum pellucidum (May, Chen, Gilbertson, Shenton, & Pitman, 2004), and more neurological soft signs (i.e., subtle indices of neurologic dysfunction that are difficult to localize to specific brain regions) (Gurvits et al., 2006). Of note, in the absence of fraternal twin pairs, it is difficult to establish whether other shared environmental factors influenced pre-trauma neurocognitive functioning and subsequent development of PTSD symptoms.

2.6. Prospective longitudinal studies

Naturalistic cohort studies that captured neurocognitive performance soon after trauma exposure have demonstrated an association between immediate, post-exposure neurocognition and subsequent PTSD symptomatology. Bustamante, Mellman, David, and Fins (2001) evaluated neurocognition and PTSD symptomatology in 38 individuals during their initial hospitalization for traumatic injuries (excluding for the presence of alteration in awareness at the time of the injury, memory disturbance for the injury, and postconcussive symptoms following the injury) and again at a six-week follow-up. Poorer verbal learning ($r = -0.32$) and recall ($r = -0.42$) during the hospitalization was associated with increased PTSD severity at the six-week follow-up assessment, and the correlations remained moderate, even after controlling for PTSD severity assessed during hospitalization. Similarly, in a sample of 131 road traffic collision survivors with mild to moderate injuries (excluding "significant" head injuries), neuropsychological performance on measures of attention/processing speed ($r = -0.21$) and executive functioning ($r = 0.28$) approximately 10 days following the collision were associated with more severe PTSD symptoms at 3-month follow-up. Likewise, at 6-month follow-up, baseline performance on measures of attention/processing speed ($rs = 0.22$, -0.25, and -0.28), verbal learning ($r = -0.25$), and executive functioning ($r = 0.23$) were associated with more severe PTSD symptoms (Suliman, Stein, & Seedat, 2014).

Kleim and Ehlers (2008) investigated the specificity of autobiographical memory recall in 203 assault survivors two weeks following the trauma, at which point less specific (i.e., more overgeneral) autobiographical memory recall was associated with acute stress disorder. The majority of the sample ($N = 190$) completed a structured diagnostic interview six months following the assault, and less specific autobiographical memory at the two-week assessment was associated with chronic PTSD and major depression at 6-month follow-up ($R^2 = 0.29$). These relationships remained when pre-trauma depression was taken into account. Overgeneral memory was specifically related to greater rumination about the trauma and perceived permanent change (Kleim & Ehlers, 2008).

Cognitive flexibility (the ability to effectively switch between two concepts) has also been implicated in the development and course of symptoms of PTSD. In a sample of 181 trauma survivors (from car accidents, terrorist attacks, work accidents, home accidents, burns, physical assault, or large-scale disaster), better cognitive flexibility one month following trauma exposure was associated with less severe symptoms of PTSD (based on structured clinical interview) 13 months later; the correlation was moderate ($r = -0.39$) and remained significant after demographic factors and trauma severity were taken into account (Ben-Zion et al., 2018). In a different sample, the same authors investigated the effects of an early neurobehavioral intervention (i.e., a daily, 30-minute computerized training program targeting executive functions and emotional reactivity and regulation) on later PTSD symptoms. Compared with a control group that engaged in classic computer games, the intervention group demonstrated greater improvement in PTSD symptoms three months post-intervention (Ben-Zion et al., 2018); the effect size was moderate (Cohen's $d = 0.63$). Improvements in cognitive flexibility in the intervention group were significantly correlated with less severe PTSD symptoms ($r = -0.40$).

Evidence from prospective studies that assessed neurocognitive abilities prior to trauma exposure suggests that pre-exposure neurocognitive integrity also influences the development of PTSD following trauma. In a sample of 1599 civilian survivors of a large bushfire affecting much of the local population, Parslow and Jorm (2007) found that better performance on neuropsychological measures of verbal working memory, verbal recall, and information processing speed were associated with lower risk of PTSD re-experiencing and arousal symptoms at an 18-month follow-up assessment. The relationship between pre-trauma neurocognition and post-trauma PTSD symptoms remained when possible confounders, including depressive symptoms and extent of trauma exposure, were taken into account. Because pre-trauma symptoms of PTSD were not measured, however, it is unclear whether preexisting PTSD symptomatology, if present, influenced the findings (Parslow & Jorm, 2007).

In a sample of 46 trainee firefighters with no prior trauma history, Bryant, Sutherland, and Guthrie (2007) investigated the relationship between autobiographical memory prior to commencing active duty and the development of subsequent PTSD symptomatology four years later after exposure to multiple traumatic events. After adjusting for trauma history and pretrauma PTSD and depression symptoms, the production at pretrauma assessment of fewer specific autobiographical memories (i.e., memories of a particular event that occurred on a specific day) in response to positive emotional words was associated with more severe posttraumatic stress symptoms four years later ($R^2 = 0.28$) (Bryant et al., 2007). The authors posited that difficulty retrieving specific autobiographical memories impedes the ability to properly contextualize trauma memories in light of positive experiences from the past, thereby increasing vulnerability for PTSD.

Schäfer et al. (2016) prospectively investigated the association between pre-deployment attentional bias and post-deployment posttraumatic stress symptoms in a sample of 144 German soldiers who deployed to Afghanistan. Pre-deployment attention bias dynamics (i.e., attention bias towards and away from angry and happy faces with attention at times preferentially directed towards stimuli and at other times away from the stimuli) interacted with the number of traumatic events during deployment in predicting greater posttraumatic stress levels at post-deployment, above and beyond the influences of pre-deployment traumatic experiences and posttraumatic stress levels (standardized $B = 0.03$–0.05 for angry and happy faces respectively). The authors highlight that dysregulated attention bias varying towards and away from positive and negative emotionally arousing stimuli may predispose individuals to the development of posttraumatic symptoms following trauma exposure.

Finally, in a prospective longitudinal study of 668 US Army Soldiers who deployed to Iraq, Marx, Doron-Lamarca, Proctor, and Vasterling (2009) found that more proficient pre-deployment performance on a measure of immediate recall of visual information was associated with less severe post-deployment PTSD symptoms. This relationship was independent of the presence of pre-deployment PTSD and of combat intensity ($R^2 = 0.33$). Further, there was an interaction effect between pre-deployment recall measures and pre-deployment PTSD symptom severity such that pre-deployment visual immediate recall and verbal learning performances were more strongly related to post-deployment PTSD symptoms (i.e., better performances associated with less severe PTSD symptoms) in the context of more severe pre-deployment PTSD symptoms. Using an overlapping sample, Vasterling et al. (2018) examined both neurocognitive performance and PTSD symptomatology at a long-term follow-up assessment conducted more than five years after the initial deployment. Findings replicated the association between better pre-deployment visual learning performance and less severe post-deployment PTSD symptoms, but extended those of Marx et al. (2009) by also revealing a relationship between better visual learning and memory performance measured soon after return from deployment and less severe symptoms of PTSD over five years later (R^2 ranged from 0.21 to 0.41). These findings suggest that neurocognitive integrity may influence both the development of PTSD and its expression over time. As with the other methodologies reviewed, prospective longitudinal cohort designs are not without limitations. Of particular relevance for this review, the follow up period of the most of the studies described above is brief relative to the sometimes-chronic course of PTSD, and therefore, studies with additional data points over a longer follow-up period will be important to further inform the influence of neurocognition on the course of PTSD.

2.7. Treatment studies

Findings from the treatment literature provide indirect support that neurocognitive skills affect the course of PTSD via the ability to benefit from treatment. Within the treatment literature, more proficient pre-treatment performance on standardized neuropsychological measures of memory (e.g., word lists and stories) has been associated with better treatment response following group and individual cognitive behavioral therapies (Haaland, Sadek, Keller, & Castillo, 2016; Scott, Harb, Brownlow, Greene, & Gur, R.C.,& Ross, R.J., 2017; Wild & Gur, 2008). Although the treatment literature does not directly examine mechanisms by which memory influences treatment response, it could be speculated that memory is associated with both generic factors such as retention of session content, as well as intervention-specific factors such as the ability to effectively retrieve trauma memories and overwrite maladaptive emotional associations required by exposure-based interventions. In addition to memory, greater efficiency in inhibitory control as suggested by more circumscribed neural activation during a Go/No-Go task predicted better treatment outcomes following an eight-week cognitive behavioral therapy intervention (Falconer, Allen, Felmingham, Williams, & Bryant, 2013). However, consistent with other studies failing to find a relationship between behavioral indices of cognitive inhibition and treatment outcomes (Haaland et al., 2016; Scott et al., 2017), behavioral performance on the Go/No-Go task was not significantly associated with treatment outcomes.

3. Compromised neurocognitive integrity as a consequence of PTSD

3.1. Theoretical conceptualizations

Neurobiological conceptualizations of PTSD are relevant to understanding the potential effects of PTSD on neurocognition. The neurobiology of PTSD has been extensively studied using a range of approaches (e.g., neuroimaging techniques, blood assays) and center largely on conceptualizations of PTSD as a fear-based disorder (see Bremner, 2007 and Pitman et al., 2012 for review). For example, Pitman et al. (2012) suggest that when individuals with PTSD encounter strongly arousing threatening stimuli the amygdala becomes over activated, leading to increased neurotransmitter (i.e., dopamine, noradrenaline, and serotonin) output to the prefrontal cortex. As a result, the prefrontal cortex goes “off-line” and inhibition of the amygdala is reduced, thereby increasing fear learning. Of relevance to neurocognition, as Pitman et al. (2012) note, when the prefrontal cortex is offline, working memory is also disrupted, with downstream implications for neurocognitive processes that rely on the integrity of the prefrontal cortex (e.g., memory encoding and retrieval). Relatedly, Aupperle et al. (2012) propose that neurobiological resources in individuals with PTSD may be over-allocated to affective processing and associated regulation networks (i.e., amygdala and medial prefrontal cortex) and under-allocated to cognitive control networks (i.e., dorsolateral prefrontal cortex) leading to diminished neurocognitive integrity, specifically in information processing speed and executive functioning.

From a cognitive perspective, the cognitive burden of PTSD symptomatology may tax neurocognitive resources that might otherwise be allocated to attentional and memory processes. For example, attentional control theory (Eysenck, Derakshan, Santos, & Calvo, 2007) proposes that anxiety is associated with increased allocation of attention to threat-related stimuli. Because attention is thought to be relatively stimulus-driven, threat (i.e., fear) related stimuli reduce attentional allocation to other more neutral tasks requiring goal-directed attention. Extending this theory to PTSD, symptoms such as hypervigilance may be associated with increased allocation of attention towards threat-related stimuli, which might then interfere with initiating more complex or effortful cognitive processes such as implementing organizational strategies to facilitate learning and memory.

The study of neurocognitive changes associated with PTSD in humans is complicated due to the complexity of psychosocial premorbid factors (including premorbid neurocognitive factors), the varying characteristics of the traumatic experiences themselves, and the complexity of the human brain and associated emotional and neurocognitive processes. In the sections below, we review literature addressing neuropsychological decrements as a potential consequence of PTSD.

4. Influence of PTSD on neurocognitive functioning

4.1. Animal literature

Indirect evidence for the effects of PTSD on human neurocognition can be drawn from findings in the animal literature illustrating the neurobiological and behavioral effects of stress. For example, early animal studies demonstrated detrimental effects of acute stress on spatial memory in rodents (Luine, Villegas, Martinez, & McEwen, 1994) and spatial working memory in monkeys (Arnsten & Goldman-Rakic, 1998; Diamond, Fleshner, Ingersoll, & Rose, 1996). Relatedly, PTSD-like behavior in rodents following single prolonged stress exposure (i.e., exposure to several successive stressors) has been associated with fear learning and neuroanatomical changes to the hypothalamic-pituitary-adrenal axis (George et al., 2015; Yamamoto et al., 2008) and impaired mental flexibility (George et al., 2015). Goodman and McIntyre (2017) found that relative to control-rodents, those that underwent single prolonged stress exposure demonstrated poorer hippocampal-dependent spatial learning, but better dorsal lateral striatum-dependent response-learning in an elevated plus maze. The authors likened the latter finding to the development of habit-like avoidant responses (e.g., substance use) to threatening stimuli in humans following exposure to traumatic stressors (Goodman & McIntyre, 2017). As noted in our review of the animal literature providing evidence that neurocognition may moderate the development and course of PTSD, though the animal literature cannot fully address the complexities of human cognition and PTSD symptoms, it provides indirect evidence that traumatic stress exposure may lead to acquired alterations in neurobiology and neurocognition.

4.2. Human analogue studies

In contrast to the previously discussed findings from the human analogue literature showing that aspects of neurocognitive control may be a predisposing factor to PTSD symptomatology, findings from Schäfer, Zvielli, Höfler, Wittchen, and Bernstein (2018) suggest that attention bias to threat (i.e., a tendency for attention to be disproportionality directed towards or away from threatening stimuli relative to non-threatening or non-trauma related stimuli) develops only as a consequence of trauma exposure. A sample of 109 healthy participants were administered a test of attention bias (i.e., a dot-probe test using emotional, neutral, and trauma-related words) before watching a trauma analogue film. Following the film, participants kept a diary of intrusions for one week and at the end of the week were re-administered the test of attention bias. Intrusive thoughts related to the film in the week following viewing of the film were associated with dysregulated attention bias (i.e., biases both towards and away from threat-relevant stimuli) (Schäfer et al., 2018). In contrast, there was no relationship between pretrauma attention bias and posttraumatic intrusions. These findings suggest that dysregulated attention bias emerged as a result of the analogue-trauma exposure, the occurrence of posttraumatic intrusions, or a combination of the two. Given that the dot-probe test included words that were related specifically to the trauma film, it is unclear whether the act of keeping a diary about the intrusions influenced attention bias in addition to any effects of the film and related intrusions. Like the analogue studies providing support that neurocognitive integrity may moderate PTSD outcomes after trauma, the studies reviewed here are limited in their generalizability to the complex presentation of clinical populations, but nonetheless, suggest that reactions to certain emotional stimuli may lead to alterations in neurocognitive functioning.

4.3. Twin studies

Findings from studies investigating neurocognition and PTSD in twin samples have been more heavily weighted in support of neurocognition as a preexisting influence on PTSD. There is, however, evidence from twin studies incorporating neuroimaging of acquired neurobiological changes associated with PTSD symptomatology. For example, in a sample of 26 Vietnam-era identical twin pairs, the twins with PTSD, but not their combat unexposed co-twins, demonstrated diminished activation in the medial prefrontal cortex when imagining scripted stressful events relative to neutral events and the effect was large ($\eta^2 = 0.34$) (Dahlgren et al., 2018). Because diminished activation was unique to the twins with PTSD, findings were interpreted to suggest that reduced activation of the medial prefrontal cortex in the face of stress was an acquired characteristic of PTSD symptomatology. Furthermore, the pattern of diminished activation for stressful events was not observed in twin pairs in which one twin was combat exposed, but neither developed PTSD, suggesting that the diminished activation was not related to combat exposure alone (Dahlgren et al., 2018). These findings are indirectly related to neurocognitive integrity, as the medial prefrontal cortex is known to be involved in aspects of neurocognition including executive functioning (e.g., Yuan & Raz, 2014) and memory encoding and retrieval (e.g., Blumenfeld & Ranganath, 2007)

Kasai et al. (2008) investigated gray matter volume in a sample of 41 Vietnam-era identical twins in which one twin was combat exposed and the other was not. Combat exposed twins with PTSD showed volume reductions in the pregenual anterior cingulate cortex relative to their co-twins who were not combat-exposed and relative to twin pairs in which one twin was combat exposed but neither twin had PTSD. In keeping with twin studies showing altered neural activation associated with PTSD, these findings suggest that volumetric reductions are acquired following PTSD development and are not familial (as would be the case if the unexposed twins showed the reduction) or acquired following combat exposure alone (as would be the case if the combat exposed, non-PTSD twins showed the reductions). The involvement of the hippocampus and anterior cingulate cortex has indirect implications for aspects of neurocognition, including learning, memory, attention, and certain executive functions. However, as the authors note and as noted above, it is possible that the neurobiological and neurocognitive patterns observed in twins with PTSD in the aforementioned studies represent vulnerability factors that were acquired prior to trauma exposure due to non-shared experiences with their co-twins.

4.4. Longitudinal studies

Longitudinal studies have also provided evidence suggesting that PTSD may adversely affect neurocognition. Yehuda et al. (2006) investigated the relationship between implicit memory (i.e., word-stem completion) and explicit memory (i.e., recall of word-pairs and a word list) and PTSD symptomatology over the course of five years in 28 older-adult Holocaust survivors and 19 non-exposed controls. Relative to the non-exposed controls, Holocaust survivors with PTSD demonstrated significantly greater decline in learning of high-associate (i.e., moderately related) word pairs and a trend towards a decline in learning of low-associate (i.e., unrelated) word-pairs over the course of five years. Although the Holocaust survivors without PTSD performed better than those with PTSD on high-associate word learning at both time points, they demonstrated a rate of decline comparable to survivors with PTSD that was not seen in the non-exposed controls, suggesting a similar, but less severe risk for accelerated aging in individuals with trauma exposure who do not develop PTSD. Among Holocaust survivors whose PTSD symptoms decreased over time, learning and memory of a word-list improved and was mediated by attention performance (Yehuda et al., 2006). Taken together, these findings suggest that at least some of the adverse effects of PTSD on neurocognition may be reversible with alleviation of PTSD symptoms.

Using a similar approach, Samuelson et al. (2009) investigated PTSD symptoms and neurocognitive functioning in 47 Vietnam era veterans several decades after trauma exposure. Over the course of the almost three-year follow-up period, veterans with PTSD, unlike those without PTSD, exhibited a significant decline from their initial assessment in delayed visual memory for emotionally neutral stimuli (facial recognition and scene recall) that was not accounted for by increasing age or change in PTSD symptom severity. Compared to veterans without PTSD, those with PTSD demonstrated a significantly greater decline in delayed recognition memory for neutral faces (Samuelson et al., 2009). Whereas individuals without PTSD showed non-significant improvement on the task, there was a medium effect for the decline on this task in the PTSD group (Cohen's $d = -0.53$). Importantly, neurocognitive declines in veterans with PTSD were not explained by age, PTSD symptom severity, or PTSD chronicity, which led the authors to speculate that other historical factors (i.e., being triggered by the political climate around the time of the follow-up assessment) accounted for the declines observed in the PTSD group. Complementing these neuropsychological studies, neuroimaging findings have shown that veterans with worsening PTSD symptoms over the course of two years exhibited volume loss in the frontal lobes, temporal lobes, and brain stem (Cardenas et al., 2011). In contrast, volume loss was not shown in veterans with improving symptoms of PTSD over the course of two years or in veterans without PTSD.

Prospective research provides opportunity to examine the effects of the development of PTSD on neurocognition. As part of the US Army cohort study described earlier (Marx et al., 2009; Vasterling et al., 2018), in a sample of 760 Army Soldiers, more severe PTSD symptoms following deployment to Iraq were associated with less proficient simple reaction time (standardized $B = -0.11$) and learning (standardized $B = -0.09$) and recall (standardized $B = -0.11$) of digit-symbol pairs adjusted for pre-deployment performance (Vasterling et al., 2012). In an overlapping sample, 315 Iraq war veterans were evaluated an average of 7.6 years following return from deployment. Increases in PTSD symptoms from pre- to post- deployment were associated with less proficient recall of word-pairs and simple reaction time at post-deployment, even following adjustment for pre-deployment performance, TBI, and severity of combat exposure. Increases in PTSD symptoms from post-deployment to long-term follow-up were associated with less proficient scores on measures of visual learning and memory ($R^2 = 0.22$–0.31, respectively) and word-pair recall ($R^2 = 0.33$–0.42, respectively) at long-term follow-up (likewise adjusted for post-deployment performance, TBI, and severity of combat exposure) (Vasterling et al., 2018).

In a previously discussed sample of 1599 brushfire survivors, Parslow and Jorm (2007) found that the participants generally improved on neurocognitive measures (interpreted as practice effects). However, the individuals with more symptoms of re-experiencing and arousal as a result of the brushfire demonstrated significantly less improvement in immediate and delayed verbal memory from pre- to post-trauma assessment when compared to those without symptoms, suggesting that symptoms of PTSD may have interfered with verbal memory processes. Complementing findings from prospective research examining neurocognition as an outcome, Admon et al. (2013) found pre-to post-combat stress exposure decrements in hippocampal volume and reductions in connectivity between the hippocampus and the ventromedial prefrontal cortex (Admon et al., 2013). As with findings supporting neurocognitive functioning as vulnerability or protective factor in the development of PTSD, longer or additional follow-up periods, though difficult to achieve, would allow for a better understanding of the influence of PTSD on neurocognition over longer periods of time.

Treatment studies.

Investigations of neurocognition over the course of treatment for PTSD have provided indirect evidence that PTSD symptomatology influences neurocognitive integrity. For example, in a sample of 42 Operation Enduring Freedom/Operation Iraqi Freedom era female veterans with PTSD who completed 16 weeks of group psychotherapy (a combination of cognitive restructuring therapy, exposure therapy, and skills training), improvement in symptoms of PTSD at the end of treatment was associated with improvements on measures of cognitive inhibition and switching ($R^2 = 0.60$) (Haaland et al., 2016). There were no changes, however, on measures of working memory or wordlist learning and memory, suggesting that certain aspects of neurocognitive functioning may be more influenced by PTSD symptomatology than others. Nijdam, Martens, Reitsma, Gersons, and Olff (2018) found improvements on a broader range of neurocognitive tasks following trauma-focused treatment. In the context of a randomized controlled trial, 88 individuals with PTSD completed neuropsychological assessments at the outset of treatment (either brief eclectic psychotherapy or eye movement desensitization and reprocessing therapy) and 17 weeks following the start of treatment. Regardless of treatment approach, participants demonstrated significant small to moderate pre- to post-treatment improvements in verbal memory, information processing speed, and executive functioning (Cohen's $d = 0.16$–0.68). Furthermore, greater improvement in PTSD symptoms was associated with better performance on neuropsychological assessments of memory ($r = 0.32$–0.54) and executive functioning ($r = -0.29$– -0.46) (Nijdam et al., 2018). Consistent with these findings, following three months of trauma-focused treatment, a small sample of 15 women with PTSD demonstrated pre- to post-treatment improvements in cognitive flexibility/set-shifting (Cohen's $d = 0.59$) and organization/planning (Cohen's $d = 0.48$) (Walter, Palmieri, & Gunstad, 2010). Finally, pharmacological treatment with paroxetine has been associated with improved verbal declarative memory (Cohen's d ranged from 0.59 to 1.17 across studies) and increased hippocampal volume in individuals with positive treatment response (Fani et al., 2009; Vermetten, Vythilingam, Southwick, Charney, & Bremner, 2003).

As with the treatment literature showing potential influences of neurocognition on ability to benefit from treatment, these findings do not directly address mechanisms by which PTSD symptoms might influence neurocognition. Nonetheless, taken together with findings that word-list memory improves with reduction of PTSD symptoms (Yehuda et al., 2006), findings from the treatment literature suggest that some effects of PTSD on neurocognition may be reversible in the context of symptom improvement. Interestingly, findings from the neuroimaging literature suggest that these improvements in neurocognitive functioning may be accompanied by alterations in brain function. Specifically, there is evidence for increased activation in cognitive control networks (Felmingham et al., 2007; Roy, Costanzo, Blair, & Rizzo, 2014; Yang et al., 2018), decreased amygdala activation (Felmingham et al., 2007; Roy et al., 2014), and increased connectivity between the two (Shou et al., 2017) following cognitive behavioral interventions for PTSD.

5. Conclusions

Studies on the relationship between PTSD and neurocognition have varied in design and outcome, and there is evidence from distinct research methodologies that the relationship between PTSD and neurocognition is bidirectional. Consistent with cognitive theories of PTSD that emphasize the importance of adequate encoding of the trauma memory (Brewin et al., 1996; Brewin et al., 2010; Ehlers & Clark, 2000; Foa & Cahill, 2001), multiple studies have suggested that more proficient memory processes may be associated with reduced risk of developing PTSD and fewer PTSD symptoms following trauma exposure (Bryant et al., 2007; Bustamante et al., 2001; Gilbertson et al., 2006; Marx et al., 2009; Parslow & Jorm, 2007; Suliman et al., 2014; Vasterling et al., 2018). Furthermore, multiple human analogue studies (Brewin & Beaton, 2002; Brewin & Smart, 2005; Streb et al., 2016; Verwoerd et al., 2009; Wessel et al., 2008) and one prospective study using a clinical sample (Schäfer et al., 2016) have implicated cognitive control processes as potentially influencing PTSD symptomatology. The findings of these studies are in line with the model proposed by Aupperle et al. (2012) that emphasizes the role of cognitive control in the development and maintenance of hyperarousal and re-experiencing symptoms through difficulty disengaging from and inhibiting responses to triggering stimuli, and thereby potentially increasing engagement in avoidant coping strategies. Our review suggests that more general intelligence and other aspects of neurocognitive functioning (e.g., attention and executive functioning more broadly) may mitigate risk of PTSD. Finally, based on treatment studies, there is evidence that the integrity of memory processes in particular may influence PTSD symptoms via treatment response, although the mechanisms of action are as yet unknown. Although not addressed by the studies reviewed, it also is possible that cognitive functioning also influences PTSD symptoms through its indirect effects on risk and resilience factors such as coping, as has been demonstrated by studies in other clinical populations, including TBI, schizophrenia, and multiple sclerosis (Krpan et al., 2007; Rabinowitz & Arnett, 2009; Wilder-Willis et al., 2002).

Conversely, findings suggesting that PTSD erodes neurocognitive integrity and is associated with increased risk of cognitive decline are consistent with neurobiological conceptualizations of PTSD that emphasize altered neurobiology as a result of trauma and/or PTSD symptomatology (e.g., Pitman et al., 2012). There is evidence that attention and memory processes are vulnerable to the effects of PTSD (Parslow & Jorm, 2007; Samuelson et al., 2009; Schäfer et al., 2018; Vasterling et al., 2012; Vasterling et al., 2018; Yehuda et al., 2006). These neurocognitive findings are supported by findings of alterations in the frontal cortex, hippocampus, and associated networks over the course of PTSD (Admon et al., 2013; Cardenas et al., 2011; Dahlgren et al., 2018; Kasai et al., 2008). Attention and memory findings are also relevant to attentional control theory (Eysenck et al., 2007), which, when extended to PTSD, would suggest that allocation of attention towards threatening stimuli might interfere with other neurocognitive processes such as learning and memory.

We propose that the relationship between neurocognitive integrity and PTSD is not only bidirectional, but also functions as a feedback loop (see Fig. 1). For some, the cycle may begin at the time of trauma exposure or in the early stages following trauma exposure with certain neurocognitive skills serving as protective factors by facilitating adequate processing of the trauma, controlled retrieval of trauma memories, and/or ability to control emotional responses to trauma reminders and direct attention. For individuals who develop symptoms of PTSD, however, PTSD may erode neurocognitive integrity, which may then increase risk of maintenance or exacerbation of symptoms by removing such cognitive control mechanisms and/or impede recovery through its potential effects on coping mechanisms and ability to benefit maximally from treatment strategies. Importantly, however, there is evidence from the treatment literature that neurocognitive performance can improve with alleviation of symptoms of PTSD, which could potentially break the feedback loop and facilitate further recovery from PTSD symptoms PTSD through improved coping.

There are several considerations either not covered by our review or as yet to be included in the literature on PTSD and neurocognitive functioning. First, it is important to highlight that the current review and the model proposed in Fig. 1 does not include the multitude of factors that may exert influence on the development and course of PTSD (e.g., trauma characteristics, social support and other interpersonal resources). Conversely, PTSD can co-occur with other conditions that influence neurocognitive functioning (e.g., substance use disorders, TBI, mood disorders). Second, though beyond the scope of this review, the potential bidirectional influences of subjective cognitive complaints and PTSD symptomatology should also be taken into consideration as subjective cognitive complaints tend to diverge from objective cognitive performance in the context of emotional distress (e.g., Donnelly et al., 2018; French et al., 2014). Although cognitive complaints are likely often mechanistically distinct from neurocognitive performance, subjective concerns are clinically relevant. Finally, future research will benefit from methodologies that build upon the existing literature. For example, cross-lagged panel designs allow examination of how variables interact with each other over time in the context of observational research.

In summary, the findings from this review implicate a functionally- and biologically-relevant avenue through which the course of PTSD might be altered. Although neurocognition is one of but many factors that may affect and be affected by PTSD, the literature on neurocognitive performance and PTSD raises the possibility that enhancing neurocognitive skills may add to the compendium of tools used to increase resilience in trauma-exposed individuals, or those at high risk for trauma exposure. Findings from the animal literature raise the question of whether pre-trauma low doses of cognitive enhancing agents may be protective against PTSD in high risk groups, possibly through facilitating more adaptive encoding of the trauma (Ritov & Richter-Levin, 2017). Within the behavioral sphere, Cognitive rehabilitation may be incorporated into treatments for PTSD with the goal of improving treatment response. For example, SMART-CPT (Jak et al., 2015), in intervention aimed at comorbid TBI and PTSD, integrates cognitive processing therapy (Resick, Monson, & Chard, 2017) with features of cognitive rehabilitation, including instruction in compensatory strategies for attention, memory, and executive functioning, use of more concrete language, and simplified instructions and has been found to be associated with improvements in PTSD symptomatology, self-reported post-concussive symptoms, and improvements in neurocognitive performance at 3-months post-treatment (Jak et al., 2019). Though not directly addressed by Jak et al. (2019), it is possible that integration of cognitive rehabilitation strategies with first line PTSD interventions may not only improve neurocognitive functioning, but may also have implications for treatment response as individuals learn to compensate for neurocognitive difficulties that may affect their ability to respond to PTSD treatment. Finally, assessment of neurocognition may be a useful metric to evaluate the effectiveness of treatments and may be warranted as an indicator of potential functional impairment in patients with PTSD.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

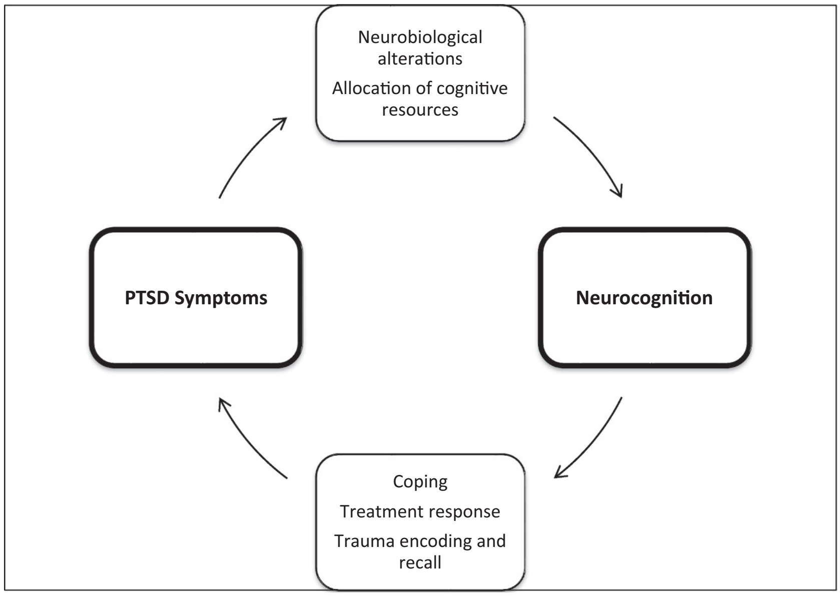

Fig. 1. Bidirectional feedback loop between PTSD and neurocognition, including potential mediators.

Declaration of Competing Interest

None.

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