



Northwest MIRECC

(VISN 20) Mental Illness Research, Education and Clinical Center

Overview

The Northwest MIRECC develops novel and improved treatments for major behavioral disorders afflicting veterans. These and other effective treatments are disseminated across veteran and military personnel health care systems through model clinical programs, educational outreach, and leadership of VA cooperative studies. Since the onset of Operation Enduring Freedom (OEF) in Afghanistan and Operation Iraqi Freedom (OIF), the Northwest MIRECC has directed major resources to the neuropsychiatric disorders highly prevalent among combat-exposed OEF/OIF returnees (posttraumatic stress disorder [PTSD] and blast concussive mild traumatic brain injury [mTBI]), and to collaborations in research, educational and treatment efforts between the MIRECC and Department of Defense components locally (Madigan AMC/Fort Lewis) and nationally (Walter Reed AMC) and Defense Centers of Excellence (DCoE).

Mission

The Northwest MIRECC applies modern genetic, neurobiologic and clinical trial methodology to the discovery and development of new and more effective treatments for major and often treatment resistant mental disorders afflicting veterans and the active duty combat personnel who will become veterans. Translational research efforts focus on treatment for PTSD and its substance abuse comorbidities (alcohol and tobacco); the chronic behavioral consequences of mTBI and its objective diagnosis through biomarkers; the elderly veteran with agitated dementia; and schizophrenia and the adverse metabolic consequences of antipsychotic drug therapy.

Research (Highlights)

MIRECC investigators discovered that the inexpensive generic drug prazosin (that blocks excessive responses to the "adrenaline" neurotransmitter norepinephrine) is highly effective for reducing and often eliminating PTSD trauma nightmares, sleep disruption and daytime hyperarousal and reexperiencing symptoms in combat veterans and in civilians. These results have led to DoD funding for a multi-site placebo-controlled prazosin trial in active duty soldiers from OIF/OEF with Madigan AMC and Walter Reed AMC, and a 13-site VA Cooperative Study (CSP #563) of prazosin for combat trauma PTSD in veterans. Encouraging results with prazosin for mTBI sleep disturbance, headaches, and cognitive impairment have led to inclusion of prazosin for mTBI in the VA/DoD treatment guidelines for mTBI. Prazosin was also demonstrated effective for alcohol dependence in both human and preclinical studies. A P20 Center to expand these alcohol dependence studies has been funded by NIAAA. Integrating smoking cessation within specialized PTSD clinics significantly improves cessation rates. MIRECC led VA Cooperative Study (CSP #519) an effectiveness trial of this approach, with results soon to be published. The MIRECC also continues to pursue cutting edge studies of genetic variants that contribute to the development of Alzheimer's disease and schizophrenia.

Clinical (Highlights)

We have developed a model Deployment Health Clinic for combat veterans returning from Iraq and Afghanistan. This integrated, multidisciplinary clinic provides "one stop shopping" post-deployment evaluations with easy access, integrated care and de-stigmatized mental health assessment and interventions. This model is being "rolled out" nationally with DHC founder and MIRECC investigator Stephen Hunt, MD leading this effort nationally. The MIRECC African-American Veterans Stress Disorders Program is a model program for African-American veterans. Co-facilitated by Vietnam First Cavalry Division combat veteran Lemanuel Jones and MIRECC Director Dr. Murray Raskind, the program has been rated significantly superior to standard PTSD psychotherapy by over 500 African-American veterans. The VISN20 MIRECC also is pioneering

with DoD collaborative approaches to behavioral disorders screening of soldiers returning from combat deployment in OIF and OEF.

Education (Highlights)

We have produced a Best Practices Manual for Posttraumatic Stress Disorder Compensation and Pension Examination. A CD-ROM independent study program has been widely disseminated across VA to complement the manual. VA Boise and VA Puget Sound MIRECC faculty are collaborating with the Office of the Chairman Joint Chiefs of Staff (Admiral Mike Mullen) to produce training and education films about PTSD and mTBI in OIF/OEF returnees as well as older veterans.

Selected Studies and Projects

Prazosin for Combat Trauma PTSD. Prazosin is a long available generic drug that easily enters the brain and blocks excess "adrenaline" stimulation. We recently confirmed in a second placebo-controlled study that evening prazosin substantially reduces or eliminates combat trauma related nightmares and sleep disruption and improves global clinical status (sense of well-being and ability to function). We are leading a VA Cooperative Study (CSP #563) and a DoD funded study in active duty soldiers to expand the prazosin database in PTSD.

VA CSP #519: Tobacco Cessation in Veterans with PTSD: Integration of Practice Guidelines.

Nicotine dependence contributes substantially to medical morbidity and mortality among veterans with PTSD. Unfortunately, referral to traditional VA smoking cessation programs results in a very low rate of cessation. We have established that integrating smoking cessation with specialized PTSD clinics significantly improves cessation rates.

Anonymous Foundation: Biomarkers and Clinical Course of Mild Traumatic Brain Injury Blast Trauma in OIF/OEF Veterans. This innovative project is studying comprehensively and longitudinally OIF returnees exposed to blast concussive trauma and with symptoms consistent with mTBI and non-blast exposed controls. It is quantifying blast exposure, characterizing subjects neuropsychologically, evaluating brain structure and function with neuroimaging (DTI, CRI, fMRI, PET) and measuring biomarkers associated with neurodegeneration in cerebrospinal fluid.

Selected Publications

McFall M, Saxon AJ, Thanneemit-Chen S, Smith MW, Joseph AM, Carmody TP, Beckham JC, Malte CA, Vertrees JE, Boardman KD, Lavori PW. Integrating smoking cessation into mental health care for posttraumatic stress disorder. *Clin Trials* 4:178-189, 2007.

Raskind MA, Peskind ER, Hoff DJ, Hart KL, Holmes HA, Warren D, Shofer J, O'Connell J, Taylor F, Gross C, Rohde K, McFall ME. A parallel group placebo controlled study of prazosin for trauma nightmares and sleep disturbances in combat veterans with posttraumatic stress disorder. *Biol Psychiatry* 61:928-934, 2007.

Taylor FB, Martin P, Thompson C, Williams J, Mellman TA, Gross C, Peskind ER, Raskind MA. Prazosin effects on objective sleep measures and clinical symptoms in civilian trauma PTSD: a placebo-controlled study. *Biol Psychiatry* 63:629-632, 2008.

Wang LY, Shofer JB, Rohde K, Hart KL, Hoff DJ, McFall YH, Raskind MA, Peskind ER. Prazosin for the treatment of behavioral symptoms in Alzheimer's disease patients with agitation and aggression. *Am J Psychiatry* 17:744-751, 2009.

Peskind ER, Petrie EC, Cross DJ, Pagulayan K, McCraw K, Hoff D, Hart K, Yu C-E, Raskind MA, Cook DG, Minoshima S. Cerebrocerebellar hypometabolism associated with repetitive blast exposure mild traumatic brain injury in 12 Iraq war veterans. *Neuroimage*, in press.

Leadership

Director – Murray Raskind, M.D.

Associate Research Director – Elaine Peskind, M.D.

Associate Education Director – James Boehnlein, M.D./Ruth Ann Tsukuda, EdD

Associate Clinical Director – Miles McFall, Ph.D.

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