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The National Center for Post-Traumatic Stress Disorder

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PTSD AND NEUROCOGNITION

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"The hurricane...has added many new dimensions to our lives, and in some cases taken things away – like our short-term memories." From "Katrina Brain attacks McGehee," published in the online edition of the *New Orleans Time-Picayune* (NOLA.com 2/20/06).

Subjective complaints of cognitive impairment among those affected by exposure to severe stress are not an uncommon or particularly new phenomenon, as reflected by the integration of concentration, attention, and memory abnormalities into PTSD diagnostic criteria. In recent years, researchers have increasingly used performance-based neuropsychological tasks as objective measures of cognitive impairment in PTSD. Correspondingly, as outlined by Southwick et al. (2005), knowledge informing the neurobiological basis of PTSD has advanced tremendously. As we learn more about the brain and PTSD, a natural question arises: How do abnormalities in brain functioning present behaviorally following trauma exposure? As a "window" into brain-behavior relationships, neurocognitive research (i.e., the study of cognition as it applies to the brain) may be particularly well-suited to help address this question.

This issue of the *Research Quarterly* addresses memory deficits and other neurocognitive correlates of PTSD, emphasizing recent advances from human subjects research in which emotionally-neutral neurocognitive tasks were central to the methods. Informative reviews of related literatures addressing information-processing biases to emotionally relevant information in PTSD (Constans, 2005), animal models of stress and cognition (Arnsten, 1998), and functional neuroimaging (Rauch et al., 2006), as well as electrophysiological (Metzger et al., 2005) findings in PTSD, can be found elsewhere. McNally (2006) provides a conceptually integrative review of new advances from the PTSD neuroimaging, information processing, and neurocognitive literatures.

Which Neurocognitive Domains Are Affected in PTSD?

In their review of the earlier literature, Horner and Hamner (2002) revealed that learning, memory, attention, and intellectual functioning have been among the most commonly studied neurocognitive domains in PTSD samples, with learning and memory studies constituting the largest proportion of these studies. Memory, however, is not a unitary construct, and it appears that not all aspects of learning and memory are equally compromised in PTSD-diagnosed individuals. Vasterling and Brailey (2005) suggest that PTSD is characterized by relatively less proficient initial registration of information and heightened sensitivity to interference, whereas there is less consistent evidence of impairment in retaining information over time. As described by Isaac et al. (2006) in a review of the literature addressing PTSD and episodic memory, this distinction is important from the perspective of brain functioning. Whereas memory retention is more closely linked to hippocampal functioning, initial acquisition has been linked to the functional integrity of the prefrontal cortex, attention, and the ability to spontaneously utilize strategic processes.

Lindauer et al. (2005), for example, found that police officers with PTSD, as compared to those without PTSD, showed heightened sensitivity to interference and made more recall intrusions (i.e., recalled words not presented on the study list) but did not differ in memory retention. Hippocampal volumes were not associated with memory performance, suggesting that the types of errors police officers with PTSD diagnoses made on memory tasks were not attributable to hippocampal size.

As a longitudinal illustration of divergence across memory measures, Yehuda et al. (2006) compared elderly Holocaust survivors to elderly comparison participants on memory and PTSD symptom measures 5 years after their initial assessment. Whereas several measures from a list learning task improved over 5 years for Holocaust survivors, verbal paired associates learning continued to be relatively impaired among the survivor group. Interestingly, improvements in list learning were associated with PTSD symptom remission. In considering the divergence in longitudinal trajectories across measures among these aging trauma survivors, the authors speculate that memory processes may be differentially affected by accelerated aging versus PTSD in trauma survivors.

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Attention can also be broken down into more basic components (e.g., distractibility, mental tracking, vigilance) that appear to be differentially affected in PTSD. Vasterling et al. (1998; 2002) found that across two groups of war-zone veterans, veterans with PTSD displayed performance weaknesses relative to no-disorder comparison samples on tasks of working memory and sustained attention, but not on tasks of attentional shifting or selection of targets from an array. Jenkins et al. (2000) similarly found that certain aspects of attentional impairment (e.g., working memory) were associated with PTSD diagnosis in rape survivors, whereas other aspects of attentional performance (e.g., shift of attention) were not.

There is also considerable empirical evidence for associations between intellectual performance and PTSD, especially on tasks of verbal intellectual functioning. The verbal and visuo-spatial dissociation on intellectual tasks is particularly interesting in light of a similar pattern of relative verbal weaknesses on learning and memory tasks, pointing to potential functional brain asymmetries in the direction of relative hypoactivation of the left hemisphere. For example, Saigh et al. (2006) found that trauma-exposed youth with PTSD performed less proficiently on verbal, but not performance (more visuospatially-oriented) subtests of the Wechsler Intelligence Scale for Children-III. Further, trauma-exposed children without PTSD did not differ appreciably from non-exposed children, suggesting that performance decrements in the PTSD group were not simply a function of trauma exposure.

Examination of executive and other cognitive skills related to prefrontal functioning constitutes an emerging area of neurocognitive research in PTSD. The abilities to plan, organize, use strategies, and inhibit irrelevant or maladaptive thoughts and actions are critical to day-to-day function. Current neurobiological conceptualizations of PTSD emphasize diminished functioning of the prefrontal cortex, but the challenge will be to identify tasks sensitive to the subregions of the prefrontal cortex most involved in the neurobiology of PTSD. That is, many traditional clinical "prefrontal" neuropsychological tasks such as those assessing mental flexibility appear to be weighted to a specific region within the prefrontal cortex known as the dorsolateral prefrontal cortex, whereas neurobiological conceptualizations of PTSD emphasize the medial and orbital aspects of the prefrontal cortex.

Alternative approaches to the study of behavioral indicators of prefrontal functioning in PTSD may prove useful. Koenen et al. (2001) provide an example of the application of experimental paradigms drawn from comparative psychology. Using delayed response, delayed alternation, and delayed matching and non-matching to sample paradigms, these investigators made preliminary conclusions that disruptions exist in specific subregions of the prefrontal cortex among participants with PTSD. In an example of another approach to examining behavioral indicators of prefrontal functioning, Vasterling et al. (1998) used traditional neuropsychological tasks but included error analysis to document PTSD-related disruption of inhibitory functions across cognitive tasks.

PTSD and Cognitive Impairment: Cause or Consequence?

Debate continues about whether PTSD causes cognitive impairment, whether pre-exposure cognitive abilities influence PTSD expression following trauma exposure, or whether the relationship between cognitive functioning and PTSD is bidirectional. The answers will have implications for both the conceptualization of the disorder and the optimal timing of relevant interventions. Recent findings from twin studies, military training studies, and longitudinal designs collectively provide preliminary evidence of potentially bidirectional relationships in which a) pre-exposure neurocognitive functioning is predictive of PTSD following trauma exposure, and b) exposure to extreme stress leads to diminished neurocognitive performance.

Using twin methodology, Gilbertson and his colleagues (2006) provided persuasive evidence that pre-exposure cognitive functioning is predictive of the likelihood of developing PTSD following trauma exposure. The study compared the cognitive performance of two groups of twins: (1) pairs in which one twin was combat-exposed and had PTSD (PTSD pair) and (2) pairs in which one twin was combat-exposed and did not have PTSD (no-PTSD pair). The remaining twin in each pair (i.e., the "co-twin") was neither combat-exposed nor suffered PTSD. The findings revealed that both combat-exposed and non-exposed brothers in the PTSD pairs performed more poorly on tasks of intellectual functioning, verbal memory, and attention than did no-PTSD twin pairs. Thus, cognitive differences between PTSD and no-PTSD pairs appeared to be more strongly linked to familial factors than to PTSD or combat exposure. The twin findings are consistent with Macklin et al. (1998), who used archival data to demonstrate that pre-exposure intellectual performance was associated with increased PTSD symptom severity following combat exposure, and Bustamante et al. (2001), who found a relationship between less proficient verbal learning and memory performances shortly after trauma exposure and the subsequent development of PTSD.

Vasterling et al. (2006) took into account pre-exposure cognitive performances in a large prospective study of Army soldiers, and found that military deployment to Iraq was associated with performance disadvantages on measures of attention, learning, and memory, but with performance advantages in reaction time efficiency. Two recent studies indicated that the significant stress associated with special operations (Morgan et al., 2006) and simulated combat (Lieberman et al., 2005) resulted in pre- to post-training declines in cognitive performances. Although findings from this body of prospective work point to cognitive alterations as a consequence of stress exposure, because cognition was measured shortly after

stress exposure, these findings do not directly address whether neurocognitive changes are transient or chronic, or whether they will become associated with PTSD.

Specificity of Cognitive Deficits to PTSD?

Not all studies have revealed associations between PTSD diagnosis and cognitive performance. Perhaps the most compelling counterexamples are derived from the large Centers for Disease Control Vietnam Experiences Survey database (see Crowell et al., 2002, as the most recent example). Collectively, these studies suggested that (1) deficits in individuals with lifetime PTSD diagnoses differed little from psychiatric or non-psychiatric samples; (2) those with lifetime PTSD and comorbidities performed more poorly than those with lifetime PTSD alone or with no psychiatric disorders; and (3) there was little difference in cognitive performances among those with current PTSD, those with lifetime PTSD, a psychiatric comparison sample, and a non-psychiatric comparison sample. There was considerable sample and measurement overlap across these studies, however, suggesting that the findings are not independent.

There are several potential sources of cognitive dysfunction in PTSD samples, including motivational deficits, and psychiatric and somatic comorbidities. Few studies have directly addressed motivational factors as a potential etiology for neurocognitive dysfunction in PTSD, although Beckham et al. (1998) demonstrated that PTSD-related cognitive deficits remained when Vietnam veterans receiving disability compensation were excluded from relevant analyses. Similarly, Vasterling et al. (2006) excluded Iraq War veterans who performed below threshold on a motivational task. These findings, the failure in many studies to find generalized deficits (as might be expected with poor effort), and the correlations of cognitive performance with other neural indicators such as electrophysiological activation (e.g., Weber et al., 2005) and neuroimaging findings (Bremner, 2006) argue against a motivational etiology for PTSD-associated performance deficits.

Studies examining the contribution of psychiatric comorbidities to cognitive deficits in PTSD have provided mixed results. Because the underlying neurobiological substrates and symptoms of PTSD overlap somewhat with emotional disorders such as non-PTSD anxiety and depression, some overlap in the cognitive profiles might be expected. With high rates of alcohol use disorder comorbidity, the influence of alcohol toxicity on neuropsychological functioning in PTSD may be particularly relevant. Using a 4-group design (PTSD+/- by alcohol+/-) and controlling statistically for the effects of depression, Samuelson et al. (2006) found that although alcohol history was associated with visual memory performance, PTSD was associated independently of alcohol history and depression with verbal memory, attention, and processing speed. Increased risk of somatic illness associated with chronic stress and physical trauma at the time of the psychological trauma may also contribute to cognitive dysfunction (cf. Sutker et al., 1990).

Clinical Implications

Ultimately, the usefulness of research examining neurocognitive functioning in PTSD will be determined by how well findings are integrated into prevention and clinical care. Several conceptual models have embraced such integration. For example, Van der Kolk (2006) described how attention and memory impairments potentially facilitate unhealthy disengagement from the present. In a cognitive neuroscience model of PTSD with implications for psychological interventions, Brewin (2001) suggested that difficulty accessing semantic trauma memories may limit the extent to which the trauma can be processed and resolved. As shown by Vermetten et al. (2003), pharmacological treatment also potentially benefits both symptom alleviation and cognitive performance. Finally, considerably more work is warranted examining potential interactive effects of trauma exposure and development stage on neurocognitive functioning (cf. De Bellis & Kuchibhatla, 2006).

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ARNSTEN, A.F.T. (1998). **The biology of being frazzled.** *Science, 280,* 1711-1712.

METZGER, L.J., GILBERTSON, M.W., & ORR, S.P. (2005). **Electrophysiology of PTSD**. In J.J. Vasterling & C.R. Brewin (Eds.), *Neuropsychology of PTSD: Biological, cognitive, and clinical perspectives* (pp. 83-102). New York: Guilford Press.

RAUCH, S.L., SHIN, L.M., & PHELPS, E.A. (2006). **Neurocircuitry models of posttramatic stress disorder and extinction: Human neuroimaging research—past, present, and future.** *Biological Psychiatry, 60,* 376-382.

SELECTED ABSTRTACTS

GILBERTSON, M.W., PAULUS, L.A., WILLISTON, S.K., GURVITS, T.V., LASKO, N.B., PITMAN, R.K., & ORR, S.P. (2006). **Neurocognitive function in monozygotic twins discordant for combat exposure: Relationship to posttraumatic stress disorder.** *Journal of Abnormal Psychology, 115,* 484-495. Neuropsychological deficits have been reported among trauma survivors with PTSD. It is often assumed that these cognitive difficulties are toxic consequences of trauma exposure. Alternatively, they may reflect preexisting characteristics that contribute to the likelihood of developing PTSD. To address this possibility, the authors evaluated cognitive performance in monozygotic twin pairs who were discordant for combat exposure. Pairs were grouped according to whether the combat-exposed brother developed PTSD. The combat-unexposed co-twins of combat veterans with PTSD largely displayed the same performance as their brothers, which was significantly lower than that of non-PTSD combat veterans and their brothers. The results support the notion that specific domains of cognitive function may serve as premorbid risk or protective factors in PTSD.

HORNER, M.D., & HAMNER, M.B. (2002). **Neuroognitive functioning in posttraumatic stress disorder.** *Neuropsychology Review, 12,* 15-30. This paper reviews the literature on performance on neuropsychological tests among individuals with PTSD. Of 19 studies, 16 reported impairment of attention or immediate memory (or both); however, most of these studies included PTSD patients with psychiatric comorbidity, so that the extent to which the observed deficits are specifically attributable to PTSD remains unclear. Other potential confounds, including medical illness, substance abuse, and motivational factors, further preclude definitive conclusions at present. Results of structural and functional neuroimaging studies of PTSD are also summarized. Two studies have reported correlations between hippocampal volume and cognitive findings in PTSD patients; functional studies have indicated specific findings in limbic regions, although the relationship of these results to neuropsychological performance remains to be explored.

ISAAC, C.L., CUSHWAY, D., & JONES, G.V. (2006). **Is posttraumatic stress disorder associated with specific deficits in episodic memory?** *Clinical Psychology Review, 26,* 939-955. People with PTSD often report difficulties remembering day to day information unrelated to their traumatic episode. In addition, structural and functional imaging techniques have identified abnormalities in the brains of people with PTSD in regions known to be important for memory functioning. Nevertheless, studies investigating cognitive functioning in people with PTSD have reported widely varying results. The aim of this review is to investigate studies reporting performance on tests of episodic memory. Specifically, papers were examined in relation to the hypothesised memory functions of the frontal lobes, the hippocampus and the amygdala. It is concluded that while there is reasonable evidence of frontal lobe involvement, memory deficits caused by hippocampal involvement have been more difficult to detect. There are no published studies looking at the involvement of the amygdala although preliminary evidence suggests that people with PTSD do have memory deficits resulting from dysfunction of this structure. Reasons for the inconclusiveness of the results are discussed.

JENKINS, M.A., LANGLAIS, P.J., DELIS, D., & COHEN, R.A. (2000). **Attentional dysfunction associated with posttraumatic stress disorder among rape survivors.** *Clinical Neuropsychologist, 14,* 7-12. PTSD is characterized by subjective reports of decreased concentration and an inability to sustain attention. Some empirical validation of these symptoms has been demonstrated via reduced performance on attentional tests among war veterans with PTSD. However, the significance of such findings is unclear given high co-morbidity with other psychiatric, neurologic, and substance abuse disorders among veterans. The present study examined neuropsychological functioning among rape survivors with PTSD, a patient population with comparatively low rates of psychiatric co-morbidity. Rape survivors with PTSD (PTSD+; $n = 15$) were compared to rape survivors without PTSD (PTSD-; $n = 16$) and age- and education-matched non-traumatized controls (CTRL; $n = 16$) on tests of attention. Performance of the PTSD+ group was significantly worse than the other groups on measures of sustained and divided attention, but not on shifting of visuospatial selective attention. Performance differences were not attributable to co-morbid psychiatric disorders or substance abuse. The implications of these findings regarding the effects of trauma on attentional functions are discussed.

KOENEN, K.C., DRIVER, K.L., OSCAR-BERMAN, M., WOLFE, J., FOLSOM, S., HUANG, M.T., et al. (2001). **Measures of prefrontal system dysfunction in posttraumatic stress disorder.** *Brain and Cognition, 45,* 64-78. Clinical observations have suggested that individuals who have suffered traumatic stressful events exhibit disruption in abilities mediated by frontal brain systems. Therefore, this study employed tasks sensitive to frontal lobe dysfunction, including delayed response (DR), delayed alternation (DA), object alternation (OA), delayed matching-to-sample (DMTS), and delayed nonmatching-to-sample (DNMTS), with participants having PTSD. Compared to controls, the PTSD participants were unimpaired on DA and DMTS, but they showed deficits on DR, OA, and DNMTS tasks. This pattern of results suggests disruption of functioning in selective prefrontal brain systems. Results are discussed in the context of the neuropsychological features of PTSD. [adapted from abstract]

LINDAUER, R.J.L., GERSONS, B.P.R., VAN MEIJEL, E.P.M., BLOM, K., CARLIER, I.V.E., VRIJLANDT, I., et al. (2005). **Effects of brief eclectic psychotherapy in patients with posttraumatic stress disorder: Randomized clinical trial.** *Journal of Traumatic Stress, 18,* 205-212. Brief Eclectic Psychotherapy (BEP) is a manualized psychotherapy for PTSD which has proven effective for police officers. This article reports on a randomized clinical trial using BEP to treat other types of PTSD patients recruited from an outpatient clinic. Twenty-four patients were randomly assigned to a treatment or a waitlist group. Assessment of PTSD was made before and after the treatment period (4 months). No significant differences between the groups were observed at pretest. By posttest, BEP had effectively reduced PTSD as well as general anxiety symptoms in the treated group of outpatients as compared to the waitlist group.

MACKLIN, M.L., METZGER, L.J., LITZ, B.T., MCNALLY, R.J., LASKO, N.B., ORR, S.P., et al. (1998). **Lower precombat intelligence is a risk factor for posttraumatic stress disorder.** *Journal of Consulting and Clinical Psychology, 66,* 323-326. The authors examined the relation between intelligence and PTSD by studying the association among precombat intelligence, current intelligence, and self-reported PTSD symptoms. Military aptitude test results were obtained in 59 PTSD and 31 non-PTSD Vietnam combat veterans who had undergone a psycho-diagnostic interview and current intelligence testing. People with lower pre-combat intelligence were more likely to develop PTSD symptoms as assessed by the Clinician-Administered PTSD Scale even after adjustment for extent of combat exposure. The association between current intelligence and PTSD was no longer significant after adjusting for precombat intelligence. These results suggest that lower pretrauma intelligence increases risk for developing PTSD symptoms, not that PTSD lowers performance on intelligence tests.

MCNALLY, R.J. (2006). **Cognitive abnormalities in posttraumatic stress disorder.** *TRENDS in Cognitive Science, 10,* 271-277. Characteristically arising in response to overwhelmingly terrifying events, 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 hyper-re-

sponsive 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.

MORGAN, C.A., DORAN, A., STEFFIAN, G., HAZLETT, G., & SOUTHWICK, S.M. (2006). **Stress-induced deficits in working memory and visuo-constructive abilities in special operations soldiers.** *Biological Psychiatry, 60,* 722-729. Preclinical and clinical studies have shown that acute stress may impair working memory and visuo-spatial ability. This study was designed to clarify the nature of stress-induced cognitive deficits in soldiers and how such deficits may contribute to operational or battlefield errors. One hundred eighty-four Special Operations warfighters enrolled in Survival School completed pre-stress measures of dissociation and trauma exposure. Subjects were randomized to one of three assessment groups (Pre-stress, Stress, Post-stress) and were administered the Rey Ostereith Complex Figure (ROCF). All subjects completed post-stress measures of dissociation. ROCF copy and recall were normal in the Pre- and Post-stress groups. ROCF copy and recall were significantly impaired in the Stress Group. Stress group ROCF copy performance was piecemeal, and ROCF recall was impaired. Symptoms of dissociation were negatively associated with ROCF recall in the Stress Group. Baseline dissociation and history of traumatic stress predicted cognitive impairment during stress. Stress exposure impaired visuo-spatial capacity and working memory. A clearer understanding may assist in identification of soldiers at risk.

SAIGH, P.A., YASIK, A.E., OBERFIELD, R.A., HALAMANDARIS, P.V., & BREMNER, J.D. (2006). **The intellectual performance of traumatized children and adolescents with or without posttraumatic stress disorder.** *Journal of Abnormal Psychology, 115,* 332-340. This study compared the Wechsler Intelligence Scale for Children-III (WISC-III) scores of traumatized youth with PTSD to the scores of trauma-exposed and nonexposed comparison groups without PTSD. All groups were free of additional major childhood psychiatric disorders. The PTSD group scored significantly lower than the comparison groups on verbal subtests, but not on performance subtests. The scores of the trauma-exposed PTSD negatives and non-trauma exposed controls were not significantly different. Accordingly, PTSD and not a history of trauma exposure in the absence of PTSD was associated with lower verbal IQ.

SAMUELSON, K.W., NEYLAN, T.C., METZLER, T.J., LENOCI, M., ROTHLIND, J., HENN-HAASE, C., et al. (2006). **Neuropsychological functioning in posttraumatic stress disorder and alcohol abuse.** *Neuropsychology, 20,* 716-726. Studies have shown differences in neuropsychological functioning between groups with PTSD and control participants. Because individuals with PTSD often have a history of comorbid alcohol abuse, the extent to which an alcohol confound is responsible for these differences remains a concern. The current study compares neuropsychological testing scores in 4 groups of veterans with and without PTSD (PTSD+ and PTSD-, respectively) and with and without a history of alcohol abuse (ETOH+ and ETOH-, respectively): n for PTSD+/ETOH- = 30, n for PTSD+/ETOH- = 37, n for PTSD-/ETOH+ = 30, and n for PTSD-/ETOH- = 31. Results showed that PTSD, when alcohol, educational level, vocabulary, and depression are controlled for, was associated with decreased verbal memory, attention, and processing speed performance. Alcohol abuse history was associated with decreased visual memory performance. By controlling for alcohol and depression, the authors can more conclusively demonstrate that verbal memory and attention differences are associated with PTSD.

VASTERLING, J.J., & BRAILEY, K. (2005). **Neuropsychological findings in adults with PTSD.** In J.J. Vasterling & C.R. Brewin (Eds.), *Neuropsychology of PTSD: Biological, cognitive, and clinical perspectives* (pp. 178-207). New York: Guilford Press. This chapter focuses primarily on information derived from research examining performance on traditional neuropsychological tasks in adults diagnosed with PTSD. The literature is summarized according to functional categorizations common to neuropsychological practice, with emphasis on studies that both include comparison samples and report univariate or multivariate comparisons organized by functional domain. Findings are integrated into three possible frameworks relative to PTSD: (1) cognitive dysfunction as a byproduct of reduced motivation or poor concentration; (2) cognitive dysfunction as a feature of neurobiological abnormalities; and (3) neurocognitive integrity as a risk-resilience factor for the development and/or maintenance of PTSD. The chapter also addresses the specificity of neuropsychological abnormalities to PTSD and the potential influence of comorbid psychopathology, somatic factors, and medications on cognitive functioning. The authors conclude that aspects of attention and memory dependent on executive control appear to be especially vulnerable in PTSD and that the pattern of deficits is closely aligned with neural abnormalities involving brain regions subserving arousal and inhibitory functions.

VASTERLING, J.J., BRAILEY, K., CONSTANS, J.I., & SUTKER, P.B. (1998). **Attention and memory dysfunction in posttraumatic stress disorder.** *Neuropsychology, 12,* 125-133. Attention and memory performances were studied in Persian Gulf War veterans with and without PTSD diagnoses. Veterans diagnosed with PTSD showed relative performance deficiencies on tasks of sustained attention, mental manipulation, initial acquisition of information, and retroactive interference. Their performances were also characterized by errors of commission and intrusion. The tendency toward response disinhibition and intrusion on cognitive tasks was correlated positively with re-experiencing symptoms and negatively with avoidance-numbing symptoms. These cognitive deficit patterns are consistent with models of PTSD that emphasize the role of hyperarousal and implicate dysfunction of frontal-subcortical systems. Results suggest that intrusion of traumatic memories in PTSD may not be limited to trauma-related cognitions but instead reflects a more general pattern of disinhibition.

VASTERLING, J.J, PROCTOR, S.P., AMOROSO, P., KANE, R., HEEREN, T., & WHITE, R.F. (2006). **Neuropsychological outcomes of Army personnel following deployment to the Iraq war.** *Journal of the American Medical Association, 296,* 519-529. The Neurocognition Deployment Health Study [NDHS], is a prospective, cohort-controlled study conducted at military installations. This report centers on 961 male and female active-duty Army soldiers drawn from the larger cohort. Deploying Army soldiers (n = 654) were examined prior to deployment to Iraq (April-December 2003) and shortly after return (within a mean of 73 days [median, 75 days]; January-May 2005) from Iraq deployment. A comparison group of soldiers (n = 307)

similar in military characteristics but not deploying overseas during the study was assessed in sessions timed to be as close as possible to the assessment of deployers. Military unit sampling procedures facilitated representation of combat, combat support, and combat service support functions among both deployers and nondeployers. Estimates for the absolute differences in adjusted mean outcome scores between deployed and nondeployed groups were determined using generalized estimating equations. Multiple linear regression analyses adjusted for battalion membership revealed that Iraq deployment, compared with nondeployment, was associated with neuropsychological compromise on tasks of sustained attention, verbal learning, and visual-spatial memory. Iraq deployment was also associated with increased negative state affect on measures of confusion and tension. In contrast, deployment was associated with improved simple reaction time. Deployment effects remained statistically significant after taking into account deployment-related head injury and stress and depression symptoms. Deployment to Iraq is associated with increased risk of neuropsychological compromise. Findings point to the need to investigate further the impact of deployment on neural functioning. Public health implications include consideration of neuropsychological compromise in health prevention and postdeployment clinical and occupational management. [adapted from abstract]

VERMETTEN, E., VYTHILINGAM, M., SOUTHWICK, S.M., CHARNEY, D.S., & BREMNER, J.D. (2003). **Long-term treatment with paroxetine increases verbal declarative memory and hippocampal volume in posttraumatic stress disorder.** *Biological Psychiatry, 54,* 693-702. Studies in patients with PTSD found deficits in hippocampal-based declarative verbal memory and smaller hippocampal volume, as measured with magnetic resonance imaging (MRI). Recent preclinical evidence has shown that selective serotonin reuptake inhibitors promote neurogenesis and reverse the effects of stress on hippocampal atrophy. This study assessed the effects of long-term treatment with paroxetine on hippocampal volume and declarative memory performance in PTSD. Declarative memory was assessed with the Wechsler Memory Scale-Revised and Selective Reminding Test before and after 9-12 months of treatment with paroxetine in PTSD. Hippocampal volume was measured with MRI. Of the 28 patients who started the protocol, 23 completed the full course of treatment and neuropsychological testing. Twenty patients were able to complete MRI imaging. Patients with PTSD showed a significant improvement in PTSD symptoms with treatment. Treatment resulted in significant improvements in verbal declarative memory and a 4.6% increase in mean hippocampal volume. These findings suggest that long-term treatment with paroxetine is associated with improvement of verbal declarative memory deficits and an increase in hippocampal volume in PTSD. [adapted from abstract]

WEBER, D.L., CLARK, C.R., MCFARLANE, A.C., MOORES, K.A., MORRIS, P., & EGAN, G.F. (2005). **Abnormal frontal and parietal activity during working memory updating in posttraumatic stress disorder.** *Psychiatry Research: Neuroimaging, 140,* 27-44. This study used event-related potentials (ERPs) to investigate the timing and scalp topography of working memory in PTSD. This study was designed to investigate ERPs associated with a specific working memory updating process. ERPs were recorded from 10 patients and 10 controls during two visual tasks where (a) targets were a specific word or (b) targets were consecutive matching words. In the first task, nontarget words are not retained in working memory. In the second task, as in delay-match-to-sample tasks, a non-target word defines a new target identity, so these words are retained in working memory. This working memory updating process was related to large positive ERPs over frontal and parietal areas at 400–800 ms, which were smaller in PTSD. Estimation of cortical source activity indicated abnormal patterns of frontal and parietal activity in PTSD, which were also observed in regional cerebral blood flow [Clark, C.R., McFarlane, A.C., Morris, P., Weber, D.L., Sonkkilla, C., Shaw, M., Marcina, J., Tochon-Danguy, H., Egan, G., 2003. Cerebral function in posttraumatic stress disorder during verbal working memory updating: a positron emission tomography study. *Biological Psychiatry 53,* 474–481]. Frontal and parietal cortex are known to be involved in distributed networks for working memory processes, interacting with medial temporal areas during episodic memory processes. Abnormal function in these brain networks helps to explain everyday concentration and memory difficulties in PTSD.

YEHUDA, R., TISCHLER, L., GOLIER, J.A., GROSSMAN, R., BRAND, S.R., KAUFMAN, S., et al. (2006). **Longitudinal assessment of cognitive performance in Holocaust survivors with and without PTSD.** *Biological Psychiatry, 60,* 714-721. There are currently no longitudinal studies of cognitive performance in older patients with PTSD. It is unclear whether relationships between memory and symptoms differ over time among older persons with and without PTSD. Twenty-eight Holocaust survivors and 19 comparison subjects were evaluated 5 years after they had received a memory assessment including paired-associates learning and the California Verbal Learning Test (CVLT). While Holocaust survivors with PTSD showed a diminution in symptom severity, they still manifested a decline in paired associates learning, suggesting an acceleration in age-related memory impairment. The survivors with PTSD showed improvements on several CVLT measures over time. These improvements correlated with symptom improvements, such that group differences at the follow-up were no longer detected. The discrepancy in the pattern of performance on these two tests of memory following symptom improvement suggests possible differentiation between aspects of memory functions associated with aging and trauma exposure and those associated with the severity of PTSD symptoms. Performance on the CVLT appeared related to clinical symptom severity while paired associate learning worsened over time in Holocaust survivors with PTSD, consistent with earlier cross-sectional findings. [adapted from abstract]

CITATIONS

Annotated by the Editor

BECKHAM, J.C., CRAWFORD, A.L., & FELDMAN, M.E. (1998). **Trail Making Test performance in Vietnam combat veterans with and without posttraumatic stress disorder.** *Journal of Traumatic Stress, 11,* 811-819.

The present study investigated variables associated with neuropsychological test performance in Vietnam combat veterans. The variables studied included PTSD, comorbid diagnoses, compensation-seeking status, anxiety and cardiac medications, and combat exposure status.

BREMNER, J.D. (2006). **The relationship between cognitive and brain changes in posttraumatic stress disorder.** *Annals of the New York Academy of Sciences, 1071,* 80-86.
The author reviewed evidence from clinical studies showing that stress is associated with changes in structure of the hippocampus, a brain area that plays a critical role in memory and memory deficits. He then described results from two studies showing that paroxetine and phenytoin may counteract the effects of stress on the brain in patients with PTSD.

BREWIN, C.R. (2001). **A cognitive neuroscience account of posttraumatic stress disorder and its treatment.** *Behaviour Research and Therapy, 39,* 373-393.
The authors reviewed research in the areas of animal conditioning, the neural systems underlying emotion and memory, and the effect of fear on these systems. He concluded that hippocampally-dependent and non-hippocampally-dependent forms of memory are differentially affected by extreme stress, and contrasts the implications of dual representation theory to those of other models of traumatic memory processing.

BUSTAMANTE, V., MELLMAN, T.A., DAVID, D., & FINS, A.I. (2001). **Cognitive functioning and the early development of PTSD.** *Journal of Traumatic Stress, 14,* 791-797.
This study examined cognitive functioning and PTSD severity in 38 participants with traumatic injuries shortly after admission to a Level I Trauma Center. Delayed recall and retroactive interference were negatively correlated with the severity of PTSD at follow-up independent of baseline PTSD severity. Relative deficits in select areas of verbal memory after a trauma may confer greater risk for developing PTSD.

CONSTANS, J.I. (2005). **Information-processing biases in PTSD.** In J.J. Vasterling & C.R. Brewin (Eds.), *Neuropsychology of PTSD: Biological, cognitive, and clinical perspectives* (pp. 105-130). New York: Guilford Press.
The author reviewed the experimental literature about how emotionally-relevant information is processed in PTSD. The chapter focuses on attentional, judgment, and memory biases for trauma-relevant information. The author concludes that PTSD is characterized by biases in processing consciously accessible stimuli, but that there is less evidence of biases on perceptual tasks in which conscious elaboration of the stimuli is minimized.

CROWELL, T.A., KIEFFER, K.M., SIDERS, C.A., & VANDERPLOEG, R.D. (2002). **Neuropsychological findings in combat-related posttraumatic stress disorder.** *Clinical Neuropsychologist, 16,* 310-321.
Neuropsychological measures of intellectual ability, learning, memory, attention, visuospatial ability, executive functioning, language, and psychomotor speed were examined in four demographically comparable groups of community dwelling veterans differing in PTSD presence and course. The four groups did not differ on the neuropsychological measures. Results further suggested that the cognitive difficulties previously linked to PTSD may actually have been secondary to preexisting individual differences or other clinical conditions coexisting with PTSD.

DE BELLIS, M.D., & KUCHIBHATLA, M. (2006). **Cerebellar volumes in pediatric maltreatment-related posttraumatic stress disorder.** *Biological Psychiatry, 60,* 697-703.
The authors compared 58 maltreated children with PTSD to two groups of children who either had no disorder or generalized anxiety disorder, by administering a comprehensive psychiatric assessment and an anatomical magnetic resonance image brain scan. The results supported cerebellar volume differences in maltreated children with PTSD.

LIEBERMAN, H.R., BATHALON, G.P., FALCO, C.M., KRAMER, F.M., MORGAN, C.A., & NIRO, P. (2005). **Severe decrements in cognition function and mood induced by sleep loss, heat, dehydration, and undernutrition during simulated combat.** *Biological Psychiatry, 57,* 422-429.
Cognitive functioning was evaluated before, during, and after an intense and stressful military training exercise. Participants showed substantial degradation in attention, memory, and reasoning.

SOUTHWICK, S.M., RASMUSSON, A., BARRON, J., & ARNSTEN, A. (2005). **Neurobiological and neurocognitive alterations in PTSD.** In J.J. Vasterling & C.R.Brewin (Eds.), *Neuropsychology of PTSD: Biological, cognitive, and clinical perspectives* (pp. 27-58). New York: Guilford Press.
Reviews preclinical and clinical data addressing the relationship between brain regions thought to be critical to the fear response and three neurotransmitter/neurohormone systems (noradrenergic system, serotonergic system, and hypothalamic-pituitary-adrenal (HPA) axis) found to be dysregulated in PTSD. The authors link neurobiological dysregulation to PTSD-related cognitive deficits such as executive functioning, vigilance, working memory, and declarative verbal learning and memory.

SUTKER, P.B., GALINA, Z.H., WEST, J.A., & ALLAIN, A.N. (1990). **Trauma-induced weight loss and cognitive deficits among former prisoners of war.** *Journal of Consulting and Clinical Psychology, 58,* 323-328.
WAIS-R and Wechsler Memory Scale (WMS) Logical Memory indices were collected from former prisoners of war (POWs) and non-POW combat veterans. Severity of POW confinement stress (reflected by trauma-induced weight loss) was predictive of long-term compromise in cognitive performance.

VAN DER KOLK, B.A. (2006). **Clinical implications of neuroscience research in PTSD.** *Annals of the New York Academy of Sciences, 1071,* 277-293.
The author discussed how neuroscience contributes to understanding the nature of traumatic stress. He concluded that effective treatment involves (a) learning to tolerate feelings and sensations by increasing the capacity for interoception, (b) learning to modulate arousal, and (c) learning that after confrontation with physical helplessness it is essential to engage in taking effective action.

VASTERLING, J.J., DUKE, L.M., BRAILEY, K., CONSTANS, J.I., ALLAIN, A.N., & SUTKER, P.B. (2002). **Attention, learning, and memory performances and intellectual resources in Vietnam veterans: PTSD and no disorder comparisons.** *Neuropsychology, 16,* 5-14.
Attention, learning, memory, and estimated intellectual potential were examined in 26 Vietnam veterans diagnosed with PTSD and in 21 Vietnam veterans without mental disorders. PTSD was associated with cognitive impairment independent of intellectual functioning.

THE BEHAVIORAL SCIENCE DIVISION

The NCPTSD Behavioral Science Division (BSD) is one of the original five sites funded in 1989. Terence M. Keane, Ph.D., was founding BSD Director and continues in that role. He shares leadership and administrative responsibilities with Deputy Director Danny Kaloupek, Ph.D., Associate Director for Education and Training Brett Litz, Ph.D., and Associate Director for Clinical Programs Lisa Fisher, Ph.D.

BSD staff are primarily clinical psychologists, each of whom has a role in the research, training, and clinical activities of the Division. BSD staff members typically obtain faculty appointments in the Division of Psychiatry at Boston University School of Medicine. This affiliation has proved beneficial to our research programs and professional development.

For over 25 years, Dr. Keane has worked to improve measurement of trauma, especially with regard to the impact of military service and combat. As a result, BSD has a tradition of specializing in the development and validation of measures for trauma exposure, stress symptoms, and PTSD diagnosis. Dr. Keane also chaired a landmark study involving over 1000 Vietnam veterans that demonstrated a strong relationship between psychophysiological reactions and PTSD status. More recently, Dr. Keane is collaborating with John Otis, Ph.D., to develop and evaluate an integrative approach to treating comorbid PTSD and chronic pain.

Dr. Kaloupek has expertise in psychophysiological measurement that he applied in assembling the laboratory used by BSD investigators for physiological studies. In recent years, Mark Miller, Ph.D., has assumed a major role in the lab and has established a productive line of investigation based around the acoustic startle paradigm. The general aim of this research is to use startle as a means for studying the impact of PTSD on the stress-sensitive hypothalamic-pituitary-adrenal (HPA) system. Dr. Miller maintains a second major line of research that relates variation in posttraumatic reactions to fundamental dimensions of personality. This work has the potential to influence clinical assessment as well as revealing the basic mechanisms of PTSD. Katherine Putnam, Ph.D., uses brain imaging (MRI) and salivary cortisol measures, among others, in studies of individuals with Borderline Personality Disorder that aim to expand understanding of how trauma exposure may cause emotional dysregulation.

Dr. Brett Litz directs a diverse research portfolio including lab-based studies that address issues related to emotion regulation. He has particular interest in the nature of stress-related emotional numbing. Dr. Litz is developing and evaluating interventions that can be delivered via the internet and self-administered. This work fits well with recent emphasis on VA services that aim to maximize an individual's strengths in promoting rehabilitation and recovery. Dr. Barbara Niles is working on projects that address diabetes self-care and control in veterans with PTSD. Dr. Niles also directs a study of "mindfulness" meditation, an alternative intervention that has shown promise for use by veterans with PTSD. Dr. Casey Taft is addressing issues tied to intimate partner violence. The primary aims of Dr. Taft's research are to increase understanding of the roles of trauma exposure and PTSD with respect to violence perpetration and the development of interventions to reduce the occurrence of violent behavior in relationships. An additional focus is the physical and psychological health impact of violence victimization.

Other senior BSD staff are Jeff Knight, Ph.D., Steve Quinn, Ph.D., and Karen Krinsley, Ph.D. The Division was extremely fortunate during the past year to recruit Denise Sloan, Ph.D., and Brian Marx, Ph.D., two established trauma experts from the academic world. They are continuing established research programs on, respectively, disclosure-based intervention and tonic immobility. Finally, we look forward to the impending arrival of Kevin Brailey, Ph.D., and Jennifer Vasterling, Ph.D., experts on the neuropsychology of PTSD.

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