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Invited review

# Executive function and PTSD: Disengaging from trauma

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ABSTRACT

Neuropsychological approaches represent an important avenue for identifying susceptibility and resiliency factors relating to the development and maintenance of posttraumatic stress disorder (PTSD) symptoms post-trauma. This review will summarize results from prospective longitudinal and retrospective cross-sectional studies investigating executive function associated with PTSD. This research points specifically towards subtle impairments in response inhibition and attention regulation that may predate trauma exposure, serve as risk factors for the development of PTSD, and relate to the severity of symptoms. These impairments may be exacerbated within emotional or trauma-related contexts, and may relate to dysfunction within dorsal prefrontal networks. A model is presented concerning how such impairments may contribute to the clinical profile of PTSD and lead to the use of alternative coping styles such as avoidance. Further neuropsychological research is needed to identify the effects of treatment on cognitive function and to potentially characterize mechanisms of current PTSD treatments. Knowledge gained from cognitive and neuroscientific research may prove valuable for informing the future development of novel, more effective, treatments for PTSD.

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"*The significant problems we face in life cannot be solved at the level of thinking that created them.*"
– *Albert Einstein*

## 1. Introduction

An estimated 50–60% of people will experience a serious trauma—as a result of combat, sexual assault, major accidents, or other real-life horrors—at some point in their lives (Kessler et al., 1995). However, only 5–10% of people are estimated to develop symptoms qualifying them for diagnosis of posttraumatic stress disorder (PTSD). This observation has led researchers to consider what factors other than the trauma itself may contribute to, or protect against, the development and maintenance of PTSD symptoms. Neuropsychological approaches may provide an important insight into susceptibility and resiliency factors by identifying pre-trauma cognitive functions that relate to subsequent development of PTSD as well as posttraumatic cognitive processes that may influence development or maintenance of the disorder. Finally, understanding these cognitive processes may provide new approaches for treatment to improve long-term outcomes of individuals with PTSD.

Although much of neuropsychological research in PTSD has focused on learning and memory, there has also been an accumulation of research examining potential "frontal lobe" or executive dysfunction. William James, in *The Principles of Psychology*, defined attention as "the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought" (James, 1890). He went on to say that "…It implies withdrawal from some things in order to deal effectively with others." In the modern world of neuropsychology and cognitive neuroscience, there are many disagreements about distinct and common definitions of attention, working memory, and executive function. For the purposes of this manuscript, we will focus on concepts that have been considered throughout the literature to be involved in maintaining successful "executive function", or the control of complex goal-directed behavior (Royall et al., 2002; Alvarez and Emory, 2006; McCabe et al., 2010). This includes 1) *attention*, or the voluntary allocation of processing resources or focusing of one's mind on a particular stimulus within the environment, 2) *working memory*, or the active maintenance and manipulation of information in one's mind over a short period of time, 3) *sustained attention*, or the maintenance of attention

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on one set of stimuli or a task for a prolonged period, 4) *inhibitory function*, involving the inhibition of automatic responses to maintain goal-directed behavior, 5) *flexibility/switching*, or the ability to switch between two different tasks or strategies, and 6) *planning*, or the ability to develop and implement strategic behaviors to obtain a future goal (Smith and Jonides 1999; McCabe et al., 2010; Carlson et al., 2005; Salthouse et al., 2003; Miyake and Shah 1999; Repovs and Baddeley, 2006).

We chose to focus on attentional and executive functions for the current review, rather than learning and memory, for two primary reasons. First, there have been several recent reviews summarizing findings related to learning and memory in PTSD—both in regards to neutral information as well as emotional information, such as with fear conditioning and extinction (Rubin et al., 2008; Johnsen and Asbjornsen, 2008; Moore, 2009). The second reason we chose to focus on executive and attentional functions is because recent research indicates that attentional modification programs may be beneficial in the treatment of anxiety disorders (Amir et al., 2009a; Li et al., 2008; Schmidt et al., 2009; Amir et al., 2009b; Najmi and Amir, 2010; Amir et al., 2008). This suggests that research related to attention and working memory function may not only increase our understanding of PTSD, but may also lead to more effective treatments for these patients.

The majority of neuropsychological research in PTSD uses cross-sectional designs from which it is impossible to determine whether any observed cognitive dysfunctions represent pre-trauma risk and resiliency factors or if they represent responses to the experience of trauma or PTSD. We therefore begin our review by discussing results from longitudinal and twin studies that may shed some light on this issue. We then synthesize results from cross-sectional studies concerning "frontal lobe" dysfunction associated with PTSD, focusing on simple attention and working memory, "higher-order" executive functions, flexibility, and inhibition, and the effects of emotional context on attention and executive function. The focus of this discussion will be on how difficulties regulating attention and inhibiting responses to stimuli (particularly emotional or trauma-related stimuli) could contribute to the clinical profile of PTSD—for example, leading to the development of alternative, potentially maladaptive, coping mechanisms. We will also discuss research concerning potential neural substrates of executive dysfunction, and the relationship between treatment and cognitive dysfunction, in PTSD. This review will not discuss the issue of comorbid disorders (e.g., traumatic brain injury, substance use disorders) and their potential influence on neurocognitive function in PTSD. We recognize the significant influence comorbid conditions can have on neurocognitive function and refer to recent articles focusing on this important and complex issue (Stein and McAllister, 2009; Samuelson et al., 2006).

## 2. Cognitive risk factors versus sequelae of PTSD

Although historically considered a controversial issue, research examining cognitive risk and resilience factors could be invaluable in understanding mechanisms for PTSD and in developing better preventive and treatment interventions. Lower IQ (often measured via military aptitude test performance) and educational achievement pre-trauma has been reported to relate to PTSD symptoms post-trauma (Gale et al., 2008; Macklin et al., 1998; Green et al., 1990; Pitman et al., 1991; Thompson and Gottesman, 2008; Vasterling et al., 2002). In most studies, the IQ range for individuals later developing PTSD, though lower than controls, is within the normal range. It has therefore been suggested that premorbid cognitive risk factors of PTSD may be relatively subtle, or relate to specific deficits in circumscribed areas measures that are difficult to ascertain retrospectively.

Recently, prospective longitudinal studies have been initiated, involving more fine-tuned assessment pre- and post- trauma (e.g., combat deployment). Parslow and Jorm (Parslow and Jorm, 2007) reported that pre-trauma performances on immediate and delayed verbal recall (California Verbal Learning Test [CVLT]) (Delis et al., 1988), working memory (digit span backward), visuomotor speed (Symbol Digit Modalities Test [SDMT]) (Smith, 1982), and verbal intelligence (National Adult Reading Test [NART]) (Nelson, 1982; Nelson and Willison, 1991) was negatively related to post-trauma PTSD re-experiencing and arousal symptoms. Marx et al. (Marx et al., 2009) conducted a similar study with veterans, and reported that pre-deployment visual immediate recall performance (Wechsler Memory Scale) (Wechsler, 1997b) was negatively related to PTSD symptoms post-deployment.

Twin studies also have the ability to highlight potential pre-trauma risk and resilience factors in PTSD (Kremen et al., 2007; Gilbertson et al., 2006). Gilbertson et al. examined neuropsychological functioning in combat-exposed individuals with and without PTSD and their high-risk and low-risk monozygotic twins. Measures of overall IQ, verbal memory (immediate and delayed recall), attention (digit span) (Wechsler, 1987), and executive function (Wisconsin Card-Sorting Test [WCST]) (Heaton, 1981) performance was decreased not only for the PTSD group, but also their twins, compared to the non-PTSD group and their twins. These results provide further support that lower pre-trauma cognitive functioning—particularly in domains of attention, executive function, and memory—may serve as a risk factor for the development of PTSD.

However, there is also evidence that pre-trauma cognitive function does not completely account for post-trauma cognitive deficits. Studies examining neuropsychological differences between individuals with and without PTSD have reported cognitive function (e.g., learning and memory) to correlate with PTSD severity above and beyond that accounted for by premorbid IQ (Vasterling et al., 2002; Gilbertson et al., 2001). It is likely there are both pre-trauma and acquired differences in cognitive function associated with PTSD. A decrease in specific cognitive functions pre-trauma may not only influence the development of PTSD, but may itself be exacerbated by the experience of trauma. The experience of trauma could cause subtle pre-trauma cognitive deficits to morph into more significant symptoms detectable not only during sensitive neuropsychological assessment, but also to patients as they try to function in their daily lives. Although cross-sectional neuropsychological studies do not provide insight into etiology, they provide important information concerning the resulting deficits associated with PTSD—which may relate not only to individuals' daily functioning and clinical symptoms, but also potentially to treatment outcome.

## 3. Attention, working memory, and executive function in PTSD

### 3.1. Attention and working memory

*Attention* and *working memory* are often measured using digit span, one-trial word recall (e.g., CVLT Trial 1), and spatial span (e.g., Crosi blocks) (Milner, 1971) tasks. These tasks require individuals to attend to a series of presented digits, words, or spatial locations and immediately recreate sequentially what was presented. Tasks such as digit span backward and letter-number sequencing (Wechsler, 1997a; Wechsler, 2008) require increased *working memory* load, as they involve greater manipulation of information held in one's mind. Decreased performance on measures of auditory attention and working memory have been found in combat- and sexual assault- related PTSD when compared to victims without PTSD and

non-trauma controls (Samuelson et al., 2006; Brandes et al., 2002; Gilbertson et al., 2001; Vasterling et al., 1998, 2002; Marmar et al., 2006; Lagarde et al., 2010; Gilbertson et al., 2001; Jenkins et al., 2000), and these deficits have been reported to correlate with PTSD symptom severity (Burriss et al., 2008). However, it should be noted that several studies have failed to identify auditory attention deficits in PTSD (Vasterling et al., 1998; Neylan et al., 2004; Samuelson et al., 2006; Leskin and White, 2007). Research has also failed to identify impairments in *visual* attention and working memory associated with PTSD (Samuelson et al., 2006; Jenkins et al., 2000). Therefore, it seems there is evidence, albeit inconsistent, that mild deficits in simple auditory attention and working memory may be one aspect of the cognitive profile of PTSD. However, it is unclear whether PTSD is associated with primary problems in attention and working memory, or whether the inconsistent findings are due to difficulties coping with and inhibiting unintentional "distracters", such as internal (e.g., emotions, cognitions) or external stimuli (e.g., environmental sounds and sights; stimuli presented in previous tasks).

### 3.2. Sustained attention and inhibitory functions

*Sustained or selective attention* is often measured via continuous performance tasks (CPT) (Loong, 1988; Conners, 1992), requiring individuals to attend to a long series of auditory or visual stimuli and respond (via a button press) when a target stimulus is presented. Studies have repeatedly found PTSD patients to exhibit impaired performance (e.g., increased omissions, commissions, or reaction time) in auditory and visual sustained attention (Vasterling et al., 1998; McFarlane et al., 1993; Wu et al., 2010; Shucard et al., 2008; Jenkins et al., 2000; Vasterling et al., 2002); except see (Golier et al., 1997), and the number of correct hits has been reported to negatively correlate with PTSD symptom severity (Vasterling et al., 2002). It should be noted that many studies using CPT tasks to assess performance in PTSD have reported increased errors of commission to distracter stimuli (Wu et al., 2010; Vasterling et al., 1998), suggesting difficulty with *inhibition* of automatic responses. Other measures requiring *inhibition* of responses include the go-nogo, stop-signal, and attention network (ANT) tasks (Shucard et al., 2008; Jenkins et al., 2000). Decreased inhibitory function has rather consistently been reported for PTSD (Falconer et al., 2008; Wu et al., 2010; Koso and Hansen 2006; Casada and Roache 2005; Shucard et al., 2008; Bressan et al., 2009; Jenkins et al., 2000; Leskin and White, 2007), and performance has been reported to relate to PTSD symptom severity (Falconer et al., 2008; Leskin and White, 2007). The color-word Stroop task examines response time to name the ink color of a color-related word (e.g., "red" printed in blue ink) and is also thought to be a measure of inhibitory function. Impaired performance on the color-word Stroop has been reported for various PTSD populations, though it is unclear whether such a deficit is specific to PTSD or a more general impairment across psychiatric disorders (Lagarde et al., 2010; Litz et al., 1996). Interestingly, several studies have also reported PTSD to be associated with increased intrusions during memory recall (Vasterling et al., 1998; Lindauer et al., 2006), which may reflect difficulty inhibiting related, but non-relevant internally-generated stimuli. Interestingly, Vasterling et al. (Vasterling et al., 1998) found the tendency to intrude information across various cognitive tasks (commissions on sustained attention and intrusions on memory measures) related to severity of re-experiencing and hyperarousal symptoms.

There seems to be growing evidence to support PTSD being associated with inhibitory dysfunction—through comparisons with control groups and correlations with symptom severity measures. Such inhibitory dysfunction may specifically relate to re-experiencing and hyperarousal symptoms. However, it is difficult to determine the directionality of this effect, given these studies rely primarily on cross-sectional designs. Heightened arousal and re-experiencing symptoms could create more distracters when an individual is attempting to concentrate on the task at hand, thereby interrupting working memory, sustained attention, and inhibitory functions. However, it is also possible that primary inhibitory dysfunction could result not only in decreased performance on cognitive tasks, but also impaired ability to inhibit emotional memories and physiological arousal in response to triggers.

### 3.3. Flexibility/switching and planning

The ability to shift between different tasks is an essential aspect of executive control. Classical measures of flexibility and switching include the Trail-Making Test (TMT, Partington and Leiter, 1949; Reynolds, 2002; Delis, et al 2001; Reitan, 1958), involving connection of "dots" while switching between letter and number (i.e., 1-A-2-B-3-C), and verbal fluency switching (as in the Delis-Kaplan Executive Function Scale [D-KEFS]) (Delis et al., 2001), involving the production of words while switching between two categories. Some studies with PTSD have reported impairment (e.g., increased time on TMT; decreased total words on fluency) on such tasks (Stein et al., 2002; Beckham et al., 1998; Jenkins et al., 2000), while others have not (Zalewski et al., 1994; Twamley et al., 2004, 2009; Lagarde et al., 2010; Barrett et al., 1996; Crowell et al., 2002; Gurvits et al., 1993; Leskin and White, 2007). Executive function measures involving the added dimensions of *planning* and strategy use include, among others, the Wisconsin Card-Sorting Test (WCST) (Heaton, 1981) and Tower of London Task (Simon, 1975; Shallice, 1982). For the most part, no consistent deficits on these measures have been reported (Vasterling et al., 1998; Lagarde et al., 2010). Although Kanagaratnam and Asbjornsen (Kanagaratnam and Asbjornsen, 2007) reported PTSD to be associated with increased number of trials to complete the first category of the WCST (indicating deficits in initial problem solving), they found no impairment on overall performance. A similar finding was reported by Twamley et al. (Twamley et al., 2009), who found PTSD to be associated with increased trials to complete the first category, but with increased overall learning efficiency. It can be argued that the WCST involves switching and flexibility similar to the Trail Making Test. However, tests such as TMT are timed and require quick attentional switching between pre-defined tasks. The WCST on the other hand is untimed and requires initial production of a strategy and subsequent switching of *strategies*—rather than flexibility and quick switching of *attention* (as with the TMT). Neuropsychological research therefore seems to provide inconsistent support for impairment in speed-reliant, attentional switching, but indicates that planning, rule-learning, and untimed strategy switching, may be mostly spared in PTSD.

### 3.4. Influence of emotional factors on executive function in PTSD

Although research examining "cognitive" and "emotional" aspects of learning in PTSD have traditionally been kept separate, it is clear these interact with one another and are intrinsically intertwined. Additionally, neural systems responsible for executive control within affective or neutral situations are most likely non-distinct and overlapping. Reflective of this, research has begun to examine cognitive function in PTSD when trauma-relevant, affective but trauma-irrelevant, or other highly-valued stimuli are involved.

PTSD has repeatedly been associated with attentional biases towards threat and negative emotional stimuli, as exhibited by

performance on the modified Stroop (Williams et al., 1996), which involves timed verbalization regarding the ink color of emotional and neutral words (Mathews and MacLeod, 1985), and dot-probe tasks (MacLeod et al., 1986), in which targets are displayed in locations closer to previously-presented trauma-relevant, generally negative, or neutral stimuli (Dalgleish et al., 2003; Foa et al., 1991; McNally et al., 1990; Chemtob et al., 1999; Mueller-Pfeiffer et al., 2010; Kimble et al., 2010); except see (Bremner et al., 2004; Kimble et al., 2009). Observed performance differences on these tasks could be due to either attentional facilitation involving *enhanced detection* of threat-relevant stimuli, or attentional interference involving *difficulty disengaging* from threat-related stimuli to focus attention on the task at hand. Recent studies suggest the bias may be most associated with attentional interference, indicating potential underlying dysfunction in disengagement and inhibition (Pineles et al., 2007, 2009).

Studies on PTSD have also examined the effects of symptom provocation prior to completion of a cognitive task (Jelinek et al., 2006, 2008). These studies corroborated previous neuropsychological findings of general working memory dysfunction in PTSD. However, results indicate that recall of emotional autobiographical events does not influence working memory function any more for PTSD patients than controls. Other studies have examined the effect of inserting emotional images into the working memory task as distractors (e.g., directly prior to number Stroop decisions or in between encoding and recall for working memory tasks). Results from these studies have been mixed, with one study reporting PTSD to be associated with worse detectability scores across working memory trials regardless of distractor type (neutral vs. trauma-related) (Morey et al., 2009), while another study reported PTSD patients to exhibit greater response latency for number Stroop after negative (versus positive or neutral) images as compared to trauma-exposed and non-trauma-exposed control groups (Mueller-Pfeiffer et al., 2010). These results suggest that the acute emotional state may not have an overwhelming effect on objective cognitive function in PTSD. Instead, these studies support the existence of underlying deficits in working memory that in some situations can be worsened by the inclusion of emotional distractor stimuli.

Decision making involves comparative valuation of potential choices and presented stimuli. Many decision making tasks (e.g., Iowa Gambling Task) have been proposed to involve not only rational input regarding the objective value of choices, but also an "emotional" or "somatic" input directing an individual towards one choice over another (Bechara et al., 2000, 2003). Decision making paradigms therefore offer a unique way of examining the influence of PTSD on functions involving affective input, valuation, and cognitive resources. Two studies have been conducted thus far to examine decision making in PTSD patients, both of which found PTSD to be associated with an increase in the number of trials needed to learn optimal patterns of responding (Sailer et al., 2008; Koenen et al., 2001). However, these tasks involve various components that, if disrupted, could account for the impairment observed in PTSD: 1) lack of motivation or reward-seeking, 2) impaired learning of response-outcome associations, or 3) lack of disengagement from a non-optimal response strategy. Further research is therefore needed to clarify these findings.

The most consistent finding in the emotional-cognition PTSD literature is on inhibitory tasks requiring quick, in-the-moment disengagement from emotional stimuli, as is involved in the emotional Stroop and dot-probe tasks. Increased hypervigilance towards threat-related materials may serve to enhance attention and reaction time to stimuli presented in the same locale. Recent evidence suggests that difficulty with subsequent *disengagement* from threat-related material may be a primary culprit influencing attention and executive dysfunction in PTSD. Obviously, if there was no initial hypervigilance towards threat, there would be no need to disengage. However, it may be possible to experience hypervigilance towards threat but retain the ability to disengage or regulate that attention. Potentially, the ability to disengage from even highly-valued stimuli could serve as a resiliency factor for preventing the development and maintenance of PTSD.

## 4. Neural correlates of attention and executive function in PTSD

Neuroimaging studies (using positron emission tomography [PET] or functional magnetic resonance imaging [fMRI]) in PTSD have primarily focused on symptom provocation or responses to trauma-related or emotional stimuli. These results have been discussed in recent reviews (Shin and Liberzon 2010; Liberzon and Sripada, 2008; Francati et al., 2007) and meta-analyses (Etkin and Wager, 2007) and suggest hyperactivation within limbic regions (particularly amygdala and insula) and hypoactivation of prefrontal regions, including anterior cingulate (ACC; including both rostral and dorsal) and ventromedial prefrontal cortex (vMPFC). A small collection of studies have been conducted to examine neural substrates of executive functions in PTSD. These studies have focused on 1) sustained attention using oddball tasks, 2) inhibitory functions using go-nogo, n-back, or continuous performance tasks, or 3) inhibitory functions during tasks involving emotional stimuli.

fMRI studies with healthy adults have shown that tasks requiring sustained attention activate medial PFC and ACC as well as parietal cortex (Kirino et al., 2000; Yamasaki et al., 2002; Fichtenholtz et al., 2004; Morey et al., 2008; Bledowski et al., 2010; Clark et al., 2000; McCarthy et al., 1997; Menon et al., 1997; Yoshiura et al., 1999), while those involving inhibitory functions activate areas of the inferior frontal cortex (IFC), lateral PFC (including ventrolateral [vlPFC] and dorsolateral [dlPFC]), and ventromedial or orbitofrontal cortex (OFC) (Aron et al., 2003; Garavan et al., 1999; Menon et al., 2001; Kiehl et al., 2000; Konishi et al., 1998; Liddle et al., 2001; Rubia et al., 1998; Bledowski et al., 2010). The lateral PFC specifically has been implicated in response inhibition—whether it be emotional or non-emotional contexts (Compton et al., 2003; Bledowski et al., 2010). However, the ACC may have some specialization in this regard, as more ventral regions are thought to be primarily involved in inhibition of responses to emotional stimuli, while more dorsal regions are thought to be involved in the inhibition of neutral information (Whalen et al., 1998; Bush et al., 1998; Mohanty et al., 2007; Yamasaki et al., 2002; Fichtenholtz et al., 2004).

PTSD has been associated with *increased* activation in dorsal ACC and other PFC regions during an auditory oddball task (Bryant et al., 2005). However, during the go-nogo task, PTSD patients exhibited *reduced* activation in the inferior frontal and ventral and dorsal lateral PFC, as well the medial OFC (Falconer et al., 2008). Activation in these areas was negatively correlated with PTSD symptom severity and rate of commission errors, suggesting that attenuated activations were not related to compensatory mechanisms but instead to the observed impairments in performance. Discrepancies between these two studies may be due to the varying degrees of working memory and inhibition required by the tasks. Along these lines, Moores et al. (Moores et al., 2008) used a task with conditions of working memory "maintenance" requiring subjects to maintain attention and respond to pre-specified target stimuli ("fixed target") and "updating" requiring subjects to respond to stimuli that matched that presented directly before it (i.e., 1-back task, "variable target"). Thus, the "updating" condition involved greater working memory load and inhibition of responses. For the updating condition, PTSD subjects had *decreased* activation in several PFC regions, including dlPFC, ACC, and inferior frontal cortex, as well

as the insula. During maintenance, there were no significant differences between groups, but there was a trend noted towards *increased* activation in lateral PFC, inferior frontal cortex, and insula. It therefore seems that PTSD may be associated with hyperactivation of prefrontal areas in response to simple sustained attention tasks, but relative hypoactivation during tasks involving inhibition or "updating". The former could reflect the hypervigilance and enhanced attention towards "triggers" associated with PTSD, while the latter could relate to decreased ability to control or inhibit these attentional resources. Alternatively, hyperactivation during sustained attention could reflect compensatory activation to maintain attention during more simple tasks, which hits a ceiling or breaks down as working memory load increases, thus failing to compensate further for more complex inhibition or "updating" tasks.

Studies involving the presentation of emotional "distracters" during working memory tasks have reported PTSD to be associated with increased activation in ventral PFC regions (e.g., ventromedial PFC) during processing of emotional distracters, but decreased activation in dorsal PFC regions (e.g., dorsal ACC, dlPFC) and parietal cortex (Morey et al., 2008, 2009; Pannu Hayes et al., 2009) during the working memory task itself. Similarly, PTSD has been associated with reduced medial PFC and rostral ACC activation during the emotional Stroop (Bremner, 2001; Shin et al., 2001). These results could be taken as support for an overactive ventral/limbic "emotional" processing stream that interferes with more dorsal prefrontal "cognitive" processing streams. However, a somewhat different interpretation could be that PTSD is associated with difficulties recruiting those regions necessary to disengage from highly-valued stimuli (e.g., dorsolateral PFC, dorsal ACC). PTSD may therefore relate to the combination of enhanced "emotional" processing networks that serve to enhance attention towards specific stimuli and decreased "inhibitory" networks meant to disengage attention and redirect it to the task at hand.

As discussed, decision making paradigms require not only attention and working memory, but also the integration of outcome valuations, and the inhibition of automatic responses (Hare et al., 2010; Kim and Lee, 2010). There is a rather extensive neuroimaging literature attempting to tease apart the various aspects of decision making and this literature primarily implicates regions of the PFC, including OFC, ACC, and dlPFC, as well as striatal systems (Rangel et al., 2008; Hare et al., 2010; Kim and Lee, 2010)—regions which have exhibited dysfunction in PTSD. Decision making paradigms therefore offer a useful framework for teasing apart PFC dysfunction in PTSD and other anxiety disorders (Aupperle and Paulus, 2010). However, there has only been one study that has used fMRI to investigate neural substrates of decision making in PTSD. Sailer et al. (Sailer et al., 2008) reported that PTSD patients were slower to learn an optimal response pattern during decision making, and also showed attenuated activation in the nucleus accumbens in response to reward. This suggests PTSD may be associated with dysfunction in reward system networks—which could contribute to decreased motivation and reward-seeking.

## 5. Treatment and cognitive function in PTSD

Cognitive processes may relate to treatment in a number of different ways. First, cognitive function may be used as a predictor of treatment outcome, or as a treatment outcome measure in and of itself. Second, cognitive factors may themselves be treatment targets to improve clinical symptoms. Thus far, there has been one study published to examine the predictive utility of cognitive function in the treatment of PTSD. Wild et al. (Wild and Gur, 2008) reported that performance on immediate recall for stories, above and beyond initial treatment severity and even attentional measures, significantly predicted improvement in symptoms after cognitive behavior therapy. Surprisingly, there have also been very few studies reporting the effects of PTSD treatment on neuropsychological function. Vermetten et al. (Vermetten et al., 2003) reported significant improvement on verbal memory after paroxetine treatment, but this study did not include a control group for comparison. Fani et al. (Fani et al., 2009) used a double-blind, placebo-controlled design and reported paroxetine treatment to be associated with a non-significant trend toward improved verbal declarative memory. Walter et al. (Walter et al., 2010) reported that trauma-focused therapy (e.g., cognitive processing therapy, prolonged exposure therapy), for a small group of women ($N = 10$), resulted in significant improvement on TMT number-letter switching and visual organization (Rey-Osterrieth Complex Figure task) (Osterrieth, 1944; Rey, 1941), with a trend towards overall improvement in executive function. Another study investigated the effects of psychotherapeutic treatment on emotional Stroop performance in PTSD and found no significant effects (Devineni et al., 2004). Due to the small number of studies using varied methodologies (e.g., medication vs. therapy; varying neuropsychological measures), it is difficult to reach any firm conclusions regarding PTSD treatment effects on neuropsychological function. Further research in this regard could be important in determining potential mechanisms of current treatments and whether such treatments are effective for both emotional and cognitive symptoms of PTSD.

A novel and interesting field of research has evolved concerning the use of attentional training itself as a treatment for anxiety disorders. This research uses a modified dot-probe paradigm to "train" individuals to respond faster to probes presented away from negative stimuli (MacLeod et al., 2002). Attention modification has been effective in reducing symptoms in social anxiety (Li et al., 2008; Schmidt et al., 2009; Amir et al., 2008), generalized anxiety (Amir et al., 2009b), and sub-clinical obsessive-compulsive disorder (Najmi and Amir, 2010). Such training is meant to contradict the automatic attentional bias towards threat observed in anxiety disorders and to facilitate attentional disengagement from threatening stimuli (Amir et al., 2008, 2009b). A recent fMRI study suggests that attention modification training may modulate lateral PFC and striatal activations during emotional working memory (Browning et al., 2010). A recent EEG study reported that attentional training in anxious individuals resulted in increased N2 amplitudes, thought to play a role in attentional control processes, and decreased P2 amplitudes, thought to be associated with emotional processing (Eldar and Bar-Haim, 2010). Thus far, there have been no published studies investigating effects of attention modification on PTSD symptoms or neural activation patterns. However, given the deficits in inhibitory and attentional functions observed in PTSD, this could be a promising area of research.

## 6. Discussion

Although PTSD does not have a substantial effect on general cognition, neuropsychological research provides evidence for subtle deficits concerning inhibition of automatic responses and the regulation of attention—in both emotional and non-emotional contexts (Falconer et al., 2008; Pineles et al., 2007, 2009; McNally et al., 1990; Kimble et al., 2010; Leskin and White, 2007). In particular, PTSD has been associated with difficulty disengaging attention from one stimulus to focus on more task-relevant stimuli (Pineles et al., 2007, 2009). Such impairment may be most evident when the "distractor" stimuli are of high value—either negative or even potentially, positive. One basic ability we have as humans is to assess the value of environmental stimuli and quickly orient attention towards stimuli as needed (e.g., through "bottom-up"

influences on attention). However, it is also important to be able to determine which stimuli are irrelevant or distracting to our current goals and disengage from those stimuli in order to orient towards those that are more goal-relevant (e.g., "top-down" regulation of attention)(Bishop, 2008). There is evidence that PTSD may be associated with enhanced activation in prefrontal networks during tasks involving non-flexible, sustained attention to a stimulus (e.g., as with the continuous performance task), but with attenuated activation of prefrontal networks on tasks requiring inhibition or flexibility in attention (Bryant et al., 2005; Falconer et al., 2008; Moores et al., 2008). This combination of neural response patterns in PTSD may relate to observed difficulties disengaging and reorienting attention to perform optimally on cognitive tasks, and may underlie at least part of the symptom profile in PTSD.

Additional prospective, longitudinal research is needed to determine whether or not inhibitory dysfunction is a pre-trauma risk and resiliency factor. However, given the pervasiveness of such dysfunction across both trauma-related (e.g., dot-probe or modified Stroop tasks) and neutral (e.g., Go-NoGo tasks) tasks, it is likely that subtle deficits in executive function pre-date the trauma and influence the development of PTSD. In particular, there may be a subtle pre-trauma deficit concerning disengagement of attention from stimuli or behaviors that are no longer relevant. This subtle deficit could be amplified when a task or situation involves highly-valued stimuli that increase the pull on attentional resources. When a trauma occurs, trauma-associated stimuli become very highly "valued"—thereby demanding greater attention and making it more difficult to disengage. In such situations, any disengagement or "switching" dysfunctions could be amplified to their extreme. Subtle deficits in inhibition and disengagement may not significantly influence daily functioning until a highly emotional or traumatic experience serves to perturbate the system. It is easy to imagine how such difficulties, when combined with a significant traumatic experience, could spiral in a way that influences the development of symptoms we label as PTSD. A chart representing how these difficulties could relate to the progression of PTSD symptoms is displayed in Fig. 1.

As documented in the literature, a high percentage of people experience symptoms of posttraumatic stress within the few weeks following trauma (Rothbaum et al., 1992; Shalev et al., 1998). Fortunately, these symptoms decrease over time for most, while for those with PTSD, symptoms remain and may even worsen with time (Orcutt et al., 2004). We therefore suggest that trauma exposure may be associated with increased attention towards trauma- or threat- related stimuli for most, if not all, individuals (Fig. 1b). However, only a subset of these individuals would have underlying deficits related to inhibition of responses (Fig. 1c) and disengagement of attention (Fig. 1e). Such deficits could contribute to development of pervasive re-experiencing and hyperarousal symptoms. Furthermore, when individuals have difficulty

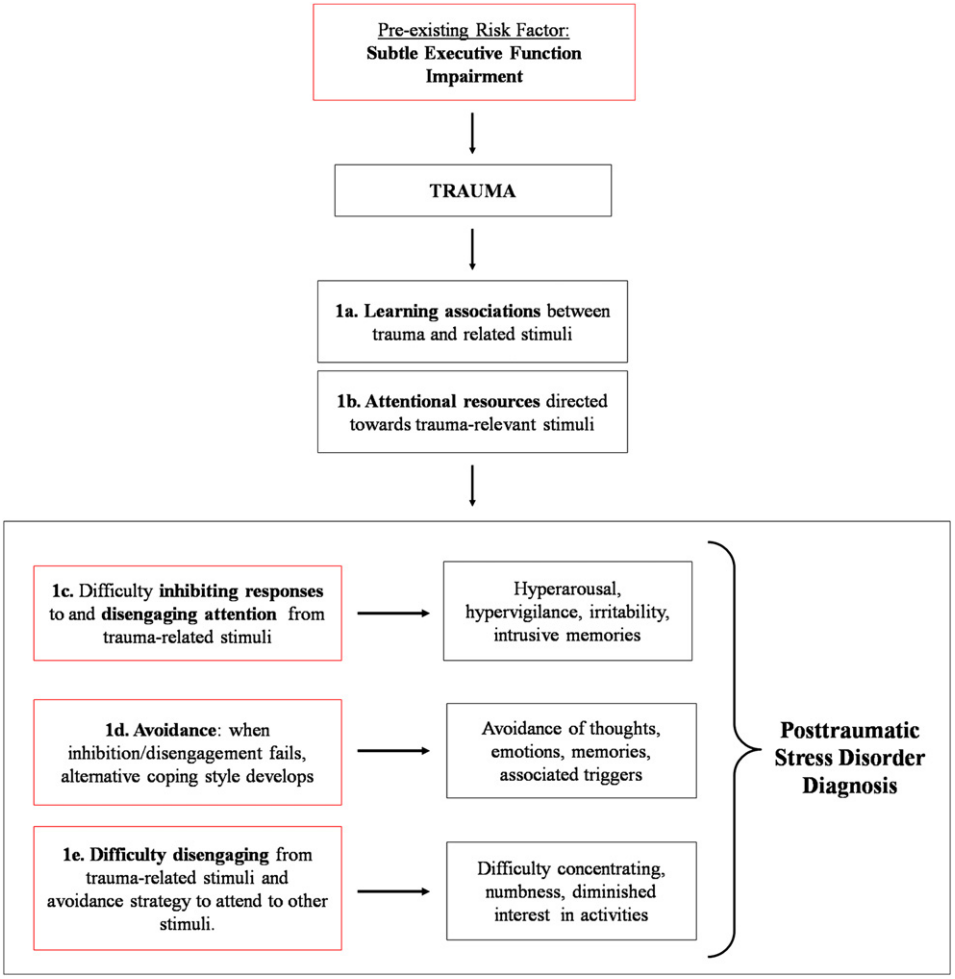


**Fig. 1.** Potential role of executive dysfunction in the development of PTSD. Most individuals experiencing a trauma may learn associations and direct attentional resources towards trauma-relevant stimuli (1a and 1b). However, subtle impairments in executive dysfunctions may relate to difficulties inhibiting responses and disengaging attention from trauma-related stimuli (1c and 1e) and lead to a reliance on avoidant coping strategies (1d), which contribute to the development of PTSD symptoms.

inhibiting responses to triggering stimuli, they may rely on other coping mechanisms—namely avoidance of arousing stimuli. In other words: if you can't inhibit it—avoid it (Fig. 1d).

Adoption of an avoidant coping strategy may be adaptive in the short term, as it decreases reliance on dysfunctional inhibitory and attentional networks. This coping strategy becomes a problem when avoiding emotional triggers also requires sacrifice of rewarding and positive aspects of a person's life. For example, a PTSD patient may avoid hospitals despite needing medical care in order to avoid smells or sights for which they have difficulty inhibiting emotional responses. Another PTSD patient may avoid previously-pleasurable activities (e.g., sports activities, family functions) due to crowds or other triggering stimuli. Persistent use of avoidance strategies keeps individuals from situations in which they could potentially learn to inhibit re-experiencing and hyper-arousal symptoms—thus helping maintain the disorder (Foa and Kozak, 1986). Difficulty disengaging from trauma-related stimuli and from adopted avoidant coping strategies, may also prevent individuals from attending to other aspects of their life—such as their family, friends, pleasurable activities, and positive emotions and cognitions in general. This in turn could contribute to the emotional numbness and depressive symptoms often experienced by PTSD patients.

One basic assumption of the most effective treatments for PTSD (e.g., Cognitive Processing Therapy and Prolonged Exposure) is that patients must decrease avoidant behaviors, habituate to triggering stimuli, learn that they can cope with strong emotions, and alter their cognitions and perceptions of the trauma, themselves, and the world in general (Foa and Kozak 1986; Foa et al., 2007; Resick and Schnicke, 1996). Such treatments disrupt avoidant coping styles and lead patients through experiences in which they can practice both habituation of emotion as well as inhibition and regulation of their automatic thoughts, feelings, and behaviors. Could treatments that more directly target inhibition, disengagement, and control of attention serve to benefit PTSD patients and decrease clinical symptoms? As discussed, there is evidence that training attention away from threat may help to reduce symptoms in other anxiety disorders. Given that between 20 and 50% of patients do not respond to current, first-line treatments for PTSD (Cukor et al., 2010; Schottenbauer et al., 2008), it is imperative that we direct *our* attentional resources towards the development and examination of such novel treatment strategies.

## 7. Conclusion

There is evidence for subtle deficits in attentional and inhibitory functions in PTSD that may predate trauma exposure, serve as risk factors for the development of PTSD, and relate to the severity of symptoms. We propose that such dysfunction could contribute to hypervigilance and arousal symptoms and the reliance on avoidant coping strategies, which are considered hallmark symptoms of PTSD. Further neuropsychological and neuroimaging research is needed to determine the exact nature of these deficits and the specific role they play in the etiology of the disorder. The use of attentional and inhibitory tasks within prospective, longitudinal studies could help in determining whether or not observed deficits are pre-trauma risk and resiliency factors. Additionally, the effect of current PTSD treatments on executive functions, as well as the effect of training in attention and inhibitory functions on PTSD symptoms, is of utmost importance. Neuropsychological, neuroimaging, and clinical research conducted thus far has led us to have specific, objective targets in sight on which treatments could potentially be aimed. It is hoped that by incorporating knowledge from cognitive and neuroscientific research, we can develop novel treatments that will allow us to more successfully treat those suffering from PTSD.

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