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Combat & Operational Stress Research Monthly

A Word from the Editor:

Dear Colleagues,

We are pleased to introduce this compilation of highly relevant research on combat and operational stress, including recent findings on the etiology, course, and treatment of Post-traumatic Stress Disorder (PTSD) and Traumatic Brain Injury (TBI). The intent of this monthly publication is to facilitate translational research by providing busy clinicians with up-to-date findings with potential to guide and inform evidenced-based treatment. We encourage you to not only use the knowledge gained here to apply to your practice, but also share the information with colleagues to initiate discussions about best practices.

In this first edition we have included not only relevant peer-reviewed research from preceding months, but also publications from the past few years that have had a high impact factor. If you have an article or other piece you would like to include in subsequent publications, please contact the editor at kimberly.schmitz@med.navy.mil. If you are interested in further pursuing a research study in combat and operational stress, but need assistance, please contact the NCCOSC Research Facilitation Department Head, Dr. Chris Johnson, at 619-532-7111 or douglas.c.johnson@med.navy.mil.

V/R,
Kimberly Schmitz,
NCCOSC Research Facilitation

Brain and Cognition

Abstracts

Gurvits TV, Metzger LJ, Lasko NB, Cannistraro PA, Tarhan AS, Gilbertson MW, et al. (2006). **Subtle neurologic compromise as a vulnerability factor for combat-related post-traumatic stress disorder: results of a twin study.**
Archives of General Psychiatry, 63(5), 571-576.

Previous studies have demonstrated subtle neurologic dysfunction in chronic posttraumatic stress disorder (PTSD) manifest as increased neurologic soft signs (NSSs). The origin of this dysfunction is undetermined. OBJECTIVE: To resolve competing origins of increased NSSs in PTSD, namely, preexisting vulnerability factor vs acquired PTSD sign. DESIGN: Case-control study of identical twins. SETTING: A Veterans Affairs and academic medical center (ambulatory). PARTICIPANTS: A convenience sample of male Vietnam veteran twins with (n = 25) and without (n = 24) PTSD and their combat-unexposed identical (monozygotic) co-twins. INTERVENTIONS: Neurologic examination for 45 NSSs. MAIN OUTCOME MEASURE: Average scores for 45 NSSs, each scored on an ordinal scale from 0 to 3, masked to diagnosis and combat exposure status.

RESULTS: There was a significant between-pair main effect of PTSD diagnosis (as determined in the combat-exposed twin) on average NSS score in the absence of a significant combat exposure main effect or diagnosis x exposure interaction. Combat veterans with PTSD had significantly higher NSS scores than combat veterans without PTSD. The "high-risk," unexposed co-twins of the former also had significantly higher NSS scores than the "low-risk," unexposed co-twins of the latter. This result could not be explained by age, number of potentially traumatic lifetime noncombat events, alcoholism, or the presence of a comorbid affective or anxiety disorder. The average NSS score in unexposed co-twins was not significantly associated with combat severity in combat-exposed twins. CONCLUSIONS: These results replicate previous findings of increased NSSs in Vietnam combat veterans with PTSD. Furthermore, results from their combat-unexposed identical co-twins support the conclusion that subtle neurologic dysfunction in PTSD is not acquired along with the trauma or PTSD but rather represents an antecedent familial vulnerability factor for developing chronic PTSD on exposure to a traumatic event.

Kremen WS, Koenen KC, Boake C, Purcell S, Eisen SA, Franz CE, et al. (2007). **Pretrauma cognitive ability and risk for post-traumatic stress disorder: a twin study.** *Archives of General Psychiatry, 64(3), 361-368.*

Cognitive deficits are associated with post-traumatic stress disorder (PTSD), but whether such deficits reflect sequelae or risk factors is not fully resolved.

OBJECTIVE:
To determine, in a representative sample, whether preexposure cognitive ability is associated with risk for PTSD, and whether that risk is genetically mediated.

DESIGN, SETTING and PARTICIPANTS:
The co-twin-control study involved 2386 male Vietnam-era twin veterans with a mean (SD) age of 41.9 (2.7) years, a population-based sample of men who were in military service during this era. Cognitive ability scores were obtained just before military induction at a mean (SD) age of 19.7 (1.5) years. Participants included only individuals who were exposed to potentially traumatic events and underwent preexposure cognitive testing.

MAIN OUTCOME MEASURES:
Armed Forces Qualification Test (of cognitive ability) percentile scores and PTSD diagnosed by means of structured interviews.

RESULTS:
We found a significant dose-response relationship between preexposure cognitive ability and risk for PTSD. After controlling for confounders, the highest cognitive ability quartile had a 48% lower risk than the lowest ability quartile (P<.001). Non-PTSD-concordant pairs had the highest scores; PTSD-concordant pairs had the lowest scores; and PTSD-discordant pairs had intermediate scores. Differences in Armed Forces Qualification Test scores within twin pairs were significant only in PTSD-discordant pairs (P=.04) and were accounted for specifically by the discordant dizygotic pairs (P=.002). Genetic influences on preexposure cognitive ability explained 5% of the variation in PTSD, but 100% of that relationship was explained by common genes.

CONCLUSIONS:
Preexposure cognitive ability is a risk or a protective factor for PTSD. The variance in PTSD explained by preexposure cognitive ability is accounted for entirely by common genetic factors. Lower cognitive ability may be a marker of less adaptive coping against adverse mental health consequences of exposure to potentially traumatic events. Further study of the potential mechanisms through which cognitive ability confers risk is needed.

Scherrer JF, Xian H, Lyons MJ, Goldberg J, Eisen SA, True WR, et al. (2008). **Posttraumatic stress disorder; combat exposure; and nicotine dependence, alcohol dependence, and major depression in male twins.** *Comprehensive Psychiatry, 49(3), 297-304.*

Combat exposure is associated with increased risk of psychiatric and substance use disorders in veterans. However, it is not known whether combat exposure independently increases risk for these disorders or whether this association is accounted for by genetic vulnerability common to post-traumatic stress disorder (PTSD). This article tests competing explanations for the association of combat exposure and PTSD with nicotine dependence (ND), alcohol dependence (AD), and major depression (MD). Data were obtained from 6099 members of the Vietnam Era Twin Registry, a national registry of male-male twin pairs who served in the military during the Vietnam era. Twin models were fit to estimate the genetic and environmental variance common and specific to Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition, lifetime diagnoses of PTSD, combat trauma, and 3 comorbid conditions: ND, AD, and MD. Variance specific to ND, AD, and MD was due to genetic factors (48%, 36%, and 12%, respectively) and unique environmental factors (36%, 42%, and 58%, respectively). After accounting for variance common to PTSD, no residual genetic and environmental variance overlapped between combat and ND, combat and AD, and combat and MD. Combat exposure is not independently associated with lifetime ND, AD, and MD. The association of combat exposure with these 3 disorders is due to genetic and unique environmental contributions in common with PTSD. These findings suggest comorbid PTSD may represent a genetically mediated vulnerability to psychopathology after trauma.

Werner NS, Meindl T, Engel RR, Rosner R, Riedel M, Reiser M, et al. (2009). **Hippocampal function during associative learning in patients with posttraumatic stress disorder.** *Journal of Psychiatric Research, 43(3), 309-318.*

In the last decade several studies have shown memory deficits in patients with post-traumatic stress disorder (PTSD) which have been associated with a reduced hippocampus volume. However, until now we do not know how or whether these structural abnormalities turn into functional abnormalities. Thus, the primary purpose of the present study was the investigation of the hippocampal function using functional magnet resonance imaging (fMRI). We compared PTSD patients and healthy control participants using an associative learning paradigm consisting of two encoding and one retrieval condition. During fMRI scanning participants had to learn face-profession pairs. Afterwards only faces were presented as cue stimuli for associating the category of the prior learned target profession and the participants had to decide whether this face belonged to a scientific or an artistic profession. Additionally, cognitive functioning, i.e. memory and attention, was examined using neuropsychological standard tests. During encoding PTSD patients showed stronger hippocampal and weaker prefrontal activation compared to healthy control participants. During retrieval the two groups did not differ neither in hippocampus activation nor in accuracy of retrieval. PTSD patients however showed a reduced activation in the left parahippocampal gyrus and other memory-related brain regions. We did not find any significant memory differences between PTSD patients and healthy control participants. The results suggest that PTSD has an effect on memory-related brain function despite intact memory functioning. In particular the hippocampal/parahippocampal regions and the prefrontal cortex show functional alterations during associative learning and memory.

Whalley MG, Rugg MD, Smith AP, Dolan RJ & Brewin CR. (2009). **Incidental retrieval of emotional contexts in post-traumatic stress disorder and depression: an fMRI study.** *Brain and Cognition, 69(1), 98-107.*

In the present study, we used fMRI to assess patients suffering from post-traumatic stress disorder (PTSD) or depression, and trauma-exposed controls, during an episodic memory retrieval task that included non-trauma-related emotional information. In the study phase of the task neutral pictures were presented in emotional or neutral contexts. Participants were scanned during the test phase, when they were presented with old and new neutral images in a yes/no recognition memory task. fMRI results for the contrast between old and new items revealed activation in a predominantly left-sided network of cortical regions including the left middle temporal, bilateral posterior cingulate, and left prefrontal cortices. Activity common to all three groups when correctly judging pictures encoded in emotional contexts was much more limited. Relative to the control and depressed groups the PTSD group exhibited greater sensitivity to correctly recognised stimuli in the left amygdala/ventral striatum and right occipital cortex, and more specific sensitivity to items encoded in emotional contexts in the right precuneus, left superior frontal gyrus, and bilateral insula. These results are consistent with a substantially intact neural system supporting episodic retrieval in patients suffering from PTSD. Moreover, there was little indication that PTSD is associated with a marked change in the way negatively valenced information, not of personal significance, is processed.

CITATIONS *Annotated by the Editor*

Belanger HG, Kretzmer T, Yoash-Gantz R, Pickett T & Tupler LA. (2009). **Cognitive sequelae of blast-related versus other mechanisms of brain trauma.** *Journal of the International Neuropsychological Society, 15(1), 1-8.*

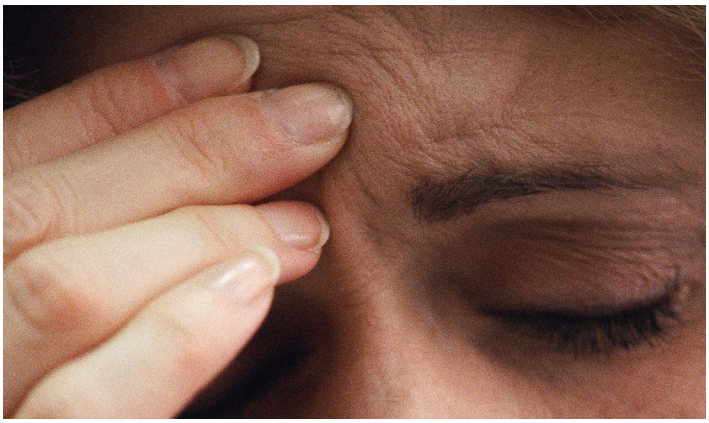
The use of improvised explosive devices has become the hallmark of modern warfare and has resulted in an ever-increasing number of blast-related traumatic brain injuries (TBIs). Despite this fact, very little is actually known about the cognitive sequelae of blast-related TBIs. The purpose of the current study was to compare patterns of performance on neuropsychological measures in subjects who have sustained TBIs as a result of blast (or explosion) with those who have sustained TBIs from non-blast or blunt force trauma (motor vehicle accident, fall, assault, etc.). No main effects were observed in analysis of covariance between blast-related TBI participants and non-blast-related TBI participants across any of the neuropsychological variables, although an interaction was observed on a visual memory test showing stronger performance for mild blast-related and poorer performance for moderate-to-severe blast-related participants compared with both non-blast groups. Overall, the results do not provide any strong evidence that blast is categorically different from other TBI mechanisms, at least with regard to cognitive sequelae on select measures. Additional findings included a marginally increased incidence of reported PTSD symptoms among blast-injured participants.

Bruce JM & Echemendia RJ. (2009). **History of multiple self-reported concussions is not associated with reduced cognitive abilities.** *Neurosurgery, 64(1), 100-106.*

In the present study, we examined the association between a self-reported concussion history and cognition using traditional and computer-based neuropsychological tests. A computerized neuropsychological battery was administered to a sample of 858 collegiate male athletes. Of this sample, 298 athletes reported a history of concussion. A traditional neuropsychological battery was administered to a separate sample of 479 male collegiate athletes, 187 of whom reported a history of concussion. Finally, both a computerized and a traditional neuropsychological battery were administered to a third distinct sample of 175 male collegiate athletes, 57 of whom reported a history of concussion. Concussion history was assessed via self-report. None of the athletes had been concussed in the 6 months before testing. No significant association was found between self-reported concussion history and performance on either computerized or traditional neuropsychological tests. Findings suggest that athletes who report a distant history of concussion have minimal enduring neurocognitive deficits. Given conflicting findings in the literature, prospective studies that attempt to identify moderating factors are necessary to help determine who is at risk for long-term cognitive difficulties after concussion.

Kennedy MR, Wozniak JR, Muetzel RL, Mueller BA, Chiou HH, Pantekoek K, et al. (2009). **White matter and neurocognitive changes in adults with chronic traumatic brain injury.** *Journal of the International Neuropsychological Society, 15(1), 130-136.*

Diffusion tensor imaging was used to investigate white matter (WM) integrity in adults with traumatic brain injury (TBI) and healthy adults as controls. Adults with TBI had sustained severe vehicular injuries on the average of 7 years earlier. A multivariate analysis of covariance with verbal IQ as the covariate revealed that adults with TBI had lower fractional anisotropy and higher mean diffusivity than controls, specifically in the three regions of interest (ROIs), the centrum semiovale (CS), the superior frontal (SPF), and the inferior frontal (INF). Adults with TBI averaged in the normal range in motor speed and two of three executive functions and were below average in delayed verbal recall and inhibition, whereas controls were above average. Time since injury, but not age, was associated with WM changes in the SPF ROI, whereas age, but not time since injury, was associated with WM changes in the INF ROI, suggesting that the effects of WM on time since injury may interact with age. To understand the utility of WM changes in chronic recovery, larger sample sizes are needed to investigate associations between cognition and WM integrity of severely injured individuals who have substantial cognitive impairment compared to severely injured individuals with little cognitive impairment.



Stahel PF, Flierl MA, Morgan BP, Persigehl I, Stoll C, Conrad C, et al. (2009). **Absence of the complement regulatory molecule CD59a leads to exacerbated neuropathology after traumatic brain injury in mice.** *Journal of Neuroinflammation, 6, 2.*

Complement represents a crucial mediator of neuroinflammation and neurodegeneration after traumatic brain injury. CD59 is the major regulator of membrane attack complex (MAC) formation and represents an essential protector from cell injury after complement activation in the injured brain. Mice deleted in the Cd59a gene (CD59a-/-) and wild-type littermates (n = 60) were subjected to focal closed head injury. Sham-operated (n = 60) and normal untreated mice (n = 14) served as negative controls. The brain-injured CD59a-/- mice showed a significantly impaired neurological outcome within 7 days, compared to wild-type controls. The serum levels of neuron-specific enolase, an indirect marker of neuronal cell death, were significantly elevated in CD59a-/- mice at 4 h and 24 h after trauma, compared to wild-type littermates. Increased neuronal cell death and brain tissue destruction was detected in CD59a-/- mice within 24 hours to 7 days after head trauma. The analysis of brain homogenates for potential mediators and regulators of cell death other than the complement MAC revealed no difference in gene expression and protein levels between CD59a-/- and wild-type mice. These data emphasize an important role of CD59 in mediating protection from secondary neuronal cell death and further underscore the key role of the terminal complement pathway in the pathophysiology of traumatic brain injury.

Abstracts

Kline AE, Hoffman AN, Cheng JP, Zafonte RD & Massucci JL. (2008). **Chronic administration of antipsychotics impede behavioral recovery after experimental traumatic brain injury.** *Neuroscience Letters, 448(3), 263-267.*

Antipsychotics are often administered to traumatic brain injured (TBI) patients as a means of controlling agitation, albeit the rehabilitative consequences of this intervention are not well known. Hence, the goal of this study was to evaluate the effects of risperidone (RISP) and haloperidol (HAL) on behavioral outcome after experimental TBI. Anesthetized rats received either a cortical impact or sham injury and then were randomly assigned to five TBI (RISP 0.045mg/kg, RISP 0.45mg/kg, RISP 4.5mg/kg, HAL 0.5mg/kg and VEHicle 1mL/kg) and three Sham (RISP 4.5mg/kg, HAL 0.5mg/kg and VEH 1mL/kg) groups. Treatments began 24h after surgery and were provided once daily for 19 days. Behavior was assessed with established motor (beam-balance/walk) and cognitive (spatial learning/memory in a water maze) tasks on post-operative days 1-5 and 14-19, respectively. RISP and HAL delayed motor recovery, impaired the acquisition of spatial learning, and slowed swim speed relative to VEH in both TBI and sham groups. These data indicate that chronic administration of RISP and HAL impede behavioral recovery after TBI and impair performance in uninjured controls.

Sumpter RE & McMillan TM. (2006). **Errors in self-report of post-traumatic stress disorder after severe traumatic brain injury.** *Brain Injury, 20(1), 93-99.*

Assessing PTSD by questionnaire can lead to false positive diagnosis after severe traumatic brain injury. Sumpter and McMillan, reported quantitative data on 34 people with severe TBI; 59% were PTSD 'cases' by questionnaire assessment, but only 3% using a structured interview. The present paper describes ways in which these individuals made errors on questionnaires. Some did not follow questionnaire instructions because of inattention and concrete thinking or instead reported effects of brain injury. Symptom overlap between TBI and PTSD, including insomnia, irritability and impaired concentration can cause errors. Brain injury can also provoke curiosity about loss of memory (during coma, retrograde and post-traumatic amnesia), decreased participation, social withdrawal and difficulty adjusting to injury that may be mistaken for fear-associated PTSD symptoms. Assessment of PTSD by questionnaire can lead to erroneous conclusions and factors related to brain injury must be carefully considered when investigating PTSD.

Ley EJ, Scehnet J, Park R, Schroff S, Dagliyan G, Conti PS, et al. (2009). **The in vivo effect of propranolol on cerebral perfusion and hypoxia after traumatic brain injury.** *The Journal of Trauma, 66(1),154-159.*

Recent epidemiologic evidence has identified beta-blockade as independently associated with improved survival in patients with isolated traumatic brain injury (TBI). Reduced sympathetic discharge and catecholamine release may improve circulation in the injured areas and influence delayed demise. The purpose of this study was to investigate the cerebral effect of beta-blockade in a murine TBI model using immunohistochemical and microPET analysis. METHODS: Balb/c mice underwent TBI as in a previously described model and were randomized to receive treatment with propranolol or placebo in a blinded fashion. Immunofluorescent images were obtained for vessel density (CD31), vessel perfusion (Ricinus communis agglutinin [RCA]-lectin), and cerebral hypoxia (hypoxyprobe-1) and compared by digital quantification. Perfusion measurements were acquired using positron emission tomography microPET scans with [64Cu]-pyruvaldehyde bis(N4-methylthiosemicarbazone) ([64Cu]-PTSM) and converted into standardized uptake values (SUV) for analysis. RESULTS: On immunohistochemical analysis, the normal mouse cerebral perfusion was a quantitated mean of 325 +/- 20, the cerebral perfusion after TBI and treatment with placebo was 113 +/- 25, and the cerebral perfusion after TBI treated with propranolol was 172 +/- 23. Immunohistochemical analysis demonstrated treatment with propranolol improved cerebral perfusion by 152% (p value <0.01) and reduced cerebral hypoxia by 24.2% (p value <0.01) compared with treatment with placebo. MicroPET imaging of the normal mouse brain after injection with placebo measured a SUV of 0.7075+/- 0.02; the normal mouse brain after treatment with propranolol measured a SUV of 0.400 +/- 0.02. After TBI and treatment with placebo, the SUV reduced to 0.395 +/- 0.01; after treatment with propranolol the SUV measured 0.515 +/- 0.04. MicroPET imaging demonstrated propranolol improved cerebral perfusion after TBI to 130% of placebo (p value <0.01). CONCLUSION: Propranolol in vivo increased cerebral perfusion and decreased cerebral hypoxia. This research demonstrates beta-blockade may prevent additional brain damage after traumatic insult and should be the focus of future clinical trials.

The following article relates to an attention modification study in the planning process at NCCOSC that will be conducted to determine if this attention modification program can aid service members with PTSD:

Amir N, Beard C, Burns M & Bomyea J. (2009). **Attention modification program in individuals with generalized anxiety disorder.** *Journal of Abnormal Psychology, 118(1), 28-33.*

Research suggests that individuals with generalized anxiety disorder (GAD) show an attention bias for threat-relevant information. However, few studies have examined the causal role of attention bias in the maintenance of anxiety and whether modification of such biases may reduce pathological anxiety symptoms. In the present article, the authors tested the hypothesis that an 8-session attention modification program would (a) decrease attention bias to threat and (b) reduce symptoms of GAD. Participants completed a probe detection task by identifying letters (E or F) replacing one member of a pair of words. The authors trained attention by including a contingency between the location of the probe and the nonthreat word in one group (Attention Modification Program; AMP) and not in the other (attention control condition; ACC). Participants in the AMP showed change in attention bias and a decrease in anxiety, as indicated by both self-report and interviewer measures. These effects were not present in the ACC group. These results are consistent with the hypothesis that attention plays a causal role in the maintenance of GAD and suggest that altering attention mechanisms may effectively reduce anxiety.

CITATIONS *Annotated by the Editor*

Lew HL, Gray M & Poole JH. (2009). **Simultaneous measurement of perceptual and motor cortical potentials: implications for assessing information processing in traumatic brain injury.** *American Journal of Physical Medicine & Rehabilitation, 88(1), 1-6.*

Psychomotor slowing is a common manifestation of traumatic brain injury. Previous electrophysiological studies of traumatic brain injury have focused on abnormal attentional and perceptual responses to incoming stimuli. We hypothesize that traumatic brain injury is also associated with abnormal cortical components of motor execution. To test this hypothesis, we analyzed event-related potentials of 22 subjects (11 with a history of severe traumatic brain injury and 11 age-matched healthy subjects) during oddball discrimination tasks. The findings from this study indicate that patients with traumatic brain injury have impairments in both the perceptual interpretation of incoming stimuli and the execution of motor responses and that both abnormalities contribute to psychomotor slowing in patients with traumatic brain injury.

Beck JG, Coffey SF, Foy DW, Keane TM & Blanchard EB. (2009). **Group cognitive behavior therapy for chronic posttraumatic stress disorder: an initial randomized pilot study.** *Behavior Therapy, 40(1), 82-92.*

Individuals with PTSD related to a serious motor vehicle accident were randomly assigned to either group cognitive behavioral treatment (GCBT) or a minimum contact comparison group (MCC). Compared to the MCC participants (n=16), individuals who completed GCBT (n=17) showed significant reductions in PTSD symptoms. Examination of anxiety, depression, and pain measures did not show a unique advantage of GCBT. Treatment-related gains were maintained over a 3-month follow-up interval.

McGhee LL, Maani CV, Garza TH, Desocio PA, Gaylord KM & Black IH. (2009). **The effect of propranolol on posttraumatic stress disorder in burned service members.** *Journal of Burn Care & Research, 30(1), 92-97.*

This retrospective study examines the relationship between PTSD prevalence and propranolol administration. The military burn center received 603 soldiers injured in OIF/OEF, of which 226 completed the PTSD Checklist-Military. Thirty-one soldiers received propranolol and 34 matched soldiers did not. In propranolol patients, the prevalence of PTSD was 32.3% vs 26.5% in those not receiving propranolol (P = .785). These data suggest propranolol does not decrease PTSD development in burned soldiers.

Rau V, Oh I, Laster M, Eger EI 2nd & Fanselow MS. (2009). **Isoflurane suppresses stress-enhanced fear learning in a rodent model of post-traumatic stress disorder.** *Anesthesiology, 110(3), 487-495.*

In a rodent model of PTSD, stress-enhanced fear learning (SEFL), rats are preexposed to a stressor of 15 foot shocks. Subsequent exposure to a single foot shock produces an enhanced fear response. The authors studied the effect of isoflurane and nitrous oxide on SEFL. They found that increasing isoflurane concentrations decreased SEFL when given during, but not after, the stressor. As with isoflurane, nitrous oxide also suppressed SEFL. These results suggest that sufficient concentrations of an inhaled anesthetic may prevent SEFL.

Stein DJ, Pedersen R, Rothbaum BO, Baldwin DS, Ahmed S, Musgnung J, et al. (2009). **Onset of activity and time to response on individual CAPS-SX17 items in patients treated for post-traumatic stress disorder with venlafaxine ER: a pooled analysis.** *The International Journal of Neuropsychopharmacology, 12(1), 23-31.*

This pooled analysis of data from two randomized, placebo-controlled trials of venlafaxine extended release (ER) (placebo, n=347; venlafaxine ER, n=340) assessed onset of activity and time to response on the 17 symptoms of PTSD measured by the 17-item Clinician-Administered PTSD Scale (CAPS-SX17). Significant separation between venlafaxine ER and placebo was observed on most CAPS-SX17 items. The results indicated that symptoms of physiological reactivity and psychological distress in response to cues, and irritability/anger outbursts show early and robust improvement with venlafaxine ER treatment, while symptoms of numbing and hyperarousal take longer.

Sun D, Bullock MR, McGinn MJ, Zhou Z, Altememi N, Hagood S, et al. (2009). **Basic fibroblast growth factor-enhanced neurogenesis contributes to cognitive recovery in rats following traumatic brain injury.** *Experimental Neurology, 216(1), 56-65.*

Stem/progenitor cells reside throughout the adult CNS and are actively dividing in the hippocampus. This neurogenic capacity of the hippocampus is enhanced following traumatic brain injury (TBI) suggesting that the adult brain has the inherent potential to restore brain cells lost to injury. This raises the possibility of developing strategies aimed at harnessing the neurogenic capacity of these regions to repair the damaged brain. One strategy is to enhance neurogenesis with cell growth factors. As basic fibroblast growth factor (bFGF) is a potent stem cell growth factor, we set out to determine if an intraventricular administration of bFGF following TBI could affect the levels of injury-induced neurogenesis in the hippocampus, and the degree to which this is associated with cognitive recovery. We found that injured rats infused with bFGF exhibited significantly enhanced cell proliferation in the hippocampus at 1 week post-TBI as compared to controls, and a greater number of the newly generated cells survived to 4 weeks post-injury, with the majority being neurons. Additionally, animals infused with bFGF showed significant cognitive improvement. Collectively, the current findings suggest that bFGF-enhanced neurogenesis contributes to cognitive recovery following TBI.

Health and Functioning

CITATIONS *Annotated by the Editor*

Belleville G, Guay S & Marchand A. (2009). **Impact of sleep disturbances on PTSD symptoms and perceived health.** *The Journal of Nervous and Mental Disease, 197(2), 126-132.*

The aim of the study was to assess the impact of sleep disturbances on PTSD symptom severity and perceived health. Ninety-two adults with PTSD were administered a Structured Clinical Interview for DSM-IV (SCID), and a series of questionnaires assessing PTSD symptom severity, perceived health, sleep, and alcohol use. Regression analyses revealed that sleep quality has an impact on PTSD symptom severity and perceived mental health, even when the effect of other potential confounding variables is controlled for. Future studies could explore whether the addition of interventions focusing on sleep help optimize PTSD treatment.

Jacobson IG, Smith TC, Smith B, Keel PK, Amoroso PJ, Wells TS, et al.; Millennium Cohort Study Team. (2009). **Disordered eating and weight changes after deployment: longitudinal assessment of a large US military cohort.** *American Journal of Epidemiology, 169(4), 415-427.*

The effect of military deployments to combat environments on disordered eating and weight changes is unknown. Using longitudinal data from Millennium Cohort Study participants who completed baseline and follow-up questionnaires (n=48,378), the authors investigated new-onset disordered eating and weight changes in a large military cohort. Deployment was not significantly associated with new-onset disordered eating in women or men. However, deployed women reporting combat exposures were 1.78 times more likely to report new-onset disordered eating and 2.35 times more likely to lose 10% or more of their body weight compared with women who deployed but did not report combat exposures.

Heppner PS, Crawford EF, Haji UA, Afari N, Hauger RL, Dashevsky BA, et al. (2009). **The association of posttraumatic stress disorder and metabolic syndrome: a study of increased health risk in veterans.** *BMC Medicine, 7, 1.*

The authors assessed PTSD-related biological burden in 253 veterans by measuring biological factors that comprise metabolic syndrome, an important established predictor of morbidity and mortality, as a correlate of long-term health risk in PTSD. The authors found that veterans with higher severity of PTSD were more likely to meet diagnostic criteria for metabolic syndrome. These findings provide preliminary evidence linking higher severity of PTSD with risk factors for diminished health and increased morbidity, as represented by metabolic syndrome.

Kibler JL, Joshi K & Ma M. (2009). **Hypertension in relation to posttraumatic stress disorder and depression in the US National Comorbidity Survey.** *Behavioral Medicine, 34(4), 125-132.*

The clinical literature increasingly indicates that cardiovascular risk factors and cardiovascular disease (CVD) are more common among individuals with PTSD. Depression also poses a risk for CVD and is often comorbid with PTSD. The authors examined relationships of lifetime PTSD and depression with high blood pressure in data from the US National Comorbidity Survey. They divided participants into 4 mutually exclusive diagnostic groups: (1) PTSD history and no depression history, (2) PTSD and depression history, (3) depression history and no PTSD history, and (4) no history of mental disorder. Hypertension prevalence was higher for the PTSD, no depression and PTSD plus depression groups compared with the depression only and no mental disorder groups. PTSD appears to be related to hypertension independent of depression. This may partially explain elevated rates of CVD in PTSD patients.

Malta LS, Levitt JT, Martin A, Davis L & Cloitre M. (2009). **Correlates of functional impairment in treatment-seeking survivors of mass terrorism.** *Behavior Therapy, 40(1), 39-49.*

This study sought to identify variables associated with functional impairment in persons exposed to terrorism. Data was collected from a sample of adults who sought treatment for psychological distress related to the 2001 World Trade Center attack. A multiple regression analysis found that PTSD numbing symptoms, beliefs about the ability to regulate negative moods, feelings of social discomfort and expectations of being disliked, income level, and relationship status significantly predicted 58% of the variance in social-occupational impairment. The results suggest that treatments targeting PTSD numbing symptoms as well as maladaptive expectations about social interactions and one's ability to manage negative affect may have utility for persons adversely affected by mass violence

Staiger PK, Melville F, Hides L, Kambouropoulos N & Lubman DI. (2009). **Can emotion-focused coping help explain the link between posttraumatic stress disorder severity and triggers for substance use in young adults?** *Journal of Substance Abuse Treatment, 36(2), 220-226.*

High rates of PTSD have been reported among people seeking treatment for substance use disorders (SUDs), although few studies have examined the relationship between PTSD and substance use in young drug users. This study compared levels of substance use, coping styles, and high-risk triggers for substance use among 66 young adults with SUD, with or without comorbid PTSD. Young people with current SUD-PTSD (n = 36) reported significantly higher levels of substance use in negative situations, as well as emotion-focused coping, compared to the current SUD-only group (n = 30). Severity of PTSD was a significant predictor of negative situational drug use, and emotion-focused coping was found to mediate this relationship.

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