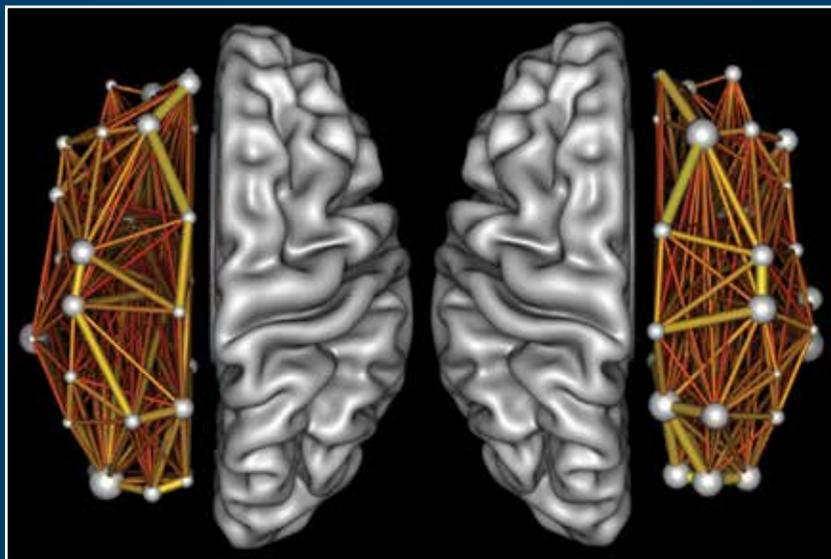


UNIFORMED SERVICES UNIVERSITY
CENTER FOR THE STUDY OF TRAUMATIC STRESS

12th Annual Amygdala, Stress and PTSD Conference: Understanding Stress

APRIL 18, 2017

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



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SPONSORED BY:

**The Center for the Study of Traumatic Stress (USU), Department of Psychiatry (USU),
Neuroscience Program (USU), Department of Family Medicine (USU), and
Department of Psychiatry (WRNMMC)**



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Department of Psychiatry (WRNMMC)**



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 *12th Annual Amygdala, Stress and PTSD Conference: Understanding Stress*.

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0900-0905	Conference Announcements — Gary H. Wynn, MD
0905-0915	Welcome and Introduction — Robert J. Ursano, MD
0915-1000	Ronald S. Duman, PhD — <i>Molecular and Cellular Studies of PTSD: Postmortem Transcriptome Analysis and Novel Therapeutic Agents</i>
1000-1045	Doug Williamson, PhD — <i>On the Road to Discovery: Identifying Novel Genes Associated with PTSD</i>
1045-1115	Coffee Break and Poster Review in Lobby
1115-1145	Discussion Panel 1 — Moderator, James Reeves, MD
1145-1245	Lunch
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1330-1415	Steven E. Bruce, PhD — <i>Examination of Neural Improvements after Cognitive Behavioral Therapy for PTSD</i>
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1600-1615	Robert J. Ursano, MD — <i>Closing Remarks and Presentation of Poster Award</i>

Conference Speakers

Regina C. Armstrong, PhD



Dr. Armstrong is Director of the Center for Neuroscience and Regenerative Medicine (CNRM). The CNRM is a collaborative intramural research program of the Uniformed Services University of the Health Sciences (USU) with the National Institutes of Health (NIH) and the Walter Reed National Military Medical Center (WRNMMC). The

CNRM focus is pre-clinical through clinical research to promote recovery from traumatic brain injury and to improve psychological health in combat casualties cared for at WRNMMC.

Dr. Armstrong earned a B.S. in Neuroscience from the University of Rochester, where she began research training in multiple sclerosis at the Center for Brain Research. She was a National Science Foundation Fellow for work toward her Ph.D. in Neurobiology at the University of North Carolina at Chapel Hill. She did postdoctoral training at the National Institute for Neurological Disorders and Stroke (NIH).

Dr. Armstrong's primary academic appointment is as Professor of Anatomy, Physiology, and Genetics in the F. Edward Hebert School of Medicine at USU. Dr. Armstrong holds secondary appointments in the Neuroscience and the Molecular and Cell Biology Graduate Programs. Dr. Armstrong received the faculty award for Outstanding Graduate Biomedical Educator from the School of Medicine in 2002. She served as Director of the USU Neuroscience Graduate Program from 2002–2008 before stepping down to begin as Director of the CNRM. Dr. Armstrong teaches in the first year medical student module on the nervous system and in several graduate student courses. Dr. Armstrong's laboratory focuses on mechanisms of damage and repair in the brain and spinal cord. This work employs diverse research approaches, from molecular techniques to neuroimaging, to address ways to improve neuroregeneration and repair capacity in the CNS. Research efforts in her laboratory have been funded through peer-reviewed competitive awards from the NIH, the National Multiple Sclerosis Foundation, and the Department of Defense.

Steven E. Bruce, PhD



Steven E. Bruce, PhD is the Director of the Center for Trauma Recovery, Director of Clinical Training, and Associate Professor of Psychological Sciences at the University of Missouri-St. Louis. He received his Ph.D. in Clinical Psychology from Virginia

Commonwealth University in Richmond, Virginia. He then completed his internship at the Medical University of South Carolina in Charleston, SC and a post-doctoral fellowship at Brown University School of Medicine in Providence, RI. Dr. Bruce is a member of several scientific organizations including the Association for Behavioral and Cognitive Therapies (ABCT) and the Society for Neuroscience (SFN) and has served on several editorial boards. He has authored or co-authored over 50 publications and over 150 presentations in the area of anxiety disorders. Dr. Bruce's primary research interests and clinical specializations include the treatment of anxiety and affective disorders, particularly post-traumatic stress disorder. Specifically, Dr. Bruce is interested in conducting translational research incorporating neuroimaging and psychophysiological assessment as both predictors and outcomes of cognitive behavioral treatment response.

Ronald S. Duman, PhD



Dr. Duman is Professor of Psychiatry and Neurobiology and Director of the Abraham Ribicoff Research Facilities at the Yale University School of Medicine. Studies from Dr. Duman's laboratory have contributed to the characteriza-

tion of the molecular and cellular actions of stress, depression, and antidepressants providing the basis for a neurotrophic and synaptic hypothesis of depression. This hypothesis is based on work demonstrating that chronic administration of a typical antidepressant or a single dose of a rapid acting agent like ketamine blocks or reverses the neuronal atrophy that is caused by stress and depression. Dr. Duman's work has demonstrated that increased neurotrophic factor levels and increased synapse formation underlie the actions of rapid acting antidepressants. These findings represent major advances in our understanding of the effects of antidepressants and provide a framework for the development of novel therapeutic agents. More recent studies from Dr. Duman's laboratory have focused on the cellular mechanisms underlying traumatic stress, including transcriptional and proteomic studies of postmortem brain tissue from PTSD subjects, and studies of novel rapid acting agents for the treatment of PTSD. Dr. Duman has been the recipient of several prestigious awards, including the Anna-Monika Prize, Nola Maddox Falcone Prize, Janssen Prize, NIMH MERIT Award, and a NARSAD Distinguished Investigator Award. He is a member of the National Academy of Sciences. Dr. Duman is author of over 300 original articles, reviews and chapters and has given over 250 invited lectures. He has also served as a consultant to Pfizer, Lilly, Johnson & Johnson, Lundbeck, Taisho, Naurex, Navitor, and Allergan.

Sandro Galea, MD, MPH, DrPH



Dr Galea is a physician and an epidemiologist. He is the Robert A. Knox Professor and Dean at the Boston University School of Public Health. Prior to his appointment at Boston University, Dr Galea served as the Gelman Professor and Chair of the Department of Epidemiology at the Columbia

University Mailman School of Public Health. He previously held academic and leadership positions at the University of Michigan and at the New York Academy of Medicine.

In his scholarship, Dr Galea is centrally interested in the social production of health of urban populations, with a focus on the causes of brain disorders, particularly common mood-anxiety disorders and substance abuse. He has long had a particular interest in the consequences of mass trauma and conflict worldwide, including as a result of the September 11 attacks, Hurricane Katrina, conflicts in sub-Saharan Africa, and the American wars in Iraq and Afghanistan. This work has been principally funded by the National Institutes of Health, Centers for Disease Control and Prevention, and several foundations. He has published over 640 scientific journal articles, 50 chapters, and 10 books and his research has been featured extensively in current periodicals and newspapers. His latest book, co-authored with Dr Katherine Keyes, is *Population Health Science*, was published by Oxford University Press in 2016.

Dr Galea has a medical degree from the University of Toronto, and graduate degrees from Harvard University and Columbia University; he has an honorary doctorate from the University of Glasgow. He was named one of TIME magazine's epidemiology innovators and has been listed by Thomson Reuters as one of the "World's Most Influential Scientific Minds" for the Social Sciences. He is past-president of the Society for Epidemiologic Research and an elected member of the National Academy of Medicine and of the American Epidemiological Society. Dr Galea has received several lifetime achievement awards for this research, including the Rema Lapouse Award from the American Public Health Association and the Robert S Laufer Award from the International Society for Traumatic Stress. He is a regular contributor to *Fortune* magazine and has

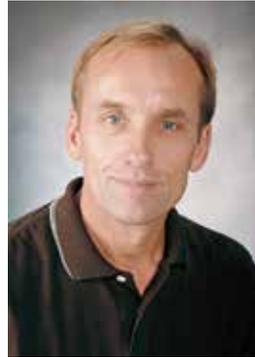
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Sandro Galea, MD, Continued

published widely in lay press including in the *Wall Street Journal*, *Harvard Business Review*, the *Boston Globe*, the *New York Times*. His research has been cited in these journals and in BBC, Slate, WBUR, and NPR, among others.

Dr Galea serves frequently on advisory groups to national and international organizations. He currently serves on the Advisory Council on Minority Health and Health Disparities and has formerly served as chair of the New York City Department of Health and Mental Hygiene's Community Services Board and as member of its Health Board.

Doug Williamson, PhD



Douglas E. Williamson is a Professor at Duke University in the Department of Psychiatry and Behavioral Sciences and the Director of the Translational Center for Stress-Related Disorders. Dr. Williamson's research interests fall within the emerging field of translational epidemiology – a discipline that considers the

population level characteristics of stress-related diseases and integrates mechanistic studies in the identification and characterization of risk factors associated with their onset.

Dr. Williamson's earlier research examined the familial aggregation of depression in children and adolescents and the role of familial risk for depression on the risk to develop depression early in the life span. This research has led to insight into potential genetic and environmental risk factors for depression and anxiety and has extended to understanding the role of the developing brain. This research has shown that adolescents at high familial risk for depression have a heightened amygdala response to stimuli and that subtle shifts in epigenetic state of gene (e.g. DNA methylation) further potentiate this heightened reactivity resulting in the emergence of initial symptoms of depression.

Currently, Dr. Williamson is leading efforts for the STRONG STAR Multidisciplinary Research Consortium to identify genetic and environmental contributors to PTSD. Toward this end, Dr. Williamson and colleagues are using population samples of active duty soldiers screened before and after deployment to identify genetic variants associated with PTSD as well as genes that are uniquely dysregulated following exposure to combat-related trauma among soldiers developing PTSD. Dr. Williamson also currently leads efforts for the Consortium to Alleviate PTSD (CAP), a national effort established as part of the White House's National Research Action Plan in 2013 to address the public health burden of PTSD. Dr. Williamson and colleagues are identifying unique genetic and epigenetic biomarker signatures of PTSD, risk to develop PTSD, and predictors of treatment response for PTSD.

Moderators

James Reeves, MD



Born in Portsmouth, Virginia and raised in Houston, Texas, CAPT Reeves graduated from Southwestern University with a degree in Biology in 1992. He completed his Doctor of Medicine at the University of Texas Health Science Center San Antonio in 1996 and his residency in psychiatry at the

University of North Carolina Hospitals in Chapel Hill where he was chief resident in 2000.

CAPT Reeves began his Navy career in 2000 as a staff psychiatrist at the Walter Reed Army Medical Center and the National Naval Medical Center. He assisted in the relief efforts both at Washington DC and New York City during 9/11 and published 3 papers on the topic. CAPT Reeves was then selected to become the 1st Marine Division (1MARDIV) psychiatrist at Camp Pendleton where he oversaw mental health for the 1st Marine Expeditionary Force in Al Anbar province, Iraq during 2004 and published in the Marine Corps Gazette on operational stress control. From 2005 to 2009 he served as the psychiatry residency director at the Naval Medical Center San Diego. In 2009 CAPT Reeves was selected to become the Office of the Secretary of Defense's (OSD) lead on global health in OSD-Policy where he oversaw the Department of Defense's \$99 million HIV/AIDS prevention program. CAPT Reeves was selected as the Director for Mental Health at Naval Medical Center Portsmouth where he led 320 personnel across Hampton Roads to include inpatient, outpatient and substance abuse services as well as 2 training programs and served on the Command Executive Board. CAPT Reeves is currently serving as the Director of Training and Professional Development for the Center for Global Health Engagement at the Uniformed Services University of the Health Sciences (USUHS). He also serves as the Specialty Leader for Navy Psychiatry where he leads the Navy's 145 psychiatrists and manages Navy mental health policy.

CAPT Reeves remains an Associate Clinical Professor of Psychiatry at the Uniformed Services University of the Health Sciences and previously served as a board examiner for the American Board of Psychiatry and Neurology. He received the 2015 Sears Award for most outstanding Navy psychiatrist.

James C. West, MD



Dr. West is Assistant Professor of Psychiatry and a Scientist at the Center for the Study of Traumatic Stress, Uniformed Services University of the Health Sciences. He earned his B.S.E. from the United States Naval Academy in 1989 and his M.D. from the University of Michigan Medical School

in 2001. He served eight years as a submarine warfare officer in the Navy and completed residency training in psychiatry at Naval Medical Center Portsmouth, Virginia. He has completed tours with First Marine Division in Camp Pendleton, California and National Naval Medical Center, Bethesda, Maryland. He deployed in 2006 to Fallujah, Iraq as Operational Stress Control and Readiness (OSCAR) psychiatrist for Regimental Combat Team 5 and in 2010 to Helmand Province, Afghanistan as Combat and Operational Stress Control Officer for Combat Logistics Regiment 15 (Fwd). He served on the leadership team integrating with Walter Reed Army Medical Center as Assistant Deputy Commander and Deputy Commander of Behavioral Health at Walter Reed National Military Medical Center.

Dr. West is a fellow of the American Psychiatric Association and currently serves as assembly representative for the Society of Uniformed Services Psychiatrists. His professional interests include research into assessment methods in psychiatry education, and translating understanding of biological underpinnings of PTSD and trauma-related disorders into more effective treatments.

Conference Leadership

Gary H. Wynn, MD LTC, MC, USA



Dr. Wynn is Associate Professor of Psychiatry 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 12th year and President of the Society of Uniformed Services Psychiatrists. In addition, Dr. Wynn has over 50 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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Conference Posters

Presented in the Lobby

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MicroRNAs Expression in Basolateral Amygdala of Rats Associated with Stress Vulnerability and Resilient Sleep Patterns: Implications for Posttraumatic Stress Disorder

Authors

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ABSTRACT

Background: Sleep problems are prevalent in military veterans with PTSD. An animal model of PTSD shows that the basolateral amygdala (BLA) mediates the effects of fear memory on REM sleep. However, the molecular mechanisms underlying through which the BLA affects sleep are virtually unknown. The main objective of this study was to identify and characterize the role of stress-associated miRNAs that mediate the relationship between stress-related memories and sleep, using an animal model of PTSD.

Methods: Adult Wistar rats were prepared for recording sleep and possible muscimol (MUS) micro-

injections into BLA. The rats were then randomly assigned to a non-stressed, home cage control group (HC), or to a shock training (ST) (20 trials, 0.8 mA, 0.5 sec, 1 min ISI) group. Based on relative amounts of REM sleep in the first 2 hrs following ST, the rats were further designated as vulnerable (Vul, lower REM) or resilient (Res, higher REM). One subgroup of rats was sacrificed at 2 hrs after ST (ST-Vul and ST-Res), and another subgroup received MUS microinjections before ST and were subsequently sacrificed at 2 hrs after context re-exposure (CTX-Vul and CTX-Res). Global miRNA expression profiles from the BLA and their alterations were generated using TaqMan[®] MicroRNA Array cards and Stat-Miner[®] software.

Results: Altered miRNAs were observed in the BLA. Animals with reduced REM sleep showed increased miRNA dysregulation. Ingenuity pathway network analysis indicates that these altered miRNAs in the BLA may play an important role in the regulation of genes associated with PTSD and sleep.

Conclusions: This study suggests that directionally different alterations in REM following stress are associated with differential miRNA expression in BLA, a region that mediates the effects of stress and stressful memories on sleep. Further studies are needed to delineate the role of these miRNAs in mediating stress outcomes.

Reversal of Stress-Induced Social Interaction Deficits by Buprenorphine

Authors

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3. Department of Pharmacology and Molecular Therapeutics, Uniformed Services University of the Health Sciences, Bethesda

ABSTRACT

Background: Post-traumatic stress disorder (PTSD) symptom clusters as defined by the DSM 5 criteria include intrusion, avoidance, altered arousal and negative cognition/mood. Frequently, patients report persistent problems with social interactions and significant detachment from others. Chronic social defeat stress (CSDS) is a widely used rodent model of stress that produces robust and persistent social interaction deficits. Avoidance of other rodents can be reversed following chronic administration of selective serotonin reuptake inhibitors (SSRIs), the only pharmaceutical class for treating PTSD approved by the U. S. Food and Drug Administration. In this study, the sensitivity of social interaction deficits evoked by 10 days of CSDS to prospective treatments for PTSD was examined.

Methods: The effects of acute and repeated treatment with low dose buprenorphine (BPN, 0.25 mg/kg/day) on social interaction deficits in male C57BL/6 mice were studied. A separate cohort of mice were treated with either the SSRI fluoxetine (FLX, 10 mg/kg/day), the NMDA antagonist ketamine (KET, 10 mg/kg/day) or the selective kappa opioid receptor antagonist CERC-501 (1 mg/kg/day). Changes in mRNA expression of *Oprm1* and *Oprk1* were assessed in a separate untreated CSDS exposed cohort.

Results: BPN significantly reversed social interaction deficits following 7 days of administration, but not after acute injection. Treatment with FLX for 7 days, but not 24 h, also reinstated social interaction behavior in CSDS-stressed mice. In contrast, CERC-501 and KET failed to reverse social avoidance. Gene expression analysis identified reduced *Oprm1* and *Oprk1* mRNA in the amygdala and hippocampus and increased expression in the frontal cortex of CSDS-exposed mice.

Conclusions: Short-term treatment with BPN and FLX normalized social interaction after CSDS. In concert with the changes in opioid receptor expression produced by CSDS, we speculate that BPN's efficacy in this model of PTSD relies on the ability of this compound to engage multiple opioid receptors.

Analysis of Traumatic Stress and Depression Self-Report Measures in a Civilian Population Sample

Authors

Pietra Bruni, BS¹, Jeffrey Girard, MS¹, Taylor Wulf, Jeffrey Cohn, PhD¹, Charles Benight, PhD²

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2. Trauma Clinical Training Program, Department of Psychology, University of Colorado, Colorado Springs, CO

ABSTRACT

Background: Research has shown the negative influence trauma exposure has on the psychological, social, emotional and health functioning of both a civilian and veteran population. The PTSD Checklist for DSM-5 (PCL-5) is a self-report measure that can be used to monitor symptom change in trauma-exposed individuals and make a provisional PTSD diagnosis. Recent psychometric evaluations have examined the correlation between scores on the PCL-5 and scores of other criterion measures. The Beck Depression Inventory (BDI) has been used in nearly all published psychometric evaluations that examine PCL-5 severity scores in relation to depression severity.

Method: This study aimed, in part, to examine the relationship between the PCL-5 and another tool

from the field of psychiatric epidemiology, the Center for Epidemiological Studies Depression Scale Revised (CESD-R). It was hypothesized that the robust interaction seen between the PCL-5 and BDI in other psychometric studies would be replicated when using the CESD-R. A sample of sixty-six (n=66) treatment-seeking women who recently experienced a traumatic event were included. Each participant completed a battery of general outcome measures, including the PCL-5 and CESD-R, once at baseline and once at the completion of a novel treatment model that facilitated engagement and self-efficacy in the trauma-exposed cohort.

Results: Descriptive statistics and measures of internal validity yielded an observed correlation between participant's responses on the PCL-5 and the CESD-R, both at baseline and at study completion. Both depressive and trauma-related symptoms decreased in the sample after completing the novel treatment approach.

Conclusion: For the DSM-5 criteria for PTSD to be met, the occurrence of negative mood and cognition must be present. A high degree of comorbidity is observed between depression and PTSD; the use of effective diagnostic measurement tools is of the utmost importance. Further work could include a comparison of multiple depression inventories used in conjunction with the study of traumatic stress.

Functional Connectivity of Centromedial-Amygdala Predicts its Response to Fearful Faces

Authors

Elisabeth C. Caparelli, PhD¹, Thomas J. Ross, PhD¹, Hong Gu, PhD¹, Xia Liang, PhD^{1,2}, Elliot A. Stein, PhD¹, Yihong Yang, PhD¹

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2. Research Center of Basic Space Science, Harbin Institute of Technology, Harbin, China

ABSTRACT

Background: The amygdala has shown to be involved in emotional processing such as responses to fearful faces. Preclinical studies have demonstrated that the central nucleus of the amygdala plays a key role in fear expression. However the specific role of the subcomponents of the human amygdala in emotional processing is much less known. In this study, we aimed to evaluate the specificity of fear/anger expression in subdivisions of the human amygdala, defined from a modularity analysis, by correlating brain activation during a face processing task with resting-state functional connectivity (rsFC) relevant to the activated regions.

Method: Resting-state fMRI (rsfMRI) and task fMRI (t-fMRI, face-task: faces (fear or anger) and shapes blocks) data from 100 adult healthy volunteers, from

the Human Connectome Project (HCP), were used in this analysis. Data were analyzed in AFNI. The t-fMRI data were modeled in a block design, contrasting face with shape condition. Partial correlation maps were calculated using individual amygdala subdivisions, obtained from a Lovain modularity analysis, as seeds. A t-test was used to determine significant activation and correlation maps; a ROI analysis was used to extract the average activation and rsFC signals from each subdivision.

Results: The modularity analysis identified three main subdivisions for the amygdala: laterobasal, centromedial (CM) and superficial. The amygdala activation in respond to fear/anger faces was localized only to the CM. In turn, the CM showed strong connectivity with the insula, dorsal ACC and striatum.

Conclusions: Our findings indicate that functional connections of the CM are associated with the degree of activation elicited by fear/anger faces. The unique functional connectivity of CM with areas belonging to the salience network suggests its involvement in the identification of the emotional significance of environmental stimuli. Finally, our findings point to the potential prediction of fear-elicited activation by intrinsic functional connectivity in this area.

Association of General Belief in a Just World and Mental Health Outcomes Following the 9/11 Terrorist Attacks

Authors

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ABSTRACT

Background: The developed world has seen a three-fold increase in terrorism since the 9/11 World Trade Center attacks, which makes research regarding the impact of mass casualties on survivors essential. Previous research has shown an association between one's perceptions of justice in the world and mental health outcomes in Indian and American students. Belief in a just world (BJW) is a construct that describes the extent to which people believe that the world is fair and everyone's fate is deserved. A study focusing on BJW and terrorism-related distress in American students after 9/11 noted that individuals who strongly endorsed BJW before the terrorist attacks experienced more distress after the attacks. The present study examined the connection between BJW and mental health after a terrorist attack.

Method: We utilized a dataset of 603 individuals who lost a family member as a result of the 9/11 attacks (83.2% female; age [M = 56.3 years, SD = 12.4]; and 90.5% White). Participants completed the General Belief in a Just World Scale (Dalbert, 1987), a validated self-report instrument that measures BJW, as well as measures of participant depression (PHQ-9), complicated grief (ICG) and posttraumatic stress disorder (PCL-C).

Results: Results of multivariate logistic regressions indicate that participants who scored lower on the General Belief in a Just World Scale endorsed threshold symptoms of depression (OR = 1.76; $p < .01$), complicated grief (OR = 1.71; $p < .01$), post-traumatic stress disorder (OR = 1.93; $p < .05$) and generalized anxiety disorder (OR = 2.25; $p < .01$).

Conclusions: These unexpected findings suggest a unique association between BJW and mental health outcomes after terrorist attacks. Additional research is needed to replicate these findings and examine how perceptions of injustice in the world affect mental health outcomes in different types of populations.

The Protective Effect of Social and Support Networks Among U.S. Army Soldiers at Risk for Suicide

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ABSTRACT

Background: *The suicide rate among US Army Soldiers has increased dramatically over the past decade; despite increased and ongoing research efforts, an understanding of risk and protective factors for suicidal behavior among Soldiers is far from complete.* The purpose of this study is to identify whether social and support networks mitigate suicide risk among US Army soldiers using a psychological autopsy study.

Methods: Data are from the Army Study to Assess Risk and Resilience among Servicemembers (Army STARRS). Soldier Health Outcomes Study - B is and Army STARRS case-control study of Soldiers who died by suicide while on active duty between

August 01, 2011–November 01, 2013. We utilized a semi-structured interview of next of kin (NOK) and first line supervisors (SUP) of 168 Soldiers who died by suicide and 389 similar living (control) soldiers matched on known sociodemographic risk factors for suicide and Army history variables to obtain information on social support networks for these Service-members.

Results: NOK of Soldiers who died by suicide reported these Soldiers were more likely to be married 2 or more times when compared to NOK reports of controls (OR = 3.1) and case NOK also reported these Soldiers had more casual acquaintances (4-5) than controls (OR = 2.9). NOK of Soldiers who died by suicide reported that these Soldiers were less likely to seek help from a chaplain or religious counselor than controls (OR = 0.4). SUP reported fewer close relationships in decedents (6 or more) (OR = 0.5) than did SUP of controls. SUP reported Soldiers who died by suicide were less likely to seek help from a mental health counselor (OR = 0.4).

Conclusions. Results suggest third parties identify differences in social networks and supports between suicide decedents and matched controls. This information may inform prevention efforts.

Promoting Family Safety Through Personal Firearm Safety Education

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ABSTRACT

Background: Every year in the United States approximately 33,000 people are killed by firearms and another 730,000 are injured. Two-thirds of firearm deaths are suicides. Since 2011, suicide has become the second leading cause of death among military members. Firearms make up 61.1% of military suicides in the United States. Personal Firearm Safety involves taking simple measures to protect the life of loved ones from injury by accidental or intentional firearm use. Previous research has shown that safe storage practices place barriers between suicidal ideation and action, thereby increasing the probability of reconsideration or intervention. Healthcare providers can use such resources for firearm counseling and education for military members and their families.

Methods: The Center for the Study of Traumatic Stress developed a collection of training materials targeting active duty and reserve service members who may own personal firearms. These materials include an in-person interactive workshop, self-guided online learning. Topics covered include: basic principles of safe firearm storage, communication between household members about firearms, and alternative storage plans for times of distress. Materials also include Fact Sheets for medical providers to discuss personal firearm safety with patients.

Discussion: Personal Firearm Safety education applies principles of safe storage and alternative storage planning. Proper storage and safety measures keep firearms out of the curious and untrained hands while still accessible for self-defense and recreational purposes. Public health interventions are an effective strategy. A past example is the dramatic reduction of automobile fatalities even as car ownership has exponentially increased in the last century. Safer manufacturing, seatbelts, speed limits, driver education, and campaigns against drunk and distracted driving have led to significantly safer roads. Just like cars, common sense interventions for personal firearms can produce fewer injuries and deaths.

Perceived Environmental Stress Mediates the Relationship Between PTSD Symptoms and Coping in a Neighborhood-Matched Substance-Using Sample

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ABSTRACT

Background: People with substance use problems living in neighborhoods with high levels of environmental stress are disproportionately likely to experience trauma and develop posttraumatic stress disorder (PTSD) symptoms. We sought to evaluate the relationships between objective and perceived measures of environmental stress and the use of maladaptive coping behaviors among both non-substance-using and substance-using participants with and without PTSD symptoms.

Methods: Participants [(255 Non-Drug Users (NDUs), 168 Marijuana and/or Alcohol Users (MAUs), and 273 Opioid and/or Stimulant Users (OSUs)] completed the Addiction Severity Index, PTSD Checklist — Civilian Version, The COPE Inventory, and the Perceived Neighborhood Scale. The

Neighborhood Inventory of Environmental Typology (NIfeTy) was used to objectively assess environmental stress of participant's home address. Regression modeling was used to assess within-group predictors of PTSD and test for mediation in the relationships between PTSD, perceived environment, and coping behaviors.

Results: Among NDUs, low sense of community partially mediated the relationship between PTSD symptoms ($p < 0.01$) and using mental disengagement ($p < 0.01$). In MAUs, higher levels of perceived crime partially mediated the relationship between PTSD symptoms ($p < 0.0001$) and using mental disengagement ($p < 0.05$), focusing on and venting emotions ($p < 0.005$), and using substances to cope ($p < 0.0001$). OSUs with PTSD symptoms perceived a significantly higher degree of crime and reported using significantly higher levels of mental disengagement, focusing on and venting emotions, and substances to cope. However, perceived crime did not predict any of the three coping behaviors ergo no mediation was inferred.

Conclusion: Perceptions of community and crime may be more predictive of PTSD symptoms than objectively assessed measures of environmental stress. These perceptions partially mediate PTSD symptoms and maladaptive coping behaviors.

Multiple Notifications of Human Remains in Families of September 11th Decedents Associated with Depression and Posttraumatic Stress Disorder

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ABSTRACT

Objective: During the September 11th terrorist attacks, the New York City Office of the Chief Medical Examiner was responsible for identifying all remains taken from Ground Zero in lower Manhattan and notifying the families of the deceased. Previous research has shown that when properly conducted, confirmation of a loved one's death (for example, through discovery of human remains) is associated with positive mental health outcomes in the bereaved; however no identified empirical studies have examined the effect of multiple notifications on family members of those killed in a terrorist attack.

Method: The present study sought to address this gap in the literature by examining a sample of 421 (83% female; $M = 57.12$ years, $SD = 12.02$; White 91%) families of September 11th decedents. Partici-

pants were asked how many times they were notified of recovery of their loved one's remains (never, once, twice, three or more times).

Results: 38.2% of respondents were never notified of human remains identification, 27.6% were notified once, 16.2% were notified twice, and 18.1% were notified three, or more times. Multivariate logistic regressions examined the contribution of frequency of notification of human remains to complicated grief (Inventory of Complicated Grief), depression (Patient Health Questionnaire-9), posttraumatic stress disorder (PTSD Checklist-Civilian), and generalized anxiety disorder (Generalized Anxiety Disorder-7). Results indicated that those who were notified three or more times were at risk for depression ($OR = 2.1$; $p < .05$) and PTSD ($OR = 3.3$; $p < .05$), but not complicated grief or generalized anxiety disorder, when compared with those that had received no notification.

Conclusions: These findings suggest a negative impact of repeated notifications of human remains on the families of 9/11 decedents. Further research should replicate these findings and future policy decisions regarding notification of family members about human remains after mass casualty events should consider these effects.

Grief, Anxiety, and Depression Independently Predict Cognitive Failures in Bereaved Family Members

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Abstract:

Background: Between 7-25% of bereaved individuals develop complicated grief (CG), characterized by persistent sense of loss, 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. It is unknown whether these difficulties generalize to cognitive failures (minor errors in thinking that interrupt physical or mental action) and whether these cognitive failures are also affected by co-morbid anxiety and depression.

Method: The present study investigated associations between cognitive failures and CG, generalized anxiety (GA), anxious arousal, and depression using participants (n=619) from the National Military Family Bereavement Study.

Results: Linear regression indicated depression ($p < .0001$), GA ($p < .034$), anxious arousal ($p < .0001$) and grief ($p = .0001$) independently predicted cognitive failures. It was expected that comorbid depression and/or GA would be associated with more cognitive failures than CG alone. To investigate, eight groups were created: high scores on three (CG, GA, and depression) measures (high; n=1), high scores on two measures and low scores on the third (n=3), high scores on one measure (n=3), and low scores on three (n=1). ANOVA was used to test CFQ differences between groups. As expected, high had the most cognitive failures. However, high did not differ from the comorbid depression and CG group, or the comorbid depression and GA group. Thus, while CG, depression and anxiety were each associated with cognitive failures, comorbid depression (with either CG, anxiety, or both) contributed to increased cognitive failures.

Conclusions: Future assessments of cognitive failures in bereaved individuals, especially with comorbid depression, can elucidate how cognitive capacity is affected in day-to-day activities, and suggest future targets for intervention and provide ecological validity for research about grief and cognition.

Community Strength and Disasters: Collective Efficacy Following the 2004 Florida Hurricanes

Authors

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ABSTRACT

Background: Natural disasters produce a range of adverse behavioral and psychological outcomes in residents of affected communities. The impact of disaster exposure on community-level characteristics, including collective efficacy (CE), also influence community strength and mental health. CE, defined as social cohesion among neighbors and willingness to intervene for the common good, is associated with lower levels of depressive symptoms and post-traumatic stress disorder following natural disasters. Perception of CE may influence the decision to relocate or remain in one's neighborhood following a disaster, such as a hurricane. This study assessed the association of relocating following a series of Florida hurricanes with CE in 592 community members.

Participants: Ages ranged from 21–72 years (median=48.5). Most were female (78%; $n=462$), currently married (69%; $n=407$), White (83%; $n=487$), and 57% had at least a BA/BS degree ($n=338$).

Procedures: Participants completed self-report questionnaires at 9 months following 4 hurricanes and 1 tropical storm in August and September 2004 and approximately 9 months after the 2005 hurricane season. Questionnaire items identified participants' zip codes and assessed CE at both time points. Relocation was defined by a participant's zip code differing between the two time points. Independent-samples and paired t-tests compared CE in those who remained in the same geographical area or relocated.

Results: In general, CE decreased from Time 1 ($M=7.76$, $SD=1.84$) to Time 2 ($M=7.54$, $SD=1.88$), $t(591)=2.97$, $p=.0031$. Among participants who did not move, CE decreased from Time 1 ($M=7.81$, $SD=1.83$) to Time 2 ($M=7.52$, $SD=1.9$), $t(532)=3.69$, $p=.0003$. For those who relocated, the change in CE from Time 1 to Time 2 was not significant, suggesting that CE level was sustained from before to after their move.

Conclusions: Individual, community and event-related factors can influence CE following a disaster. Optimizing CE prior to and following disasters may hold promise to offer significant public health benefits.

Regression Modeling of Post-Deployment Survey Data Identifies Areas of Needed Resiliency Training

Authors

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ABSTRACT

Background: The population lifetime exposure rate to traumatic events is approximately 90%, with PTSD prevalence among combat veterans at 23%. Identifying factors differentiating those who experience trauma and develop PTSD versus those who do not develop PTSD is a major research question. Resiliency is a possible explanation. The U.S. Army Comprehensive Soldier Fitness program trains personal resiliency, but does not address other areas that may be contributing factors (e.g., social support from one's family or unit). As such, we sought to examine how extraneous factors such as family issues and social support affected PTSD severity. We hypothesized that pre-deployment trauma exposure, combat exposure, anxiety while deployed, post-de-

ployment support networks, and negative post-deployment life events would be significant predictors of PTSD symptom severity.

Methods: We collected data from previously deployed service members (n=81 [74 males], age=32.9±6.9 years). We used multiple-regression modeling to determine the best fitting model associated with resiliency factors predicting PTSD symptom severity using the Deployment Risk and Resiliency Inventory, Combat Exposure Scale, and Life Events Checklist.

Results: The model that best fit our data included combat exposure, anxiety about self and family while deployed, post-deployment support, negative life events post-deployment, and an interaction between combat exposure and anxiety while deployed ($F(5, 75) = 35.42$; $p < 0.001$; $R^2 = 0.70$). Contrary to our hypothesis, pre-deployment trauma exposure variables were not significant predictors. The data did support our hypothesis that combat exposure, anxiety while deployed, post-deployment support networks, and negative post-deployment life events were significant predictors.

Conclusions: These data suggest that including how to deal with family issues while deployed and post-deployment resiliency training that includes the family may have a transformative impact on Army resiliency training.

Effects of Isoflurane Anesthesia and Intravenous Morphine Self-administration on Regional Cerebral Glucose Metabolism in Sprague Dawley Rats: ^{18}F -FDG PET/CT Study

Authors

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ABSTRACT

Background: Over the past decade of military operations in Iraq and Afghanistan, more than 50,000 U.S. service members have been wounded in action. A previous study found that 44% of 2,597 active duty soldiers who had been deployed to Iraq and Afghanistan experienced chronic pain, lasting at least three months (Toblin, Quartana et al. 2014). Therefore, efficient pain management and prevention of opioid drug misuse represent a major challenge in the military community. Despite these epidemiological findings, biological factors that are associated with opiate abuse are not well characterized.

Method: We investigated the effects of 1) isoflurane anesthesia during [^{18}F]-fluoro-deoxy-glucose (FDG) uptake and 2) intravenous morphine self-administration (MSA) on regional glucose metabolism (BGluM) using positron emission tomography (PET) and computed tomography (CT). Jugular vein cannulated adult male Sprague-Dawley rats self-administered either saline or morphine (0.5 mg/kg/infusion, 4hrs/day) for 12 days. All animals were scanned twice with FDG-PET/CT at a baseline (pre-self-administration) and 2 days after the last self-administration session. After the intravenous injection of FDG, one group (n=14) was anesthetized with isoflurane and the other (n=16) was kept awake during FDG uptake (45 min).

Results: Isoflurane anesthesia, as compared to the awake condition, reduced BGluM in the olfactory, cortex, thalamus, and basal ganglia, while increasing BGluM in the midbrain, hypothalamus, hippocampus, and cerebellum. Morphine self-administered animals exhibited withdrawal signs, drug seeking, and behavioral sensitization to morphine challenge (0.5 mg/kg). At two-day withdrawal, BGluM in the striatum was selectively increased in morphine self-administered animals as compared to that of saline self-administered animals.

Conclusions: Increased BGluM in the striatum following chronic MSA may have functional significance in opiate abuse. The current findings demonstrate the utility of combining an intravenous drug self-administration paradigm and a non-invasive brain imaging technique to better understand biological mechanisms associated with opiate abuse.

Effect of Intravenous Ketamine on Corticosterone and Brain-Derived Neurotrophic Factor in Sprague-Dawley Rats

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ABSTRACT

Background: Corticosterone (CORT) and brain-derived neurotrophic factor (BDNF) mediate stress and memory. Alterations of CORT and BDNF following trauma are implicated in post-traumatic stress disorder (PTSD). Since ketamine is administered in the immediate period after injury, its impact on PTSD is of interest. Currently, the short-term effects of intravenous (IV) ketamine infusion on CORT and BDNF using a rat fear-conditioning (FC) model are unknown. *Aim:* To characterize plasma CORT at 2 and 4h and plasma BDNF at 4h following IV ketamine infusion after FC.

Methods/Design: Male Sprague-Dawley rats (300±25g) with indwelling jugular vein catheters

were separated into 4 groups (n=12/group). Group 1 (SAL) = no FC + 2h saline infusion. Group 2 (KET) = no FC + IV ketamine bolus & 2h infusion. Group 3 (FC) = FC and saline infusion. Group 4 (FC/KET) = FC + IV ketamine bolus + 2h infusion. *Fear-Conditioning:* Rats underwent 3 pairings of a 20s tone (75dB) that co-terminated with footshock (0.8mA x 0.5s). *Drug:* Rats received an IV ketamine bolus (5 mg/kg) and a 2h IV ketamine infusion (20 mg/kg/h). *Plasma:* CORT and BDNF concentrations were measured at 2h and 4h after FC using enzyme-linked immunosorbent assay (ELISA).

Results: IV ketamine infusion significantly increased CORT levels compared to SAL at the 2h time point. There were no differences in CORT levels between SAL and FC groups at 2h and no difference in CORT between all groups at 4h. Ketamine decreased peripheral BDNF concentrations in ketamine treated rats at 4h.

Implications: High-dose steroid administration immediately following trauma may be associated with reduced incidence of PTSD. On the other hand, reduced production of BDNF may be associated with impaired memory formation. Our results suggest that a high-dose ketamine infusion may offer protective effects for the development of stress related disorders following a fear triggering event.

Heterogeneity of the DSM-5 PTSD Diagnostic Criteria: A Quantitative Analysis

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ABSTRACT

Background: The diagnostic criteria for PTSD have been criticized for permitting extremely high levels of heterogeneity. In *DSM-IV*, PTSD had one of the highest number of possible diagnostic combinations and disjoint combinations (those sharing no symptoms), and these both increased eight-fold in *DSM-5*. However, observed coherence (homogeneity) for *DSM-IV* in empirical samples is substantially higher than theoretical levels.

Methods: We examined coherence of *DSM-IV* and *DSM-5* PTSD and major depressive disorder (MDD) in trauma-exposed undergraduates ($N=302$). PTSD diagnosis was based on a lenient (symptoms only) or stringent rule (symptoms plus a moderate cutoff on total severity score).

Results: Preliminary analyses revealed several important results. First, disjoint PTSD combinations were rare for the lenient rule and absent for the stringent rule. Second, coherence was higher for the stringent rule. Third, coherence was higher for *DSM-IV* PTSD using the lenient rule but higher for *DSM-5* using the stringent rule. Last, coherence for *DSM-5* using the stringent rule was comparable to coherence for MDD, with an average shared proportion of symptoms of about two-thirds.

Conclusions: We demonstrate empirically that *DSM-5* PTSD criteria yield moderate coherence, comparable to that for MDD and substantially higher than theoretical levels. Although *DSM-5* is more heterogeneous than *DSM-IV* as predicted, requiring a severity cutoff score considerably decreases heterogeneity. Future work will include two additional samples with combined $N=4000+$.

Aberrant Default Mode Connectivity Associated with Combat-Related Posttraumatic Stress Disorder

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ABSTRACT

Background: Posttraumatic stress disorder (PTSD) is estimated to affect at least 20% of returning Iraq/Afghanistan war veterans. As a result, several studies have sought to identify potential biomarkers and neural signatures associated with the condition. Here, we contribute to the literature by examining neural functional connectivity and graph theory metric differences between combat-veterans with and without PTSD during resting state functional magnetic resonance imaging (fMRI) acquisition.

Method: Thirty-eight participants (23 combat-veterans without PTSD/15 combat-veterans with PTSD) underwent fMRI on a Siemens 3T scanner at the Auburn University MRI Research Center (T2*-weighted multiband echo planar imaging,

TR=600ms, TE=30ms, FA=55°, multiband factor=2, slice gap=1mm, voxel size=3×3×4mm, 1000 volumes). Standard preprocessing was applied, and data were motion corrected and scrubbed. Functional connectivity and graph theory metrics were derived using ‘conn’, an open-source toolbox for Matlab. For functional connectivity analyses, we used a seed-to-voxel approach, with seeds being the anterior and posterior cingulate cortices (ACC/PCC). Data were thresholded at $p_{\text{voxel-level}} > 0.05$ and FDR-corrected $p_{\text{cluster-level}} > 0.05$.

Results: Analyses revealed increased connectivity of the ACC and PCC with bilateral anterior paracingulate cortex in combat-veterans without PTSD compared to those with PTSD. The reverse contrast (combat-veterans with PTSD > combat-veterans without PTSD) revealed increased connectivity between the ACC and the precuneus, PCC, left hippocampus and parahippocampus, and portions of the right prefrontal cortex. PCC connectivity differences emerged with combat-PTSD being associated with increased connectivity to bilateral temporal cortices, bilateral middle/posterior paracingulate, and sensory processing regions throughout the parietal lobe.

Conclusions: Supporting results from previous studies, we identified disruptions to critical neural hubs involved in the default mode network. We did not find support for specific deficits using graph theory metrics, but encourage the use of this novel analytic technique in future datasets. Results suggest that specific functional connectivity differences may differentiate those combat veterans with and without PTSD.

Use of Neuromodulation Techniques in the Treatment of Post-Traumatic Stress Disorder

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ABSTRACT

Background: Post-traumatic stress disorder (PTSD) is characterized by the presence of intrusive, avoidant, and hyperarousal symptoms, and negative alterations of mood and cognition, following a traumatic exposure. Symptoms must last more than thirty days and be accompanied by social and occupational impairment. PTSD has an estimated lifetime prevalence of 7% among adult Americans with a higher prevalence in combat veterans and victims of sexual assault. Only two FDA-approved clinical treatments exist and treatment resistance remains a significant problem. Neuromodulation, the process of stimulating or inhibiting nerve conduction, presents a unique opportunity to treat PTSD.

Methods: A literature search was conducted on PubMed for English articles published through

November 2016 on the topics of transcranial magnetic stimulation (TMS), cranial electrotherapy stimulation (CES), vagal nerve stimulation (VNS), deep brain stimulation (DBS), and electroconvulsive therapy (ECT) in the treatment of PTSD.

Results: TMS has some evidence of efficacy in PTSD treatment, has few side effects, and does not require anesthesia or surgery. While CES is frequently used by military and VA hospitals, and per patient reports has positive side effects, there are no controlled studies to its effects. However, CES has an excellent safety profile. VNS, DBS, and ECT, by contrast, all have strong evidence for their roles in other disorders, but their specific use for PTSD has not yet been determined. Current research for VNS and DBS is limited to pilot and animal studies, and these modalities are higher risk to patients than TMS or CES as they require surgery.

Conclusions: Neuromodulation techniques are promising treatment modalities for patients with PTSD. With the exception of TMS, evidence is currently limited. Due to their higher safety profile, CES and TMS have high potential for primary care distribution. VNS, DBS, and ECT should be considered for patients with severe refractory PTSD.

Neurophysiology of Aggression in PTSD

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ABSTRACT

Background: Traumatic stress in many PTSD patients leads to explosive anger and, all too often, violence. Herein a rat model of fight and flight is utilized toward finding Where in the brain violence foments and How. Where? Areas tested are the ventromedial hypothalamus (VMH), medial amygdala (MeA), and lateral septum (LS), previously implicated in attack, and the hippocampus (HC), since flashbacks and nightmares are fundamental to PTSD. A first step toward How is to associate synaptic transmission in and between these regions with behavioral attack.

Methods: Synaptic transmission can be assessed in the behaving rat by recording (1) the magnitude of evoked excitatory postsynaptic field potentials (fEPSPs) and (2) alpha and theta “brain waves” (endogenous electric field oscillations of 5-8 Hz (theta) and 8–12 Hz (alpha)) which represent rhythmic syn-

chronous activity of populations of neurons associated with attention and sleep. Procedures included 1) implanting microelectrodes in VMH and MeA for stimulation and in HC and LS for recording fEPSPs and alpha/theta waves, 2) evoking rat attack using the resident/intruder paradigm and theta patterned electrical stimulation in VMH/MeA, 3) recording fEPSPs in response to a continuous probe stimulus along with alpha/theta waves, and 4) recording video of attack behavior simultaneous with recorded fEPSPs and alpha/theta waves.

Results: 1) Theta patterned stimulation in VMH/MeA evoked attack in Resident rats challenged with an Intruder rat. In one rat the attacks were delayed by a week, consistent with the delayed onset of symptoms as can occur in PTSD. 2) During the attack, the fEPSP flattened out in HC and LS, then bounced back afterwards. 3) Alpha waves became prominent during standoff such as preceded attack. Very similar alpha waves were also recorded during sleep.

Implications: 1) VMH and MeA are key in evoking attack. 2) HC and LS are active leading up to and following attack, possibly processing “cognitive” information later assimilated during sleep.

Accelerated Resolution Therapy: Short-Term Trauma-focused Therapy for Operational Military Environments

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ABSTRACT

Background: The treatment of post-traumatic stress disorder (PTSD) and other trauma-related symptoms are difficult to treat in operational military settings due to limited resources, time, and mission requirements. Current evidence-based therapies including cognitive processing therapy (CPT), prolonged exposure therapy (PE), and eye movement desensitization and reprocessing (EMDR) require weekly sessions for two to three months; thus, they are typically not suitable for operational settings. In 2014, Military Medicine published an article on Accelerated Resolution Therapy (ART), which described it as a short-term trauma-focused therapy that may require only 2–5 hours of treatment per patient. Based on these findings, ART could be considered as a potential therapy modality suitable for operational military settings. ART was subsequently tested in such a setting by an outpatient psychiatrist at the Adult Behavioral Health Clinic, Camp Humphreys, Republic of Korea, from October 2015–October 2016.

Method: The presenter has over 10,000 beneficiaries in his area of responsibility. 1-2 hours of ART was incorporated into his daily clinic schedule. ART was used to treat post-traumatic stress disorder and other trauma-related symptoms.

Results: Approximately 150 sessions of ART were provided, averaging 1–2 hours of ART on most weekdays. On average, patients receiving ART returned for 0-3 follow up ART sessions after the initial session, depending on number of traumas and symptom severity. An estimated 75% of ART patients endorsed significant subjective benefit from ART, an estimated 20% had a neutral-mild clinical response, and approximately 5% were unable to tolerate or complete the therapy. No serious adverse reactions occurred during ART sessions.

Conclusions: Given these results ART should be considered as a potential treatment for PTSD and trauma-related symptoms particularly in settings with resource limitations such as operational military environments.

Decomposition of Daily Variation in the Posttraumatic Stress and Depression Symptoms in U.S. Military Service Members: Trait, State and Error

Authors

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ABSTRACT

Background: Rates of posttraumatic stress disorder and depression are high in US military service members. Little is known about how posttraumatic stress and depression symptoms are experienced throughout the day. Using ecological momentary assessment (EMA) methodology, this study assessed individual daily variation of Posttraumatic Stress Symptoms (PTSS) and depression symptoms in current and former US military service members.

Method: Forty participants completed symptom assessments four times per day for 15 consecutive days. PTSS were assessed with eighteen items from the PCL-5. Depression symptoms were assessed with six items from the PHQ-9. Linear mixed models were used to explore the within-individual covariance structure that (level-1) daily diary assessment

nested within (level-2) subjects. For each outcome, analyses were conducted with two steps. The first step was to test the first-order autoregression assumption, AR(1), against compound symmetry, CS, about within-person variation. In the second step, a modified AR(1) model, AR(1) + measurement error, was further specified which decomposes the error term into two parts, one for autocorrelation and the other for measurement error. Model fit was compared across models specifying CS, AR(1), and the modified AR(1) for the within-subject covariance structure.

Results: For both outcomes, the model with AR(1) covariance structure provided a much better fit to the data when compared to a CS structure, and the model with the modified AR(1) error structure further improved model fit. The between-subject variation, or “trait-like” differences, consisted of 76.8% of total variation in PTSS and 77.4% in depression symptoms. The “state-like” component consisted of 14.3% in PTSS and 16.3% in depression symptoms. The measurement error variance consisted of 8.9% in PTSS and 6.2% in depression symptoms.

Conclusions: Exploring appropriate error covariance structure in mixed models is useful to better understand between- and within-individual variation of posttraumatic stress and depression symptoms in EMA studies.

Dissociable Meta-Analytic Networks Contribute to Post-Traumatic Stress Disorder

Authors

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ABSTRACT

Background: From a neurobiological perspective, post-traumatic stress disorder (PTSD) is among the better-understood psychiatric conditions. However, enhanced understanding has not produced reliable biomarkers that may serve as diagnostic criteria. Here, we sought to establish which brain regions show consistent PTSD-related functional changes across neuroimaging studies within a meta-analysis framework. To provide enhanced interpretation, we used auxiliary analyses to fractionate impacted brain regions into sub-networks and determine which psychological processes those sub-networks may subserve.

Methods: We identified published neuroimaging studies that reported functional brain differences between patients with PTSD and (a) patients with trauma exposure without PTSD and/or (b) controls (groups were collapsed) as whole-brain coordinates in stereotaxic space. First, we assessed statistical convergence across activation increases (PTSD>Controls) and decreases (PTSD<Controls) ($p_{\text{cluster-corrected}} < 0.001$; $p_{\text{voxel-wise}} < 0.05$). We then parsed impacted

brain regions into sub-networks using fractional similarity network analysis (FSNA), revealing regions that exhibited co-occurring diagnosis-related changes across studies. Finally, we established which psychological processes were associated with these sub-networks using paradigm classification analysis.

Results: We identified 44 studies, representing data from 707 patients and 758 controls. Specifically, sub-network 1 (amygdala, hippocampus, and DLPFC) represented distributed increased activation associated with inducing emotions and processing emotional content. Also, sub-network 2 (insula, cingulate, and occipital lobe) and sub-network 3 (occipital lobe and cuneus) represented distributed increased activation linked with monitoring environmental cues and subsequent evaluation. Finally, sub-network 4 (PCC, DMPFC, and DLPFC) and sub-network 5 (ACC, VMPFC, and VLPFC) represented distributed decreased activation associated with decision-making, response inhibition, and effortful and sustained attention.

Conclusions: Our results indicate that PTSD is associated with several region-specific changes across the brain. Deeper understanding of the neural systems that may be impacted by PTSD is important for establishing reliable biomarkers that are specific and sensitive, capable of serving as diagnostic criteria and therapeutic targets.

Association Between Leukocyte Telomere Length and Hostility in Soldiers Deployed During the Iraq and Afghanistan Wars

Authors

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ABSTRACT

Background: Hostility is a common form of emotionally charged angry behavior. The association between telomere and greater levels of hostility has been observed in the civilian population. To investigate the relationships between hostility and leukocyte telomere length (LTL) in military service members, we conducted a study in subjects (n=474) from the US Army service members.

Method: Hostility was measured with five items from the Brief Symptom Inventory (BSI). The items for hostility are divided into two clusters: controlling anger (HC) and impulsive hostility (HI). The HC

items include: feeling easily annoyed or irritated, temper outbursts that you could not control, and getting into frequent arguments; the HI items include: having urges to beat, injure, or harm someone else and having urges to break or smash things. Participants rated each item by indicating how much that problem had bothered or distressed them (0 = "not at all" to 4 = "extremely") in the past month. The LTL was assessed using quantitative polymerase chain reaction methods. Regression analyses were conducted to determine the association of hostility and telomere length.

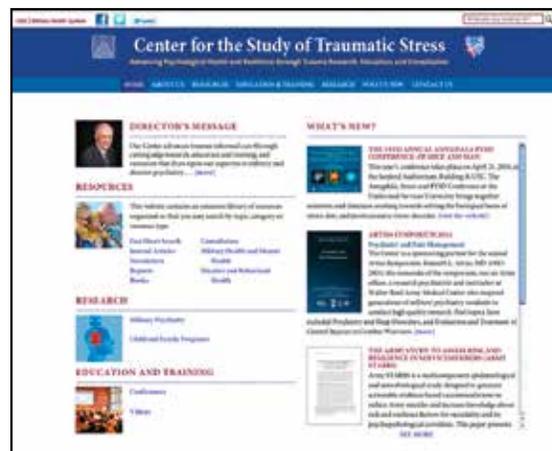
Results: Univariate regression showed that the total of score of hostility was negatively associated with LTL (CI= -0.06 to -0.002, Beta= -0.095, p <0.039). Also, univariate regression revealed the significant correlation between LTL and scores of both hostility impulse (CI= -0.108 to -0.009, Beta= -0.106, p < 0.021) and hostility control (CI= -0.071 to -0.002, Beta= -0.095, p <0.004), indicating that the association between hostility and LTL may be associated with controlling anger or impulses. Multiple regression analyses showed that the HC could not enter the equation, while the HI was still negatively correlated with the T/S ratio (P=0.021), indicating that LTL was affected by hostility impulse.

Conclusion: Our data indicate that prevention and treatment efforts designed to reduce hostility may help mitigate risk for accelerated cellular aging.

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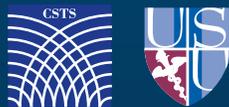
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