Cognitive abnormalities in post-traumatic stress disorder

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Characteristically arising in response to overwhelmingly terrifying events, post-traumatic stress disorder (PTSD) is a disorder of memory: sufferers seemingly relive their trauma in the form of involuntary recollection. Prominent cognitive abnormalities, especially in memory functioning, have motivated research designed to elucidate the mediating mechanisms that produce PTSD symptoms, especially those involving involuntary recollection. Recent developments suggest a pathophysiological model of PTSD which includes hyporesponsive prefrontal cortical regions and/or a hyperresponsive amygdala. Other work has also identified above-average cognitive ability as a protective factor and below-average hippocampal volume as a vulnerability factor for PTSD among the trauma-exposed. These attempts to elucidate the mediating mechanisms of PTSD have been both cognitive and, more recently, cognitive-neuroscientific in emphasis.

Introduction

Post-traumatic stress disorder (PTSD) is an anxiety disorder that develops usually in response to an overwhelmingly terrifying, often life-threatening event [1]. Symptoms include avoidance of reminders of the trauma, irritability, sleep disturbance, exaggerated startle, and emotional numbing. But its hallmark characteristic is the recurrent, involuntary recollection of the trauma in the form of intrusive thoughts, nightmares, and vivid sensory memories (‘flashbacks’). Rather than merely remembering it as an event from their past, PTSD sufferers seemingly relive the trauma with all its original emotional intensity [2].

Striking disturbances in cognition, especially memory, have prompted research on the cognitive mechanisms of PTSD. Early studies are reviewed elsewhere [3]; recent breakthroughs are reviewed here. The most important developments include phenomenological studies that have yielded clues about how traumatic experiences are represented in memory; the incorporation of neuroimaging methods into studies on intrusive cognition that have led to a model of the pathophysiology of PTSD; and studies convincingly showing that above-average cognitive ability serves as a resilience factor and that small hippocampi serve as a risk factor for PTSD among the trauma-exposed. Finally, cognitive science methods have been brought to bear on the most explosive issue in the trauma field: the debate regarding allegedly repressed and recovered memories of childhood sexual abuse (CSA) (see Box 1).

Phenomenological and meta-cognitive findings

Among sufferers of PTSD, memory for trauma can be expressed in different ways, and phenomenological research has provided clues to how memory for trauma is represented in memory [4]. For example, a person might experience repetitive, unwanted thoughts about the trauma, such as ‘Why did this thing happen to me?’, or experience intrusive memories of the trauma, such as vivid, sensory ‘snapshots’ of a horrific accident [5]. One study revealed that intrusive memories typically involved brief, visual flashbacks of stimuli that preceded the most terrifying aspect of the trauma rather than the most painful or distressing aspect of the experience per se [6]. Flashbacks, it seems, embody the antecedents – the ‘warning signals’ – that predicted the most worst part of the event. For example, one survivor of a head-on collision reported flashbacks of the headlights of the oncoming vehicle, not of the crash itself. Other work shows that flashbacks are more likely to involve certain sensory modalities than others. Visual flashbacks are most common, followed in frequency by bodily/kinesthetic (e.g. pains), auditory, olfactory, and gustatory ones [5].

Intrusive cognition about the trauma is expressible in language, and includes narrative descriptions of the trauma itself and meta-cognitive appraisal of the meaning of one’s acute PTSD symptoms. Although the sensory reexperiencings are especially dramatic features of PTSD, they are less frequent than intrusive thoughts about the trauma. A study of assault victims indicated that trauma memories are more disorganized among those with PTSD symptoms, and that the magnitude of disorganization predicts subsequent PTSD pathology [7]. Victims suffering PTSD symptoms did not exhibit disorganization when recounting a non-traumatic, control event dating from the time of the trauma. Early work on disorganized narrative memory for trauma did not incorporate control events, and disorganization itself appeared to be an artifact of limited verbal ability [8].

Meta-cognitive appraisal of one’s acute post-traumatic symptoms predicts whether one will develop chronic PTSD [9,10]. For example, if flashbacks are interpreted as harbingers of impending psychosynthesis, or if exaggerated startle reactions and nightmares are interpreted as signs
Traumatic dissociative amnesia theorists hold that the more emotionally distressing a trauma is, the more likely some victims will be unable to remember it, thanks to either repression or dissociation [54]. Unfortunately, these theorists often misconstrue the very studies they cite in support of the phenomenon. Common misconstruals include confusing everyday forgetfulness that develops after a trauma with an inability to remember the trauma itself; confusing a reluctance to disclose a trauma with an inability to remember it; confusing a failure encode every aspect of a traumatic experience with an inability to remember that one has been traumatized; and confusing not thinking about something for a long time with an inability to remember it [55].

These theorists propose that victims of childhood sexual abuse (CSA) often acquire an ability to dissociate their attention from inescapable abuse episodes, thereby attenuating the emotional impact of the experience, and rendering it difficult to recall many years later [56,57]. To test whether adults with CSA histories are characterized by heightened ability to disengage attention and forget threat cues, researchers have used directed forgetting procedures. One study involved three groups of subjects: women with CSA-related PTSD; women exposed to CSA, but without psychiatric illness; and nonabused control women [58]. They viewed a series of words on a computer screen that were either trauma-related (e.g. incest), positive (e.g. carefree), or neutral (e.g. banana). Each word was replaced with an instruction to forget or remember the word. After this encoding phase, subjects were told to recall as many words as possible, irrespective of instructions. The results revealed that subjects with PTSD did exhibit memory deficits, but only for positive and neutral words they had been told to remember. Contrary to the dissociation hypothesis, they remembered the trauma words all too well, including those they were supposed to forget.

Subsequent experiments have involved subjects who reported histories of having forgotten and then recovered their abuse memories, report never having forgotten their abuse, report no history of abuse, or who claim to harbor repressed memories of CSA that they still cannot recall. To test this hypothesis, researchers have conducted experiments involving either item-cuing directed forgetting (i.e., instruction to forget or remember follows each word) or block-cuing directed forgetting (i.e., the instructions occur after an entire block of words). In none of these experiments has any subject reporting CSA – either continuous, recovered, or repressed memories – exhibited heightened forgetting of trauma words [59–62].

of personal weakness, trauma victims are at heightened risk for failing to recover from the acute effects of trauma exposure. Although risk factor research typically entails identifying variables, pretrauma, that predict the onset of PTSD symptoms, work by Ehlers and her colleagues indicates that meta-cognitive appraisals of initial symptoms predicts the maintenance of PTSD.

Brewin [11] has suggested that memories associated with trauma are encoded in a dual-representation system: a verbally accessible one, and a situationally accessible one. The former can be accessed voluntarily, and mediates intrusive cognition about the trauma, whereas the latter mediates sensory relivings of the trauma itself, and is triggered involuntarily by cues reminiscent of those present during the experience (e.g. Ehlers’s ‘warning stimuli’).

Intrusive cognition and the emotional Stroop effect

Emotional Stroop studies have provided evidence consistent with complaints about intrusive, unwanted thoughts about trauma. Patients with PTSD, relative to trauma-exposed individuals without the disorder, take longer to name the colours of words related to their trauma (e.g. firefight) than to name the colours of other negative words (e.g. filthy), positive words (e.g. friendship), or neutral words (e.g. concrete) (e.g. [12]). Despite PTSD patients’ attempts to attend to word colour, the meanings of trauma words intrude, capturing attention, and slowing colour-naming.

With few studies [13], most studies have replicated this effect in subjects whose PTSD arose in response to diverse stressors (e.g. rape, disaster, combat) [14]. In a novel application of the paradigm, Buckley et al. [15] had professional actors attempt to simulate the effect after informing them how PTSD patients characteristically respond. The actors, however, exhibited slow overall colour-naming rather than just delayed colour-naming of trauma words. The authors concluded that the emotional Stroop could help discriminate genuine PTSD sufferers from those malingering the disorder. Concerns about individuals simulating PTSD to obtain financial compensation have been growing [16]. One extremely worrisome study revealed that 59 out of 100 men presenting with Vietnam-related PTSD decades later had no evidence of trauma exposure in their personnel files, and some of them had never served in Vietnam at all [17]. Yet nearly all had received the diagnosis of PTSD from assessing clinicians.

Neural mechanisms of the emotional Stroop effect

The neural mechanisms that mediate the emotional Stroop effect in PTSD have recently been illuminated by functional imaging studies. In a positron emission tomography (PET) study, Bremner et al. [18] found that women with sexual abuse-related PTSD, relative to victims without PTSD, exhibited less anterior cingulate activation during the emotional Stroop task. Anterior cingulate activation levels did not differ between the groups when they performed a standard Stroop task, thereby implying that the activation deficit was confined to processing trauma-related information.

Likewise, using functional magnetic resonance imaging (fMRI), Shin et al. [19] found that Vietnam veterans with war-related PTSD exhibited attenuated rostral anterior cingulate activation when exposed to trauma-relevant words in the emotional counting Stroop. In this task, participants view displays containing from one through four copies of a word that varies in emotional valence (e.g. firefight, firefight, firefight) and must press a key corresponding to the correct number (e.g. [3]). To the extent that the emotional meaning of the word captures attention, the participant will be slowed in counting the number of copies of the word on the screen.

Findings from emotional Stroop research support a pathophysiologic model of PTSD that highlights abnormalities in medial prefrontal cortex (PFC) and amygdala [20–22]. The medial PFC comprises anterior cingulate cortex (ACC), subcallosal cortex, and medial frontal gyrus. Its downward projections inhibit activation of amygdala; an intact medial PFC is essential for extinguishing conditioned fear [23]. Intrusive, distressing recollections of the trauma, accompanied by heightened physiologic
arousal, are consistent with either a hyper-responsive amygdala, a hypoactive medial PFC, or both [24].

**Evidence of prefrontal abnormalities**

In a recent fMRI study, Shin and her colleagues provided further evidence in support of this model [25]. They found that PTSD participants exhibited heightened amygdala responses (Figure 1a) and attenuated medial prefrontal cortex responses to pictures of fearful versus happy facial expressions (Figure 1b). Indeed, in the PTSD group, both signal changes in the amygdala and symptom severity were negatively correlated with signal changes in the medial prefrontal cortex (Figure 1c). Shin et al.’s study on exaggerated amygdalar responses to (supraliminal) fearful faces dovetails with previous work showing that briefly presented and backwardly masked fearful faces provoke heightened amygdalar responses in PTSD participants [22]. In further support of this model, PTSD patients exhibit diminished medial prefrontal/anterior cingulate activation while being exposed to trauma-related pictures [26], sounds [27], or traumatic imagery scripts [28] (Figure 2).

As Shin et al. [24] have emphasized, not only have researchers found reduced medial PFC activation in PTSD, but they have also found smaller ACC volumes in persons with PTSD relative to trauma-exposed individuals without the disorder [29–31]. Moreover, two of these studies revealed that the smaller the ACC volume, the worse the severity of PTSD symptoms [30,31]. In one study [30], most subjects had recovered from PTSD, thereby suggesting that smaller ACC volume constitutes either a preexisting vulnerability factor or a ‘scar’ from the disorder rather than a correlate of the illness itself.

**Neurocognitive impairment, cognitive ability, and PTSD**

In addition to experiencing intrusive recollection of traumatic experiences, PTSD sufferers often complain about difficulty concentrating and remembering things in everyday life. Although results have sometimes been inconsistent, it appears that many patients with PTSD do exhibit learning and memory deficits, mainly for verbal material [32]. In one of the most methodologically sound investigations, Gulf War veterans with PTSD, relative to healthy veterans, exhibited deficits on tests of sustained attention, working memory, initial learning, and retroactive interference [33]. Difficulty ignoring distracting information was positively correlated with self-reported severity of intrusive recollections of war trauma.

Rather than being either a toxic consequence of exposure to trauma or a consequence of PTSD itself, neurocognitive abnormalities might constitute risk factors for PTSD among those exposed to trauma. Neurological soft signs, including many datable to childhood (e.g. attention deficit problems, delays in learning to walk and talk), are twice as common among trauma-exposed people with PTSD than trauma-exposed people who did not develop the disorder [34]. Also, several studies have documented that lower scores on intelligence tests are associated with severity of PTSD symptoms, even when controlled for extent of trauma exposure [35,36]. A prospective longitudinal study of Vietnam veterans confirmed that lower intelligence, measured before deployment to the war zone, predicted severity of PTSD symptoms decades later, even when extent of combat exposure was controlled for [37]. Importantly, there was no significant correlation between severity of PTSD symptoms and change in measured intelligence, thereby showing that chronic PTSD itself does not lower IQ. Likewise, a prospective study from Israel also revealed that lower IQ was a risk factor for PTSD among those subsequently exposed to traumatic events [38].

**The role of IQ**

Is lower intelligence a risk factor for PTSD or is higher intelligence a resilience factor? Several studies now indicate that the latter is the case [37,39,40]. In all three
studies, the PTSD group scored in the average range on standardized IQ tests, whereas the trauma-exposed group without PTSD scored about a standard deviation above the mean. Breslau et al. [39] obtained IQ scores from six-year-old children from either inner city or suburban neighborhoods in the Detroit metropolitan area. They later assessed them at age 17 for exposure to trauma and PTSD. Youths whose IQ at age 6 was greater than 115 not only had decreased risk of exposure to traumatic events by age 17, but they also had lower risk of developing PTSD if they had been exposed to trauma. Because an IQ within one standard deviation above the mean did not confer significant protection against developing PTSD following trauma, Breslau et al. concluded that high IQ is protective.

**Twin studies**

Gilbertson et al. [40] administered a battery of IQ and other neurocognitive tests to monozygotic twin pairs. There were four groups: men who had been exposed to combat in Vietnam and who had developed PTSD; their identical co-twins who had not been exposed to combat and who did not have PTSD; men who had been exposed to combat in Vietnam, but did not have PTSD; their identical co-twins who had not been exposed to combat and who did not have PTSD. The findings were remarkably consistent: on nearly every test, combat veterans with PTSD performed in the normal range, as did their identical twin brothers. However, they consistently performed poorer than did combat veterans without PTSD, and their identical twin brothers. Test performance within twin pairs, regardless of trauma exposure, was remarkably similar. Taken together this important study suggests several conclusions. First, trauma exposure per se exerts little or no effect on IQ or on other measures of neurocognitive functioning. Second, because the non-exposed, healthy co-twins of the subjects with PTSD scored essentially the same on these tests, performance is best attributable to genes. Third, because the PTSD patients scored within the normal range on all but one test, one must conclude that elevated scores are protective. For example, the mean IQ in the PTSD group was 105, whereas the mean IQ in the healthy combat veteran group was 118. Moreover, over 40% of the healthy combat group had IQs in the superior range (over 120).

**Overgeneral autobiographical memory**

When asked to recall a specific personal memory in response to a cue word, such as happy, depressed individuals [41] and those who had recently attempted suicide [42] experience difficulty doing so. Unlike healthy control subjects who experience little difficulty remembering an episode from their past (e.g. ‘I was happy on the day we left for holiday last summer’), they retrieve ‘overgeneral’ memories that either reference an extended period longer than a single day (e.g. ‘I was happy during the summer after high school graduation’) or reference a category of event, but not a specific episode (e.g. ‘I am happy when I am playing tennis’). Difficulties recalling specific memories from one’s past predicts difficulty in recovering from depression [43] as well as deficits in problem-solving ability [44].

People exposed to trauma, especially those who develop PTSD, are often characterized by overgeneral autobiographical memory. In one study [45], Vietnam veterans with PTSD, relative to healthy veterans, exhibited difficulty retrieving specific autobiographical memories, a deficit exacerbated by exposure to a war-related videotape.

Other studies have emerged on overgeneral memory among trauma survivors [46]. Most studies have revealed an association between overgeneral memories and reports of early childhood trauma [47], whereas others have not [48]. An overgeneral mode of retrieval might serve an emotion-regulation function by enabling distressed individuals to avoid dwelling on disturbing events from their past [49].

**Hippocampal volume**

Although difficulty retrieving specific autobiographical memories could reflect a strategic attempt to regulate distress provoked by retrieval of disturbing memories, it might also indicate compromised integrity of the hippocampus, a structure integral to autobiographical memory. In fact, beginning with Bremner et al.’s [50] seminal study, many researchers have reported that individuals with PTSD have smaller hippocampi than do either non-trauma-exposed control subjects or trauma-exposed individuals without PTSD [51,52]. One hypothesis was that excessive release of the stress hormone cortisol either during exposure to extreme trauma or throughout the course of illness of those with PTSD might have neurotoxic effects, causing hippocampal atrophy. Skeptics, however, have stressed that the duration of exposure during acute trauma is too short to produce seemingly irreversible atrophy, and that most studies have shown that cortisol levels are in the low-normal range in people with chronic PTSD [2].

A landmark study by Gilbertson et al. [53] has shown that small hippocampi are very likely to constitute a vulnerability factor for developing PTSD among those exposed to trauma. This research group assessed hippocampal volume in monozygotic twin pairs: 17 pairs in
which one twin developed combat-related PTSD from serving in Vietnam and whose twin was healthy and had not seen combat, and 23 twin pairs in which one had seen combat in Vietnam, but had no PTSD, and whose twin had neither seen combat nor had PTSD. Replicating previous findings, Gilbertson et al. found that veterans with PTSD had smaller hippocampi than combat veterans with PTSD. However, the healthy, non-trauma-exposed co-twins of the subjects with PTSD had hippocampi that were just as small as those of their brothers. Not only do these findings imply that combat exposure does not produce hippocampal atrophy, they also indicate that small hippocampi might reflect a genetic (or at least constitutional) vulnerability for developing PTSD among the trauma-exposed.

Concluding remarks
Recent work has addressed the cognitive neuropsychiatry of PTSD from different angles and from multiple levels of analysis ranging from meta-cognitive appraisals of acute symptoms to volumetric analyses of specific brain regions implicated in symptom production. Participants in these studies, however, developed PTSD from diverse stressors (e.g. sexual abuse; combat), pointing to a likely source of heterogeneity in the findings (see Box 2).

Several general conclusions are suggested by this research, as well as questions for further work (see Box 2). First, intrusive recollection of traumatic events seem mediated by functional abnormalities in a brain circuit comprising amygdalar hyper-responsivity, prefrontal hyporesponsivity, or both. Emotional Stroop and neuroimaging studies provide data consistent with this model. Second, phenomenological research points to two representational formats underlying intrusive cognition, one reflecting memories about the trauma and one reflecting memories of the trauma. This distinction is especially important because memories about the trauma, including narrative disorganization and meta-cognitive appraisal of acute symptoms, are harbingers of the failure of symptoms to remit. Third, certain correlates of PTSD, ranging from verbal memory problems, relatively lower IQ, overgeneral memory, and small hippocampi could be vulnerability factors for PTSD among the trauma-exposed rather than either a direct consequence of exposure or a correlate of the illness itself. Moreover, not all of these factors are best characterized as true deficits. Indeed, IQ studies indicate that it is above-average intelligence counts as resilience or protective factor against PTSD among those exposed to trauma. As evident from this review, two major trends are emerging in the trauma field. Clinical researchers investigating information-processing abnormalities in PTSD have begun to shift their methodological focus from a purely cognitive one to a cognitive neuroscience one. They have also endeavored to discriminate between those abnormalities integral to the illness from those constituting preexisting vulnerability factors.

Box 2. The expanding domain of trauma
PTSD was originally conceptualized as a syndrome developing following exposure to horrific events lying outside the bounds of everyday experience. Canonical stressors included rape, combat, and imprisonment in a concentration camp. Yet in recent years, a ‘conceptual bracket creep’ in the definition of trauma has occurred whereby ordinary stressors are now deemed capable of causing PTSD [63]. The disorder is now being diagnosed among people whose stressor events range from exposure to sexually obnoxious jokes in the workplace [64] to giving birth to a healthy baby after an uncomplicated delivery [65]. One epidemiological survey [66] showed that nearly 90% of American adults qualify as trauma survivors – as trauma is currently defined. This development has direct implications for the cognitive neuropsychiatry of PTSD because the expanding definition of trauma threatens to undermine our chances of elucidating the psychobiological mechanisms that mediate the disorder. A survivor of a fender bender is unlikely to have much in common with a survivor of the Nazi Holocaust. Moreover, the more the concept of ‘traumatic stressor’ is broadened, the less plausibly we can assign causal significance to the stressor itself, and the more we must emphasize preexisting personal vulnerability factors. Yet shifting the causal burden away from the stressor undercut the very rationale for having a diagnosis of PTSD in the first place.

Box 3. Questions for further research
- Where, in the frontal—amygdalar circuit that apparently mediates intrusive PTSD symptoms, does the dysfunction lie? Does it predate exposure to trauma and the emergence of PTSD, or does it constitute vulnerability to the illness?
- How does elevated (verbal?) cognitive ability buffer trauma-exposed individuals against developing PTSD? Can the coping methods apparently used by these individuals be taught to others to foster resilience?
- What mechanisms mediate intrusive memory of the trauma versus intrusive memory about the trauma?
- Does the inciting trauma – childhood sexual abuse versus combat in adulthood, for example – make any difference to the cognitive neuropsychiatry of PTSD? Or does anyone qualifying for the diagnosis share the same pathophysiology, regardless of the triggering event?

References
1 Psychiatric Association (2000) Diagnostic and Statistical Manual of Mental Disorders (4th edn)