



American College of Neuropsychopharmacology

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Researchers Use New Techniques to Assess PTSD

Findings from Two Studies with Newly Returning Veterans Presented

NASHVILLE, TN (December 8, 2009) – Working with Iraq and Afghanistan veterans, scientists have identified measurable traits that may be useful to evaluate PTSD and develop new treatments. Using blood analysis and brain imaging techniques, scientists have identified possible characteristics, known as candidate biomarkers, for patients with PTSD. Progress in this area could lead to earlier diagnosis and enable individuals to receive personalized treatment strategies, which could greatly improve the therapeutic outcomes for many veterans who have served in the U.S. military since September 11, 2001.

Two separate abstracts describing these advances were presented at the annual meeting of the American College of Neuropsychopharmacology (ACNP) this week.

Candidate Biomarkers

Veterans of Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) frequently experience high rates of PTSD along with symptoms of depression and pain. However, little is known about why these symptoms occur together or the most effective treatments that can be used to alleviate them. One approach that may yield new insights is to search for biomarkers—indicators of a biological state that can be easily and reliably measured in people with an illness—to see if their presence or absence can predict symptoms that an individual will experience and identify optimal treatment strategies.

Dr. Christine Marx and her team at Duke University and the Durham VA Medical Center sought to determine if there are biomarkers that are associated with PTSD symptoms. They hypothesized that veterans who have PTSD (and who often experience depression and pain symptoms) show changes in neurosteroids, which are brain chemicals thought to play a key role in responsiveness to stress.

Dr. Marx based her approach on prior work involving animal models showing that levels of neurosteroids found in blood samples accurately reflect levels found in the brain. In her current research, Dr. Marx measured blood neurosteroid levels in 90 male OEF/OIF veterans to examine whether they may be predictive of PTSD, depression, and pain symptoms. These researchers found that several candidate biomarkers could be important to identifying the changes that occur in the brain with PTSD, which could aid

in the development of more effective treatments. “The neurosteroid allopregnanolone looks like a particularly promising biomarker that we might use to help assess symptom severity in PTSD, depression, and pain disorders, understand their neurobiological underpinnings, develop new treatment options, and predict therapeutic response,” said Marx, an Associate Member of ACNP.

“We’ve now developed a method that can rigorously quantify neurosteroids in blood and may help us identify people at risk at earlier timepoints, which could enable us to better tailor treatment options to each individual,” she added.

Marx and her team are now completing a treatment study in veterans with mild traumatic brain injury (TBI) using the neurosteroid pregnenolone. Preliminary results from this small randomized controlled trial suggest that increases in neurosteroid levels following this intervention predict PTSD symptom improvement in veterans with TBI.

Dr. Marx cautioned that biomarker research in psychiatric disorders is currently in its earliest stages. However, recent studies are yielding important clues to understanding and treating these illnesses. Her work was funded by the Veterans Administration, National Institutes of Health, the Department of Defense, and NARSAD.

Brain Function Changes

Trials currently underway that test treatments for PTSD have shown a tremendous amount of individual variability in the responses to psychotherapy and medication. Alexander Neumeister, MD and his team at Yale University School of Medicine sought to better understand why veterans with PTSD that also have depression, alcohol or substance abuse and suicidality vary so widely in responses to treatment. They created individual risk profiles examining brain function and whether the presence of other disorders along with PTSD affect the treatment outcome and symptom recovery.

Researchers used a collection of powerful brain imaging techniques—including functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) on a high resolution research tomograph (HRRT)—to examine activity within different parts of the brain, focusing on structures known to be involved in the regulation of mood, anxiety and suicidality.

Dr. Neumeister and his team found veterans with PTSD that also experienced depression, alcohol or substance abuse and suicidality show changes in the brain that are very different from veterans with only PTSD. “Veterans with a single diagnosis PTSD look very different in a neurobiological sense than veterans with dual diagnoses of PTSD with depression,” said Neumeister, a Member of ACNP. “These differences can have huge implications for treatment.”

Neumeister explained that giving a group of antidepressants called SSRIs to patients with both depression and PTSD will often treat the depression but not necessarily the PTSD. SSRIs may also help patients with impulsive symptoms and high anxiety. Yet, if the patient is also alcohol dependent, those treatments are often ineffective.

Equipped with more knowledge about the underlying neurobiology of PTSD, scientists will be able to develop more effective treatments, which is especially helpful for veterans who were previously reluctant to seek help. “Once veterans see this is a neurobiological disorder in which their brain acts differently in terms of circuitry and chemical function; oftentimes it motivates them to seek treatment,” said Neumeister.

Although such fMRI and PET studies are often expensive, Neumeister is optimistic that these findings in terms of subgroups and treatment effectiveness can be generalized to a wider group of veterans, which might enable the use of a more restricted set of diagnostic tools in the future.

Future work will focus on adding measurements of other types of brain activity, which will help to refine the neurobiological profiles. “Ultimately, we are trying to develop a neurobiological profile that describes people who are resilient to the impact of trauma,” added Neumeister, whose work is funded by the National Institutes of Health (NIMH, NIAAA), the Department of Veterans Affairs, NARSAD, the Patrick and Catherine Weldon Donaghue Medical Research Foundation, and the National Center for PTSD.

Marx is a co-applicant on a provisional patent application for neurosteroids and methods of lowering cholesterol; no patent issued; no licensing in place. She is also an unpaid scientific advisor/board member for NeuroScience Pharmaceuticals.

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ACNP, founded in 1961, is a professional organization of more than 700 leading scientists, including four Nobel Laureates. The mission of ACNP is to further research and education in neuropsychopharmacology and related fields in the following ways: promoting the interaction of a broad range of scientific disciplines of brain and behavior in order to advance the understanding of prevention and treatment of disease of the nervous system including psychiatric, neurological, behavioral and addictive disorders; encouraging scientists to enter research careers in fields related to these disorders and their treatment; and ensuring the dissemination of relevant scientific advances.