



# VISN 6 Mid-Atlantic MIRECC Post Deployment Mental Health

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## Educational Opportunities

Continuing Education Archives hosted by  
the VISN 22 MIRECC

VA Desert Pacific Health Care Network

<http://www.mirecc.org/education-frames.html>

This page contains links to lecture material presented at previous MIRECC sponsored accredited continuing education (CE) conferences. You may obtain CE credit by viewing selected presentations on-line and completing the associated evaluation.

## Neuroactive Steroids and Psychiatric Disorders

by Christine Marx, MD

It has been known since the 1980's that the synthesis of steroids occurs in the brain as well as in peripheral organs. The enzymes required for their synthesis are present in both neurons and glia. Some of these neurosteroids have been shown to interact with neurotransmitter receptors, including GABA, glutamate, glycine, and serotonin, allowing them to modulate brain activity quickly and directly. Although clinical studies of neuroactive steroids are relatively few in number at the present time, converging evidence suggests that these molecules may be relevant to the pathophysiology and pharmacological treatment of many psychiatric disorders. This is an active area of investigation for the VISN 6 MIRECC.

Several lines of evidence support the relevance of neurosteroids to psychiatric disorders. Neuroactive steroids are important in neurodevelopment and regulate neuronal cytoarchitecture, suggesting a potential role for these molecules in the pathophysiology of psychiatric disorders demonstrating a neurodevelopmental component and neuronal cytoarchitectural alterations such as schizophrenia. Neuroactive steroids are also differentially regulated in males and females, and may therefore modulate the neurobiology of sex differences observed in a variety of

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## Upcoming Events

### *Battlefield to Home: The Spectrum of Combat Stress and the Impact on the North Carolina Mental Health System*

July 21, 2005

Searle Center, Duke University, Durham NC

The purpose of this meeting is to examine and discuss current practices and strategies for dealing with combat stress and related mental health issues within both the active military, VA, and community health settings. The target audience includes VA physicians, psychologists, and social workers, Department of Defense representatives, public health practitioners, Vet Center representatives, and community mental health providers interested in the topic and treatment of Combat Stress among deployed and returning military personnel and their family members. The deadline for registration is July 8, 2005.

For more information contact: [Barbara.Phipps@lm.va.gov](mailto:Barbara.Phipps@lm.va.gov)

## Updates

### *Clinical Education Projects Program*

The response to the call for proposals for the Mid-Atlantic (VISN 6) MIRECC Clinical Education Projects Program was exceptional. A total of 19 proposals were submitted, involving personnel at almost all the VISN's medical centers. A very wide range of innovative educational and clinical interventions were proposed. These are presently under review. Final decisions will be announced by June 30, 2005.

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## Neuroactive Steroids and Psychiatric Disorders

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psychiatric illnesses.

Of particular interest clinically is the evidence that neurosteroids may be involved in antidepressant and antipsychotic drug action. Allopregnanolone and its stereoisomer pregnanolone are among the most potent known GABA<sub>A</sub> receptor modulators, stronger than either barbituates or benzodiazepines. In a clinical study of fifteen patients with major depression, cerebrospinal fluid (CSF) levels of allopregnanolone were decreased compared to control subjects. Following treatment with fluoxetine or fluvoxamine (both specific serotonin reuptake inhibitors, SSRIs), CSF allopregnanolone levels increased in subjects with depression, correlating strongly with improvements in depressive symptoms. Since then it has been demonstrated that several SSRIs increase synthesis of allopregnanolone, supporting the possibility that SSRI-induced allopregnanolone biosynthesis may be relevant to SSRI therapeutic actions in depression and anxiety disorders. Animal studies suggest that neuroactive steroids may also be involved in antipsychotic drug action. Our studies in rats, for example, indicate that the second-generation antipsychotics clozapine and olanzapine increase allopregnanolone in cerebral cortex and hippocampus. Since GABAergic neurotransmission appears to be altered in schizophrenia, antipsychotic-induced elevations in allopregnanolone may be relevant to this component of schizophrenia pathophysiology. If clozapine or olanzapine also induce elevations in allopregnanolone in humans, it is possible that allopregnanolone may contribute to the efficacy of these antipsychotics.

Neuroactive steroids may also be neuroprotective. Allopregnanolone has anticonvulsant effects in a variety of animal seizure models. A synthetic homologue of pregnanolone sulfate inhibits NMDA-induced current and cell death in rat hippocampal neuronal cultures and significantly reduces cortical and subcortical infarct size in rats. DHEA (dehydroepiandrosterone) and its sulfated derivative DHEAS protect rodent embryonic cerebral cortical neurons from anoxia, a neurodevelopmental stressor associated with increased schizophrenia risk. DHEA also protects neurons against glutamate and amyloid  $\beta$ -protein toxicity, glucocorticoid toxicity, and numerous other insults resulting in oxidative stress. Since a number of neuroactive steroids demonstrate prominent neuroprotective effects in a variety of rodent experimental systems, these molecules may function to modulate neuronal insults leading to psychiatric morbidity and merit further exploration in the clinical realm.

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## New Projects

### *My HealtheVet Mental Health Portal*

The MIRECC Education component is collaborating with other MIRECCs to assist in the development of the Mental Health Portal for the My HealtheVet website. The participating MIRECCs will conduct Focus Groups with veterans and their families in order to identify what they need to better understand their own behavioural health concerns and/or diagnoses and treatment.

## Publications

Taber KH, Strick PL, Hurley RA. Rabies and the Cerebellum: New Methods for Tracing Circuits in the Brain. *J Neuropsychiatry Clin Neurosci* 2005 Spring; 17(2): 133-139.

## Community Outreach

### National Guard Family Readiness Day

Saturday June 25, 2005  
Raleigh, NC



MIRECC faculty from the Durham VAMC staffed a booth at the North Carolina National Guard Family Readiness Day on June 25th 2005. The event at the RBC Center was held to honor and welcome home the 30th Combat Brigade of the North Carolina National Guard (nicknamed "Old Hickory") that returned from a deployment to Iraq about six months ago. The MIRECC group (Rajendra Morey MD, Mimi Butterfield MD, Rich Weiner MD, PhD, Chris Marx MD) mingled and conversed with Guard members and their families as a way of conducting outreach and to recruit Guard into the MIRECC OEF/OIF registry.

Upon the entering the registry, those who served in OEF/OIF will complete a 90 minutes of questionnaires about combat exposure, depression, anxiety, and substance use; then provide a sample of blood for analysis of neuroactive substances and genetics. The registry will serve as a point of entry into other MIRECC research studies.



## Neuroactive Steroids and Psychiatric Disorders

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Neurosteroids interact with the hypothalamic-pituitary-adrenal (HPA) axis and so may be important in stress-related illnesses. Allopregnanolone, for example, is known to increase with stress. Stress-induced elevations in this neurosteroid would ultimately suppress the HPA axis. It has been hypothesized that stress-induced allopregnanolone induction may therefore represent an endogenous autoregulatory mechanism to restore homeostasis following a stressful event. Since many psychiatric disorders are stress-sensitive, and illnesses such as depression demonstrate a dysregulation in stress hormones (including cortisol), neuroactive steroid modulation of the HPA axis may have important clinical ramifications.

Given accumulating evidence suggesting that neuroactive steroids may be important in psychiatric disorders and treatment strategies, the possibility that neuroactive steroids (or the enzymes leading to neurosteroid biosynthesis) may serve as targets for pharmacological intervention has received increasing attention. Limiting factors in drug development have included the rapid metabolism and poor water-solubility of neuroactive steroids, but efforts are currently underway to address these difficulties. At this time it appears likely that neuroactive steroid drug development initiatives will yield a number of promising compounds to be utilized in the treatment of neuropsychiatric disorders in future years.

## Updates

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### **Research**

MIRECC personnel at the Durham VAMC/Duke University site have inducted their first research subjects. Hampton VAMC and Salisbury VAMC are in the process of obtaining project approval from their local IRBs and expect to begin subject recruitment soon.

### **National MIRECC 2005 Conference**

#### **Risk, Rehabilitation, and Recovery: Treating Mental Illness in the VA**

The recent National MIRECC conference (June 6-8, 2005) brought together representatives of all 10 MIRECCs as well as mental health experts from DoD, VA, and national mental health organizations. Several members of the VISN 6 MIRECC made presentations. Dr. Gregory McCarthy, Director of the VISN 6 MIRECC, presented "Post-Deployment Health and Adjustment", an overview of the focus and goals of our MIRECC. Dr. Harold Kudler, Director of the VISN 6 MIRECC Clinical Component, presented "Findings of the Joint DoD/VA Conference on Post Deployment Mental Health" (see vol 1(2) of this newsletter for his article on this topic). Dr. Robin Hurley, Director of the VISN 6 MIRECC Education Component, chaired two breakout sessions on "The Veteran and New Wars: Differences, Changes, Expectations". Dr. Katherine Taber, Assistant Director of the VISN 6 MIRECC Education Component, participated in the National MIRECC Education planning session for new educational initiatives.