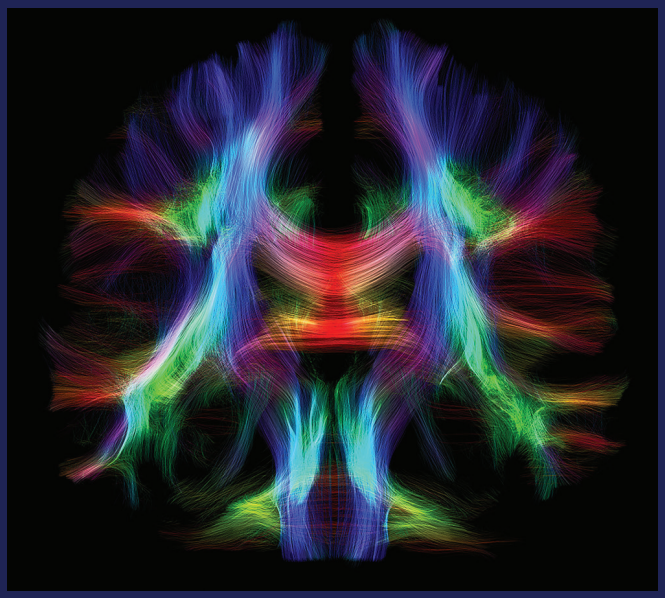
UNIFORMED SERVICES UNIVERSITY

CENTER FOR THE STUDY OF TRAUMATIC STRESS

PROGRAM
13th Annual Amygdala, Stress and PTSD Conference: The Sequela of Trauma

APRIL 17, 2018

Sanford Auditorium & Lobby, Building B
Uniformed Services University, Bethesda, MD



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The Amgydala, Stress and PTSD Conference at the Uniformed Services University brings together scientists and clinicians working towards solving the biological basis of stress, fear, and posttraumatic stress disorder.

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Background

The Center for the Study of Traumatic Stress (CSTS) of the Uniformed Services University (USU) in collaboration with the USU Department of Psychiatry, USU Neuroscience Program, USU Department of Family Medicine, and the Walter Reed National Military Medical Center (WRNMMC), Department of Psychiatry, is pleased to present the *13th Annual Amygdala, Stress and PTSD Conference: The Sequelae of Trauma*.

The Amygdala, Stress and PTSD Conference at the Uniformed Services University brings together scientists and clinicians working towards solving the biological basis of stress, fear, and posttraumatic stress disorder.

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Conference Speakers

Ruth Lanius, MD, PhD

Ruth Lanius, MD, PhD, Professor of Psychiatry is the director of the posttraumatic stress disorder (PTSD) research unit at the University of Western Ontario. She established the Traumatic Stress Service and the Traumatic Stress Service Workplace Program, services that specialize in the treatment and research of Posttraumatic Stress Disorder (PTSD) and related comorbid disorders. She currently holds the Harris-Woodman Chair in Mind-Body Medicine at the Schulich School of Medicine & Dentistry at the University of Western Ontario. Her research interests focus on studying the neurobiology of PTSD and treatment outcome research examining various pharmacological and psychotherapeutic methods. She has authored more than 100 published papers and chapters in the field of traumatic stress and is currently funded by several federal funding agencies. She regularly lectures on the topic of PTSD nationally and internationally. She has recently published a book 'Healing the traumatized self: consciousness, neuroscience, treatment' with Paul Frewen.

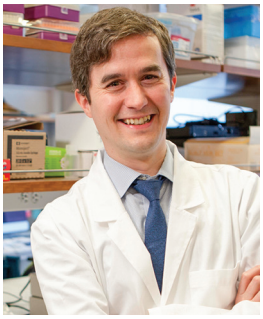
Roberto Lewis-Fernandez, MD

Roberto Lewis-Fernández, MD is a Professor of Clinical Psychiatry at Columbia University and the Director of the New York State Center of Excellence for Cultural Competence and the Hispanic Treatment Program, and the Co-Director of the Anxiety Disorder Clinic, at New York State Psychiatric Institute. His research focuses on developing culturally valid interventions and instruments to enhance patient engagement, reduce misdiagnosis, and help overcome disparities in the care of underserved cultural groups, especially Latinos. He also studies the way culture affects individuals' experience of mental disorder and their help-seeking expectations, including how to explore this cultural variation during the psychiatric evaluation. He led the development of the DSM-5 Cultural Formulation Interview, a standardized method for cultural assessment for use in mental health practice, and was the Principal Investigator of its international field trial. He is Chair of the Cultural Committee of the Group for the Advancement of Psychiatry, President of the Society for the Study of Psychiatry and Culture, President-Elect of the World Association of Cultural Psychiatry, and Past President of the American Society of Hispanic Psychiatry. He was a member of the NIMH National Advisory Mental Health Council and Chair of the Cross-Cultural Issues Subgroup of DSM-5. Currently, he is Co-Chair of the ICD-11 Working Group on Culture-Related Issues and a member of the Working Group on Somatic Distress and Dissociative Disorders. He is also Chair of the DSM Review Committee for Internalizing Disorders. His awards include the 2014 Simón Bolívar Award and the 2018 Health Services Senior Scholar Research Award of the American Psychiatric Association, the 2014 Creative Scholarship Award of the Society for the Study of Psychiatry and Culture, and the 2015 Multicultural Excellence Award of the New York State Chapter of the National Alliance on Mental Illness.

Rajita Sinha, PhD

Dr. Rajita Sinha, is the Foundations Fund Endowed Professor in Psychiatry, Neuroscience and Child Study at the Yale University School of Medicine. She is also the Chief of the Psychology Section in Psychiatry and Co-Director of Education for the Yale Center for Clinical Investigation. Her PhD was in Biological Psychology and she then retrained in Clinical Psychology and is a licensed Clinical Psychologist with expertise in mood, trauma, anxiety and addictive disorders. She is the founding director of the Yale Interdisciplinary Stress Center that focuses on understanding the sex-specific neurobiology of stress, trauma and resilient versus vulnerable coping mechanisms that promote neuropsychiatric diseases such as alcoholism, other substance abuse, PTSD and other chronic diseases. Her lab also develops and tests novel treatments to address these processes to prevent relapse and risk of stress-related chronic diseases. Her research has been supported by a series of NIH funded research projects continuously for over 20 years and she has published over 250 scientific peer reviewed publications in these areas. She currently serves on the NIH/NIAAA Advisory Council and also on the Expert Scientific Panel for the NIH Common Fund's Science of Behavior Change program. She has served on many other NIH special emphasis panels, review committees and workshops, presented at numerous national and international conferences, and her work is widely cited. She has been featured as an expert on stress and trauma and its effects on memory, cognition, emotion and health behaviors for numerous news outlets including the Dr. OZ Show, NBC Nightly News, CNN Health, Wall Street Journal and USA Today to name a few. She also conducts workshops, lectures and retreats on stress management, self-care for the stressed professional and for senior executives, and on ways to reduce stress to enrich and enhance work, family and life.

Conor Liston, MD, PhD



Conor Liston, MD, PhD is an Assistant Professor of Neuroscience and Psychiatry in the Brain and Mind Research Institute and Department of Psychiatry at Weill Cornell Medicine. His laboratory operates at the interface between basic circuit neurobiology and biological psychiatry. The long-term goals of his research program are 1) to define mechanisms by which neuronal subtypes in the prefrontal cortex (PFC) interact to support learning, memory, and motivated approach and avoidance behaviors, and 2) to understand how these processes are disrupted in chronic stress states and in stress-related neuropsychiatric disorders. To this end, his laboratory employs an approach that integrates optogenetic tools and genetically encoded calcium indicators with two-photon imaging and functional MRI, and they are actively developing new methods for quantifying cortex-wide circuit dynamics in topologically defined neuronal subtypes. His work has been recognized with awards from the Brain and Behavior Research Foundation, the Whitehall Foundation, the Klingenstein-Simons Foundation, and the Rita Allen Foundation, among others. Prior to starting his lab at Weill Cornell, he completed his undergraduate training at Harvard College; his PhD, MD, and residency training at the Rockefeller University and Weill Cornell; and a postdoctoral fellowship in the Stanford University laboratory of Dr. Karl Deisseroth.

M. Katherine Shear, MD

Dr. M. Katherine Shear is the Marion E. Kenworthy Professor of Psychiatry and the founding Director of the Center for Complicated Grief at Columbia School of Social Work. Dr. Shear is a clinical researcher who first worked in anxiety, depression. For the last two decades she has focused on understanding and treating people who experience persistent intense grief. She developed and tested complicated grief treatment (CGT) a short-term targeted intervention and confirmed its efficacy in three large NIMH-funded studies. CGT is strength-based and focused on fostering adaptation to loss. Dr. Shear is widely recognized for her work in bereavement, including both research and clinical awards from the Association for Death Education and Counseling and invited authorship of articles for Uptodate and the New England Journal of Medicine.

Moderators

Derrick Hamaoka, MD

Col (Dr.) Derrick Hamaoka serves as the Assistant Chair, Medical Education, for the Uniformed Services University of the Health Sciences Department of Psychiatry. Col Hamaoka is a graduate of the Uniformed Services University of the Health Sciences School of Medicine (1999) and the University of Texas Health Science Center Psychiatry Residency Program (2003). Prior to serving in his current position, he was the Associate Program Director, University of Texas Health San Antonio Psychiatry Residency Program, leading one of the largest programs in the nation and responsible for the majority of the active duty Air Force psychiatry pipeline. He holds the Air Force Medical Corps Academic Grand Master (ME) Special Experience Identifier (SEI). He also serves as the Defense Institute for Medical Operations director and subject matter expert for the Mental Health Services After Disasters & Combat course, providing support/education for recent missions to Iraq, Sierra Leone, Tunisia, Colombia, Mexico, and Slovakia.

LTC Vincent F. Capaldi

LTC Vincent F. Capaldi, II, MC, USA, is the Chief of the Department of Behavioral Biology, Center for Military Psychiatry and Neuroscience Research, at the Walter Reed Army Institute of Research in Silver Spring, MD. He currently serves as an associate professor in the departments of Internal Medicine and Psychiatry at the Uniformed Services University of the Health Sciences in Bethesda, MD. He is also the program director of the National Capital Consortium combined Internal Medicine and Psychiatry residency training program and chair of the Biomedical Ethics Committee at Walter Reed National Military Medical Center

LTC Capaldi completed dual residency training in Internal Medicine and Psychiatry and fellowship in Sleep Medicine at Walter Reed National Military Medical Center. LTC Capaldi holds board certifications from the American Board of Psychiatry and Neurology and the American Board of Internal Medicine to practice General Psychiatry, Internal Medicine, and Sleep Medicine. In 2013, LTC Capaldi was elected as a Fellow of the American Psychiatric Association and the American College of Physicians and currently serves at the president of the Society of Uniformed Services Psychiatrists.

In January, 2013, LTC Capaldi was appointed as officer in charge (OIC) of the Restoration Program at Bagram Air Field, Afghanistan. As OIC, LTC Capaldi was responsible for the comprehensive behavioral health restoration program, all clinical operations, and prevention activities for over 45,000 NATO troops stationed across Afghanistan.

LTC Capaldi has published over 30 peer reviewed scientific articles and book chapters on various topics such as sleep disorders, traumatic brain injury, and post stroke depression that have appeared in several medical journals. He serves as the Psychiatry & Clinical Psychology Disorders Capabilities Manager and Steering Committee Chair for Physiological Health and Performance in the Military Operational Research Program, MRMC.

Conference Leadership

Gary H. Wynn, MD
LTC, MC, USA

Dr. Wynn is Associate Professor of Psyc12hiatry and Neuroscience and Assistant Chair of the Department of Psychiatry at the Uniformed Services University of the Health Sciences. He is a Scientist at the Center for the Study of Traumatic Stress. He is also a Distinguished Fellow of the American Psychiatric Association and on the editorial boards of Psychosomatics and the Journal of Neuroscience Research. Dr. Wynn received his education at the United States Military Academy at West Point and Uniformed Services University of the Health Sciences. He completed a dual residency in psychiatry and internal medicine at the Walter Reed Army Medical Center in Washington, DC. During his military career Dr. Wynn has served as a Division Psychiatrist (2nd Infantry Division, Korea), Assistant Chief of Inpatient Services (Walter Reed), and as a Research Psychiatrist (Walter Reed Army Institute of Research) prior to transitioning to the Uniformed Services University of the Health Sciences.

Dr. Wynn has served as a frequent member of DoD level committees and working groups on the topics of PTSD and suicide. He currently serves as the Chair for the DoD's Joint Program Committee working group on Diagnosis and Treatment of PTSD. Dr. Wynn has served as a member of VA Merit Review Boards, as a member of a National Institutes of Mental Health Data Safety and Monitoring Board, and as US Representative to the NATO Human Factors in Medicine panel on technology in military mental health. He is the recipient of the AMEDD "A" Proficiency Designator, the Rundell Award, the Artiss Award, and three Meritorious Service Medals as well as a member of the Order of Military Medical Merit. Dr. Wynn is Chair for the Amygdala, Stress, and PTSD conference currently in its 13th year and past President of the Society of Uniformed Services Psychiatrists. In addition, Dr. Wynn has over 60 publications including being co-author and editor of three books.

Robert J. Ursano, MD

Dr. Ursano is Professor of Psychiatry and Neuroscience and Chairman of the Department of Psychiatry at the Uniformed Services University of the Health Sciences, Bethesda, Maryland. He is founding Director of the Center for the Study of Traumatic Stress. In addition, Dr. Ursano is Editor of *Psychiatry*, the distinguished journal of interpersonal and biological processes, founded by Harry Stack Sullivan. Dr Ursano completed twenty years service in USAF medical corps and retired as Colonel in 1991. He was educated at the University of Notre Dame and Yale University School of Medicine and did his psychiatric training at Wilford Hall USAF Medical Center and Yale University.

Dr. Ursano served as the Department of Defense representative to the National Advisory Mental Health Council of the National Institutes of Mental Health and is a past member of the Veterans Affairs Mental Health Study Section and the National Institute of Mental Health Rapid Trauma and Disaster Grant Review Section. He is a Distinguished Life Fellow in the American Psychiatric Association and a Fellow of the American College of Psychiatrists. Dr. Ursano was the first Chairman of the American Psychiatric Association's Committee on Psychiatric Dimensions of Disaster. This work greatly aided the integration of psychiatry and public health in times of disaster and terrorism. Dr. Ursano was an invited participant to the White House Mental Health Conference in 1999. He has received the Department of Defense Humanitarian Service Award and the highest award of the International Traumatic Stress Society, The Lifetime Achievement Award, for "outstanding and fundamental contributions to understanding traumatic stress." He is the recipient of the William C. Porter Award from the Association of Military Surgeons

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Robert J. Ursano, MD, Continued

of the United States, the William Menninger Award of the American College of Physicians and the James Leonard Award of the Uniformed Services University. He is a frequent advisor on issues surrounding psychological response to trauma to the highest levels of the US Government and specifically to the Department of Defense leadership..

Dr. Ursano has served as a frequent member of the National Academies of Science, Institute of Medicine Committees and working groups including the Committee on Psychological Responses to Terrorism, Committee on PTSD, the Committee on Compensation for PTSD in Veterans and the Committee on Nuclear Preparedness; and the National Institute of Mental Health Task Force on Mental Health Surveillance After Terrorist Attack. In addition, he has served as a member of scientific advisory boards to the Secretary of Health and Human Services for disaster mental health and the Centers for Disease Control for preparedness and terrorism. Dr. Ursano is co-principal investigator of the largest NIMH grant ever given for the study of Suicide in the U.S. Army. In collaboration with his co-principal investigators at Harvard University, the University of Michigan and Columbia University the Army- STARRS grant will be the Framingham Study of suicidal behavior, and address a national as well as DoD mental health need. In 2014, Dr. Ursano and Dr. Matthew Friedman of the VA National Center for PTSD co-founded the Friedman-Leahy Brain Bank supported through Senator Patrick Leahy (D-VT). It is the first human brain bank dedicated to PTSD. This joint effort of many people was a 12 year project developing concepts, pilot data and support. Dr. Ursano has over 300 publications. He is co-author or editor of eight books.

Conference Committee

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Scientist
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We extend special thanks to:
Robyn Hulvey, CMP, CGMP
Assistant Director of Meetings
Office of Education & Meetings
Henry Jackson Foundation for the Advancement of Military Medicine

Conference Posters

Presented in the Lobby

Continued

Chronic Mild Traumatic Brain Injury Altered Serum MicroRNAs and their Association with Fear Behavior of Posttraumatic Stress Disorder

Authors

Nagaraja S. Balakathiresan, PhD[1], Manish Bhomia, PhD[1], Anna E. Tschiffely, PhD[2], Richard McCarron, PhD[2,3], Stephen T Ahlers, PhD[2], and Barbara Knollmann-Ritschel, MD[1]

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1. Department of Pathology, Uniformed Services University of the Health Sciences, Bethesda, MD
2. Neurotrauma Department, Naval Medical Research Center, Silver Spring, MD
3. Department of Surgery, Uniformed Services University of the Health Sciences, Bethesda, MD

ABSTRACT

Background: Blast-related traumatic brain injury (TBI) has been a major cause of injury in military personnel and combat veterans. A striking feature of combat-acquired mild TBI (mTBI) is the co-existence of post-traumatic stress disorder (PTSD). However, the molecular mechanisms underlying the association of mTBI and PTSD are virtually unknown. MicroRNAs (miRNAs) are posttranscriptional gene regulators of diverse biological processes. In this study, we sought to identify miRNAs in blast-related mTBI in the absence of psychological stressors that may induce PTSD-related traits.

Methods: Anesthetized adult male rats were exposed to repetitive low-intensity blast overpressure (BOP), one exposure (11 psi) per day was administered for 3 consecutive days, to create mild TBI. Serum and amygdala samples were collected at the sub-acute and chronic time points of post-BOP animals; TaqMan based serum miRNA profiling was performed. MiRNA data analysis was carried out to identify the statistically significantly altered miRNAs. Bioinformatic analyses were carried out to identify the potential targets of PTSD-related traits by the BOP chronic mTBI associated miRNAs.

Results: Serum miRNA profiling data analysis showed 2 miRNAs at 2 weeks, and 30 miRNAs at 5-6 months post-BOP were upregulated from samples collected comparison to sham controls. Comparison of BOP chronic miRNAs with a panel of nine stress-responsive miRNAs using the tail shock PTSD rat model from an earlier study, showed five BOP chronic miRNAs (miR142-5p, -19b, -1928, -421, and -674*) could be potential PTSD miRNA biomarkers. Bioinformatic approach indicated that BOP chronic TBI miRNAs might play a potential role in the regulation of fear behavior associated genes.

Conclusions: This study suggests that the BOP chronic TBI miRNAs may play a potential role in the regulation of genes associated with the development of PTSD.

Riluzole for PTSD: Efficacy of a Glutamatergic Modulator as Augmentation Treatment for Combat-Related Posttraumatic Stress Disorder

Authors

David M. Benedek, MD[1], Patricia T. Spangler, PhD[1], James C. West, MD[1], Catherine L. Dempsey PhD, MPH[1], Kyle Possemato, PhD[2], Shannon McKenzie, BA[2], Andrea Gould, BA[1], and Mark Jimerson, BA[1]

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1. Center for the Study of Traumatic Stress, Department of Psychiatry, Uniformed Services University of Health Sciences, Bethesda, MD
2. Syracuse VA Medical Center, Syracuse, NY

ABSTRACT

Background: Posttraumatic stress disorder (PTSD) is a chronic and seriously debilitating anxiety disorder that develops in some individuals following exposure to severe trauma. Current pharmacological treatment for PTSD, and particularly combat-related PTSD, is suboptimal, thus there is a need to develop novel treatments. Riluzole is a glutamatergic modulator with demonstrated antidepressant and anxiolytic properties in human trials. This randomized controlled trial evaluated the efficacy of acute riluzole augmentation treatment in veterans with PTSD, with or without mild traumatic brain injury, who were suboptimally responsive to standard pharmacologic treatments for PTSD.

Methods: Seventy OEF/OIF/OND veterans, aged 18 to 65 were enrolled from Walter Reed National Military Medical Center and the Syracuse Veterans' Affairs Medical Center in an 8-week randomized, double-blind, placebo-controlled trial. Participants met criteria for PTSD as determined by a score ≥40 on the Clinician-Administered PTSD Scale (CAPS-IV). Participants were randomized (1:1) to treatment with riluzole or placebo and continued on their current medications. Outcome variables included PTSD, depression, and anxiety, which were assessed at baseline, mid-point, and post-treatment. Multivariate analyses controlled for covariates (gender, race, age, marital status and pay grade).

Results: ANOVA results suggested there were no significant differences in PTSD (F (1, 59) = 2.75, p ≤.103), depression (F =.04, p ≤. 833) and anxiety (F = 1.28, p ≤ .263) symptoms. However, there was a significant difference in global functioning between participants randomized to riluzole compared to placebo (F = 6.62, p ≤.03).

Conclusions: The lack of significant effects of riluzole as augmentation treatment for PTSD in service members may be explained by a therapeutic effect of conducting serial psychological assessments and this may have accounted for a significant placebo effect. Further research is needed in a larger sample and across multiple types of military treatment facilities to ensure generalizable results.

Changes in State Anxiety Over 62 hours of Sleep Deprivation and Subsequent Recovery

Authors

Alexxa F. Bessey, MPS[1], Nora E. Prindle, MPS[1], Meghan Powers Armstrong, BS[1], Tina Burke, PhD[1], Vincent F. Capaldi, ScM, MD[1], Thomas J. Balkin, PhD[1], Tracy Jill Doty, PhD[1]

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1. Walter Reed Army Institute of Research, Silver Spring, MD

ABSTRACT

Background: Previous work has indicated increases in self-reported anxiety following one night of total sleep deprivation (TSD). This study extends previous work by assessing the effects of two nights of sleep deprivation on state anxiety as well as the effect of a single night of recovery sleep.

Methods: Seventeen healthy adults (7 females) ranging from 18–33 years of age participated. Self-reported state anxiety was assessed using the Spielberger State Trait Anxiety Inventory (STAI-S). The STAI-S was administered at 10am, 1pm, and 4pm under four sleep conditions 1) Baseline: day following one night of 8 hours of time-in-bed (TIB), 2) TSD1: day following one night of TSD, 3) TSD2: day following two nights of TSD 4) Recovery: day following 12 hours TIB after 62 hours of TSD. The data were analyzed with a 4 (Sleep Condition) x 3 (Time of Day) mixed linear model.

Results: There was a significant main effect of Sleep Condition, $F(3,192) = 15.94$, $p = 2.70 \times 10\text{-}9$. Post-hoc tests revealed that anxiety was significantly increased after one night of TSD compared to baseline ($p=0.009$). Additionally, anxiety reported following two nights of TSD was further increased compared to one night of TSD ($p=0.0008$). This increase in self-reported anxiety was reversed after one night of recovery sleep (decreased compared to TSD2, $p = 2.50 \times 10\text{-}9$; no difference compared to baseline, $p=0.37$). There was no main effect of Time of Day nor was there a significant interaction between Sleep Condition x Time of Day.

Conclusion: The present findings suggest that state anxiety levels, as measured by the STAI-S, increase across two nights of TSD and return to baseline following a single night of recovery sleep. These preliminary findings suggest that a single 12-hour period of sleep is sufficient for restoring baseline levels of state anxiety — a finding that has implications for determining appropriate 'recycle rates' (duration between missions) for Soldiers and others involved in continuous operations.

Daily Variation in Post Traumatic Stress Symptoms (PTSS) in Individuals With and Without Post Traumatic Stress Disorder

Authors

Quinn M. Biggs, PhD, MPH[1], Robert J. Ursano, MD[1], Jing Wang, PhD[1], David S. Krantz, PhD[1], Russell B. Carr, MD[2], Gary H. Wynn, MD[1], Deborah Probe, MA[1], Nicole M. Dacuyan, BS[1], and Carol S. Fullerton, PhD[1]

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2. Walter Reed National Military Medical Center, Bethesda, MD

ABSTRACT

Background: Little is known about the extent to which post traumatic stress symptoms (PTSS) vary from day to day. This study examined the variation of the PCL-5 total score and subscale scores by the day of the week, and whether day of week variation differs between individuals with and without PTSD.

Methods: Subjects ($N = 80$) were assessed for probable PTSD at enrollment. Using an ecological momentary assessment methodology, PTSS were assessed four times daily by self-report for 15 days. Linear mixed models were used to assess daily variation in the PCL-5 total score and four subscale scores (intrusion, avoidance, negative cognition, hyperarousal).

Results: The PCL-5 total score and all four subscale scores were higher on weekdays (Monday through Friday) versus weekends (Saturday and Sunday) in those with PTSD, but there were no weekday/weekend differences among those without PTSD. The PCL-5 total score and three subscales scores (intrusion, avoidance, hyperarousal) varied across the seven days of the week among participants with PTSD, but not among those without PTSD.

Conclusions: These first preliminary results indicate that among individuals with PTSD, post traumatic stress symptoms vary by the day of the week, with more symptoms on weekdays compared to weekends. Determining the factors associated with daily variation in PTSD symptoms may be important for treatment of PTSD.

Recent Stressful Experiences and Resilience Among US Army Soldiers At Risk for Suicide: Results from the Army Study to Assess Risk and Resilience among Servicemembers (Army STARRS)

Authors

Catherine L. Dempsey, PhD, MPH[1], David M. Benedek, MD[1], Matthew K. Nock, PhD[1], Tsz Hin Ng, MPH[1], Charlotte Riggs, MS[1], Pablo Aliaga, MS[1], Nicole Caulfield, BA[1], and Sydney DeStefano, BS[1]

Affiliations

1. Center for the Study of Traumatic Stress, Department of Psychiatry, Uniformed Services University of Health Sciences, Bethesda, MD
2. Department of Psychology, Harvard University, Boston, MA

ABSTRACT

Background: To identify the extent to which the presence, severity, and accumulation of stressful events (military/deployment-related and family/social-related) are risk factors for suicide.

Methods: Data are from the Army STARRS. Next of kin (NOK) and first line supervisors (SUP) of 168 Soldiers who died by suicide and 389 similar living (control) soldiers provided data via structured interviews. Multivariate logistic regression accounting for complex survey design was used to examine the association between recent stressors and suicide.

Results: NOK and SUP (retrospectively) reported recent interpersonal stressful events and increased risk of suicide: a spouse or partner left them (OR=7.8; OR=14.0); serious ongoing arguments or break-up with a close friend or family member (OR=4.6; OR=11.8) and some type of perceived failure or humiliation (OR=20.3; OR=16.4). Severity of occupational, legal and interpersonal stressful experiences were reported: career or job (OR = 4.6; OR = 3.2), social life (OR=2.4; OR = 13.4), love life (OR = 3.2; OR =7.8); family relations (OR = 6.0; OR = 4.2); and legal difficulties (OR = 3.7; OR = 5.5). Third parties also reported poor adaptation to change (OR=4.4; OR=3.8), difficulty managing stress (OR=3.3; OR=10.9) and inability to bounce back from setbacks (OR=6.5; OR=17.7).

Conclusions: This study identified several recent stressful experiences in the month prior to death associated with increased risk of suicide; specifically, relationship problems, career/job, legal difficulties and perceived failure or humiliation. Results suggest that ability to handle stress and to adapt to change may be useful predictors of suicide.

Profiles of Complicated Grief Symptoms and Depression Differentiate Types of Cognitive Failures in Bereaved Family Members

Authors

Joscelyn Fisher, PhD[1], Jing Zhou, MS[1], Alex Liu, MPH[1], Bilal Ali, BA[1], and Stephen Cozza, MD[1]

Affiliations

1. Center for the Study of Traumatic Stress, Department of Psychiatry, Uniformed Services University of the Health Sciences, Bethesda, MD

ABSTRACT

Background: Between 7-25% of bereaved individuals develop complicated grief (CG), characterized by persistent sense of bitterness and loss of meaning in life (Newson et al., 2001; Kersting et al., 2011; Prigerson et al., 1995). CG is also associated with memory and attention difficulties.

Objective: To determine whether these difficulties generalize to cognitive failures (minor errors in thinking that interrupt physical or mental action) and whether specific symptoms of CG are more associated with certain types of cognitive failures than others.

Method: Associations between types of cognitive failures (memory, distractibility, blunders, memory for names) and symptoms of CG (yearning, anger/bitterness, shock/disbelief, estrangement from others, hallucinations of the deceased) in participants (n=447) from the National Military Family Bereavement Study were investigated using linear regression. Depression scores were included as a covariate in each of the regression models because depression is often co-morbid with grief and can also lead to cognitive failures.

Results: CG symptoms of anger, estrangement and shock and depression predicted distractibility. In contrast, only shock and depression predicted both memory and blunders. None of the CG symptoms predicted memory for names, though depression was a significant predictor.

Conclusions: These symptom profiles and their associated pattern of cognitive failures provide evidence of individual differences in how cognitive capacity is affected in day-to-day activities following bereavement, suggesting future targets for intervention.

Clinical Response Profiles in Bereaved Family Members Fourteen Years after the September 11th Terrorist Attacks

Authors

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ABSTRACT

Background: Bereavement research on sudden, violent deaths often focuses on immediate or short-term effects, rather than long-term effects.

Objective: To determine long-term (nearly 15 years post death) patterns of clinical outcomes in family members who lost loved ones on September 11, 2001.

Methods: 603 family members were recruited to complete an online survey about their experiences and current symptom profiles. The questionnaire assessed background demographics, lifetime trauma history, prior mental health treatment requirements, interim life events, income adequacy, use of grief services and satisfaction with social support. To determine symptom profiles of individuals, latent class analysis was conducted.

Results: The analysis yielded three groups: *Healthy*, *Subclinical Symptomatic*, and *Highly Symptomatic and Impaired*. Much of the sample (68.4%) was in the *Healthy* group, endorsing low levels of grief, depression and generalized anxiety. The *Subclinical Symptomatic* (16.3%) and *Highly Symptomatic and Impaired* (15.4%) each had higher probabilities of meeting cutoffs for depression, grief and generalized anxiety. Both of these symptomatic groups also described fewer positive interim life events after 9-11 than the Healthy group. However, members in the *Highly Symptomatic and Impaired* group were more likely to have grief-related impairment and to have experienced lifetime traumas. 60% of participants in the *Highly Symptomatic and Impaired* group endorsed threshold level symptoms for PTSD compared to practically none in the other two groups.

Conclusions: Programmatic support needs to target the *Highly Symptomatic and Impaired* group and clinicians must be prepared to identify and meet the needs of these individuals. Programs should be developed to address risk contributors to these clinical outcomes. Monitoring of those in the *Subclinical Symptomatic* group is also required.

Effect of Stress and Polytrauma in a Rat Model

Authors

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ABSTRACT

Background: A stressful environment may influence the outcome of wounded persons and may trigger or exacerbate PTSD after traumatic brain injury (TBI). The current study evaluates the impact of acute stress in a polytrauma rat model.

Methods: Stress was produced by a 45-minute immobilization period and rats were then instrumented under ketamine anesthesia for blood collection (t1). Polytrauma was produced by blast overpressure and controlled hemorrhage (t2). Rats were monitored for 3 hours simulating MEDEVAC-transport time (t3). Rats were then euthanized immediately after t3 or after a minimum of 48 hour recovery (t4). Corticosterone, ACTH, and ACTH receptor gene expression were measured at these time points. Rats were distributed into the following groups: no-stress + no-injury (n=9 for t3 and n=14 for t4), no-stress + injury (n=7 for t3 and n=11 for t4), stress + no-injury (n=10 for t3 and n=13 for t4), and stress + injury (n=8 for t3 and n=10 for t4). Physiological parameters were monitored throughout the study.

Results: Animals in the stress group had higher HR than the no-stress group at t1. Corticosterone and ACTH levels were low and similar for all conditions at t1 and t2 and then became elevated in all groups at t4 for corticosterone and at t3 for ACTH. The ACTH receptor gene expression indicated a trend to higher values at t4 for the stressed animals being injured or not. **S**urvival after injury was 83% in both stress and no-stress groups vs 100% in controls.

Conclusion: Overall, corticosterone and laboratory outcomes were not significantly affected following acute stress in ketamine anesthetized rats. Mortality was primarily due to polytrauma with co-morbidities appearing at t4 post trauma. The effect of ketamine anesthesia or the surgery may have overshadowed the effect of the initial stress.

Prevalence of Mental Health Conditions in Bereaved Military Service Widows: A Longitudinal Case-Controlled Study

Authors

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ABSTRACT

Background: Bereavement is associated with deleterious psychiatric effects, particularly for young widows and/or when deaths are sudden and violent. Deaths of military service members are often sudden and violent and impact young widows, yet little research systematically examines psychological consequences of military bereavement. Further, few studies include control groups or examine changes in psychiatric functioning pre- and post-bereavement.

Methods: Using outpatient medical records from wives of active duty service members (n=1375), we compared prevalence of mental health conditions and mental health care visits among bereaved widows to matched (age, baseline physical and mental health utilization. service member spouse deployment and rank), time-yoked controls (n=1375), from one year prior (Yr-1) to two years following (Yr+1 and Yr+2) service member death. Prevalence risk ratios and confidence intervals were used to compare prevalence rates of psychiatric conditions and outpatient mental health visits among spouses over time.

Results: Spouses were an average of 32.2 years old (SD=8.4). Service member deaths related to combat (30.0%), non-hostile in-theater (9.3%) or others outside theater (60.7%). Compared to controls, prevalence of both unique psychiatric conditions (depression, adjustment disorder, PTSD) and any psychiatric disorder significantly increased from Yr-1 to Yr+1 and Yr+2 for cases. Cases, but not controls, had significantly greater outpatient mental health visits following service member death (Yr+1 and Yr+2, vs. Yr-1).

Conclusions: Bereavement among a large sample of young military widows was associated with increases in diagnosis of depression, adjustment disorder, and PTSD and overall rates of psychiatric conditions. This was accompanied by increases in mental health service utilization. Present data lack information related to complicated grief diagnosis, which may have been coded as another disorder. However, these novel findings can inform improved intervention and screening for bereaved military spouses.

Gene Expression Based Measures of Chronic Stress Exposure

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ABSTRACT

Background: The risk of developing post-traumatic stress disorder (PTSD) in response to stress exposure may be dose-dependent, increasing with both the severity of the stressors as well as cumulative exposure to multiple stressors. Effects of stress are likely to be encoded, in part, by changes in the gene regulatory network. We tested these hypotheses and showed that we can construct a stress-sensitive gene expression (SSGE) index that functions as a measure of stress exposure.

Methods: Male rats were exposed to one of six different three-week long stress paradigms: social isolation, social defeat, social defeat with isolation, grid housing, chronic variable stress (CVS), and chronic shock (CS). RNA sequencing was used to measure changes in the transcriptome of the adrenal gland following exposure to the two most intense stress protocols, CVS and CS. Expression changes in candidate genes were confirmed using real-time PCR. Selected genes, whose expression levels consistently changed, were used to construct a SSGE index that was then validated across all six stress models.

Results: The SSGE index allowed a diagnostic distinction between control and stressed animals, detecting every type of stress exposure in a manner that was relatively independent of the modality of stress and that paralleled the intensity of stress exposure in a dose-dependent manner. There were also a subset of modality-specific genes that could distinguish between types of stress protocols.

Conclusions: A sensitive, quantitative, and robust measure of chronic stress exposure can be constructed from gene expression data. The SSGE index could reliably assess stress exposure across a wide range of stress modalities. Gene expression indexes may prove to be a useful adjunct to behavioral and hormonal measures of stress exposure since they are relatively inexpensive to implement and many steps can be automated to be scaled for large numbers of animals.

Poor Responses to Intravenous Morphine Analgesia Predict Opioid Addiction Vulnerability in Sprague-Dawley Rats

Authors

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ABSTRACT

Background: More than 110 Americans die every day after overdosing on opioids and the misuse of and addiction to opioids is a national crisis that costs $78 billion a year due to healthcare, lost productivity, addiction treatment, and criminal justice involvement. Therefore, developing improved strategies for pain management and opioid addiction are urgently needed.

Methods: We investigated association between responses to intravenous (IV) morphine analgesia and development of morphine addiction using a rodent model. Adult male Sprague-Dawley rats with indwelling catheters in the jugular vein were screened based on their analgesic responses to an IV bolus morphine (2.5 mg/kg) using a hot plate test.

Results: Using a median split of hot plate data, the animals were divided into 2 groups: Good Analgesia (GA) including top 50% and Poor Analgesia (PA) including bottom 50% of the animals. The animals were allowed to self-administer either IV saline or morphine (0.5 mg/kg/injection) 4 hours per day for 15 days. Morphine self-administering animals displayed reduced defecation, urination, and delayed body weight gain as compared to the saline self-administering animals. Among the morphine animals, acquisition of morphine self-administration (MSA) behavior was not different between the GA and the PA group. However, the PA group escalated morphine intake and exhibited a greater locomotor activity during the maintenance phase of MSA, as compared to those of the GA group.

Conclusion: The current results suggest that certain individuals showing poor responses to opioid analgesia may be at increased risk of developing opioid addiction after repeated use of opioids. Therefore early identification and intervention of vulnerable individuals to opioid addiction may improve the current opioid crisis in the U.S.

Fear Learning Deficits and Myelin-Related Structural Changes in a Blast Model of Mild Traumatic Brain Injury (mTBI)

Authors

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ABSTRACT

Background: PTSD and other psychiatric symptoms are often comorbid with mild traumatic brain injury (mTBI). In military and civilian settings, some mTBI results from exposure to blasts. We used a mouse blast model to investigate whether emotional and cognitive effects are seen at acute and long-term time points from the blast injury, detect structural alterations of glial cells and myelin, and infer which brain region(s) are mostly affected.

Methods: We subjected cohorts of mice to one or four blasts (once a day) and performed cued fear learning/extinction/retrieval/renewal or trace fear conditioning tests. Two days after the behavior test, we perfused and collected the brain tissues under deep anesthesia, and performed RT-qPCR for glial/myelin-related genes from several brain areas. Other cohorts were perfused for immunohistochemical and electron microscopy analyses.

Results: Following single or repeated blast exposures, fear extinction learning and retrieval/renewal were not markedly altered when tested at various time points after the injury. However, in a trace fear conditioning test, a form of associative leaning, blast produced an impairment in the temporal organization of fear behavior in relation to the onset and offset of the conditioned stimulus. RT-qPCR analysis for glial markers revealed altered expression of myelin-related genes in the hippocampus 2-4 weeks after blast and a more widespread effect 8 weeks after blast. Myelin basic protein staining and nodes of Ranvier marker staining by immunohistochemistry supported these alterations at the protein level.

Conclusions: We revealed learning deficits in both single and repeated blast exposure. Moreover, we found that the blast is affecting the myelin in specific brain areas, viz., hippocampus and corpus callosum. These observations suggest possible therapeutic opportunities for blast injury.

Family Risk Factors for Child Neglect Types

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ABSTRACT

Background: Child neglect is the type of child maltreatment most commonly reported in the U.S. and most frequently associated with child fatality. However, neglect remains understudied compared to other types of child maltreatment. Although recent empirical research suggests that neglect is a heterogeneous phenomenon characterized by distinct types, the factors that increase the likelihood of different types of neglectful parenting are largely unknown.

Objectives: To advance knowledge concerning risk factors for specific types of child neglect, this study examined family factors associated with five neglect types including *failure to provide physical needs*, *lack of supervision*, *emotional neglect, moral-legal neglect*, and *educational neglect* in substantiated cases of child neglect.

Methods: Data were drawn from 390 case files of substantiated child neglect in U.S. Army families. Multivariate logistic regression was used to examine unique associations between each family factor and elevated risk of each neglect type in models with family demographic characteristics included as covariates.

Results: Approximately 73% of families reported at least one of the 15 risk factors examined. Neglect types were associated with relatively distinct constellations of family risk factors. Family mental health problems and larger family size were associated with risk of failure to provide physical needs, childcare problems and larger family size were associated with risk of supervisory neglect, and family disagreements were associated with risk of emotional neglect. None of the family factors were associated with elevated risk of moral-legal or educational neglect.

Conclusions: Findings provide evidence of family factors differentially associated with elevated risk of physical, supervisory, and emotional neglect. Results inform the development of targeted preventive interventions for families affected by different neglect types.

Post-Traumatic Stress Disorder in Female Service Members and Veterans

Authors

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ABSTRACT

Background: The response to horrific events can lead to post-traumatic stress disorder (PTSD) (Eagle & Kaminer, 2015). As the number of women serving in the U.S. military increases, it is important to determine what female veterans know about PTSD. The purpose of this study was to determine if an educational program on the symptoms and treatment of PTSD increases the knowledge level of female veterans and encourages them to seek medical and mental health care.

Methods: Forty-four U.S. female reservists, Guardsmen, and veteran volunteers from a military base in New Jersey participated in this quantitative pre-test/post-test educational intervention study. Prior to the intervention participants completed a consent, demographics form and pre-test to obtain baseline knowledge. After watching introductory slides and five, three-minute videos from the National Center for PTSD, participants completed a post-test, an evaluation of the videos, and a survey of intent to seek medical and/or mental health care.

Results: Using SPSS Version 24, the dependent *t*-test was calculated. The mean of the post-test 21.0, was significantly higher than the pre-test, 15.59, $t(43) = -11.472$, $p = .000$. Descriptive statistics were conducted for the survey of intent with 18 of the 44 participants indicating they would seek medical care; 19 indicating they would seek mental health care.

Conclusions: After completing this educational program on PTSD, participants were able to define and recognize symptoms of PTSD; discuss current types of evidence-based treatments for PTSD; and indicate willingness to seek medical and mental health care. There was a statistically significant improvement in the knowledge level of the participants following the educational program.

Sub-Anesthetic Intravenous Ketamine Infusion Enhances Fear Memory and Brain Glucose Metabolism (^{18}f-Fdg Pet) in Sprague-Dawley Rats

Authors

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ABSTRACT

Background: Ketamine is the most common battlefield analgesic administered to traumatically injured service members in Afghanistan. However, the impacts of peri-trauma ketamine administration on the development of post-traumatic stress disorder (PTSD) are controversial and remain largely unknown. Moreover, there is a gap between pre-clinical and clinical studies because they utilize different doses and routes of ketamine administration.

Methods: We investigated the effects of different doses of intravenous ketamine infusion on fear memory and *in vivo* regional brain glucose metabolism (BGluM) in rats. Male Sprague-Dawley rats received a sub-anesthetic ketamine infusion (0, 2, 10, or 20 mg/kg, over 2 hours) either immediately after or 1 day after auditory fear conditioning (3 tone and footshock [0.6 mA, 1-sec] pairing). Fear memory retrieval, extinction, and renewal were tested on days 2, 3, and 4 post-fear conditioning and ketamine infusion. The effects of ketamine infusion (0 and 10 mg/kg) and fear memory retrieval on BGluM were measured using 18F-fluoro-deoxyglucose positron emission tomography (FDG PET) and computed tomography (CT).

Results: The ketamine infusion, both immediately after and 1 day after fear conditioning, dose dependently enhanced cued fear memory retrieval, delayed fear extinction, and enhanced contextual and cued fear renewal in rats. The ketamine infusion (10 mg/kg) increased BGluM in the hippocampus, amygdala, hypothalamus, and midbrain, while decreasing it in the cerebellum of rats.

Conclusion: The current findings suggest that sub-anesthetic doses of ketamine infusion following traumatic events may enhance fear memory via activation of brain regions that are critical for fear and stress.

Self-Reported Insomnia Symptoms Prior to a Simulated Deployment Training Operation Robustly Predicts Post-Training Posttraumatic Stress Symptoms in the Warfighter

Authors

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ABSTRACT

Background: This study investigated the relationships between self-reported sleep quality and posttraumatic stress symptoms (PTSS) in a large military unit prior to and immediately following a simulated deployment training operation.

Methods: 427 US Army Soldiers (24.9 y/o ± 5.57; 89% male) self-reported on Insomnia Severity Index (ISI) items, total sleep time(TST) extracted from the Pittsburgh Sleep Quality Index (PSQI), and the Posttraumatic Stress Disorder Checklist-Military Version, four-item version (PCL-4) pre- and post-training.

Results: Group differences in TST were found between number of years served in the military, [pre: F (2, 355) = 3.91, p = .021; post: F (2, 309) = 3.35, p = .036] and rank type, [pre: F (3, 375) = 2.75, p = .042; post: F (3, 325) = 5.59, p < .001.] ISI items indicated subthreshold insomnia at pre-training (M = 8.33 ± 3.72) and post-training (M = 8.35 ± 3.84). Soldiers had significantly less PTSS pre-training compared to post-training, t (346) = -5.07, p < .001. Group differences in PTSS were found in rank type, [post: t (67.68) = -2.24, p = .028], and in number of years served in the military [pre: F (2, 356) = 4.39, p = .013; post: F (2, 306) = 3.10, p = .047]. Multiple linear regression models showed pre-training ISI items and TST both individually and synergistically predicted post-training PTSS. However, the final model determined to best fit the data contained only ISI as a significant predictor of PTSS, β = .35, p = .001 and explained 44.2% of model variance, R^2 = .20, F (1, 55) = 13.35, p = .001.

Conclusion: This study is one of the first of its kind showing military-related factors help to characterize and predict sleep quality and PTSS in Soldiers. Future research will test the effectiveness of sleep-related interventions for reducing PTSS risk in Soldiers.

Neurophysiology of Anger in PTSD

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ABSTRACT
Background: Traumatic stress in PTSD patients may lead to explosive anger, but not necessarily violence. To help target interventions to reduce anger prior to becoming violence, the research herein is directed at neurophysiology of anger per sé.

Methods: A rodent model of anger is developed in which theta-frequency electrical stimulation in medial amygdala of a resident rat ("θ MeA") results in the resident pushing, pining, and putting its mouth to the throat of the intruder — that is, being angry — but not biting the intruder, which is being violent. Using implanted electrodes, (1) magnitude of evoked synaptic transmission and (2) frequency of local field oscillation (LFO or EEG) are measured in medial amygdala (MeA), hippocampus (HC), pyriform cortex (Pyr), and lateral septum (LS):

Results:
1. θ MeA evokes behaviorally evinced anger in the rat, but not violence.
- During this anger, synaptic transmission from MeA to HC and Pyr, but not LS, is enhanced, 200% to HC, 100% to Pyr.
- No enhancement was recorded during vigilance or chases.

2. LFO in HC, LS, Pyr:
- Varies between 7 Hz and 8Hz theta at rest.
- Complex waves lasting a few seconds appear during vigilance, chase, and anger. These waves are an order of magnitude greater in amplitude than the baseline theta, and composed of the full range of frequencies - delta, theta, alpha, beta, gamma.
- Ongoing analysis is determining which components of the LFO in each structure are correlated with which behavior or behaviorally evinced emotion.

Conclusions: Whereas anger is a state-of-mind described by humans, its animal equivalents can only be inferred. Regardless, that this state is distinct from violence in a rat model suggests there may be targets specific for anger intervention.

Association of N-Acetylaspartate Concentration in Anterior Cingulate and Amygdala with Treatment Response to Riluzole Augmentation for Posttraumatic Stress Disorder

Authors

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ABSTRACT

Background: Drugs that alter neuronal survival pathways through reduction of glutamate activity may play a role in reversing the loss of neuronal integrity and possible focal atrophy in regions of the brain implicated in the pathophysiology of posttraumatic stress disorder (PTSD). Riluzole is a glutamatergic modulator with demonstrated antidepressant and anxiolytic properties. Proton magnetic resonance spectroscopy (^{1}H MRS) studies using N-acetylaspartate-to-creatine (NAA/Cr) ratios have found reduced NAA/Cr ratios in the hippocampus and anterior cingulate (ACC) of PTSD patients. This randomized controlled trial evaluated the efficacy of acute riluzole augmentation treatment in veterans with PTSD, with or without mild traumatic brain injury, who were suboptimally responsive to trial with an SSRI or SNRI.

Methods: Thirty-two OEF/OIF/OND veterans, aged 18 to 65 at Walter Reed National Military Medical Center with suboptimal response to SSRI or SNRI treatment for PTSD were randomized to augmentation with riluzole or placebo for 8 weeks. ^{1}H-MRS acquisition was performed on a 3.0 Tesla GE750, targeting a 20x20x20cm voxel in midline ACC and a 15x12x12cm voxel in right amygdala. We assessed pre-to-post-treatment NAA/Cr ratios and absolute NAA concentrations. We hypothesized that (1) NAA/Cr ratios and absolute NAA concentration in the amygdala and ACC would increase after 8-week treatment with riluzole.

Results: ^{1}H-MRS imaging results will indicate whether there was a significant difference in response to riluzole versus placebo as measured by changes in pre- to post-treatment NAA/Cr ratios and absolute NAA concentration in the anterior cingulate and amygdala.

Conclusions: ^{1}H-MRS imaging results may provide evidence of riluzole's efficacy in increasing neuronal health in the ACC and amygdala as evidenced by changes in pre- to post-treatment NAA/Cr ratios in the ROIs. This indicator of neuronal integrity in the areas of interest may serve as a biomarker for treatment response.

Daily Influence of Sleep Duration on Post Traumatic Stress Symptoms in Individuals with and without Post Traumatic Stress Disorder

Authors

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ABSTRACT

Background: This study examined the daily association between PTSS and sleep duration in individuals with and without PTSD.

Methods: Subjects (*N* = 80) were assessed for probable PTSD at enrollment (n = 42 with PTSD, n = 38 without PTSD). Using an ecological momentary assessment methodology, PTSS were assessed four times daily by self-report for 15 days (range = 0-180). Sleep duration was assessed daily, and partitioned into overall (person mean) and daily (difference between hours of sleep during the previous night and person mean). Linear mixed models were used.

Results: Preliminary results indicate that among individuals with PTSD, there was a negative association between daily sleep duration and PTSS. One more hour of sleep than usual was associated with a decrease of 1.23 in PTSS the following day. Among individuals without PTSD, overall sleep duration was negatively associated with PTSS, but PTSS did not vary by sleep duration on a daily basis.

Conclusions: These first preliminary findings support the possibility that sleeping longer is a means to reduce PTSS in individuals with PTSD. Assessing and monitoring changes in sleep and PTSS across time may therefore lead to a better understanding of individual sleep patterns and their effect on PTSS.

Genetic Association of FKBP5 with PTSD through Mitochondrial Dysfunction

Authors

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ABSTRACT

Background: Post-traumatic stress disorder (PTSD) is a debilitating mental disorder with prevalence rates of more than 7% in the US population[1] and 12% in the military.[2] FKBP5, a glucocorticoid-regulated immunophilin, is thought to be associated with PTSD. However, the underlying mechanisms are unknown.

Objectives: We use both in *vivo* and *in vitro* methods to study the association of FKBP5 with PTSD in a high-risk military population.

Methods and Results: Samples (n=3890) were collected from US Army service members between 2008 and 2016. PTSD symptoms were assessed using the PTSD Checklist (PCL). All study procedures were approved by the Institutional Review Board at USUHS and all participants were given written informed consent. We first demonstrate that four single-nucleotide polymorphisms (SNPs, rs3800373, rs9296158, rs1360780, rs9470080) covering the FKBP5 gene are associated with lifetime PTSD in soldiers, using genotyping. An up-regulated FKBP5 protein and increased cortisol levels were also observed in soldiers with PTSD using enzyme-linked immunosorbent assay. Accordingly, treatment of SH-SY5Y cells with dexamethasone (Dex), which resembles the traumatic condition *in vitro*, led to a FKBP5 mitochondrial redistribution and subsequent changes in mitochondrial membrane potential ($\Delta\Psi m$) and mitochondria reactive oxygen species (mROS). The FKBP5 inhibitor FK506 pharmacologically attenuated these effects of Dex, indicating that FKBP5 is necessary for the regulation of mitochondrial function. Further studies found that FKBP5 co-localizes with the mitochondria in leukocytes of PTSD subjects. In addition, we found significant down-regulation of mitochondrial complexes I, II and III in PTSD compared to non-PTSD controls, supporting our finding of possible mitochondrial dysfunction in this disorder.

Conclusions: Our study provides new insight into a mechanism of FKBP5 in PTSD. Specifically, FKBP5 is associated with PTSD through its mitochondrial redistribution leading to mitochondrial dysfunction during stress and therefore represents a promising treatment target.

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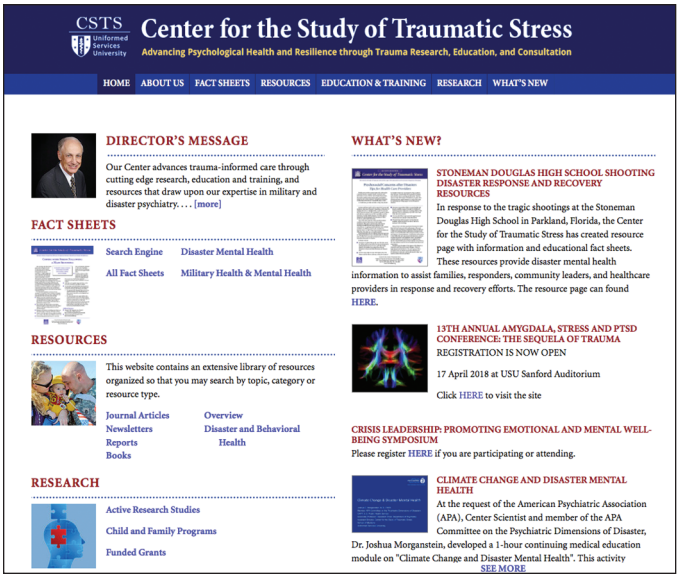
The Amygdala, Stress, and PTSD Conference, in conjunction with the Center for Deployment Psychology at the Uniformed Services University is pleased to offer up to 4.75 continuing education credits for Physicians, Psychologists, Social Workers, and Nurses. The credits are available through live in person attendance and as a webinar.

Continuing Education made possible in part by the generous support of the Center for Deployment Psychology.



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