



## Scientists Identify New Approaches to Treating PTSD

March 1, 2010

AUSTIN, Texas — Drugs known as HDAC inhibitors may prove useful in treating post-traumatic stress disorder (PTSD), according to a study conducted by faculty at The University of Texas at Austin's Waggoner Center for Alcohol and Addiction Research.



The study, the results of which were recently published in *Neuropsychopharmacology*, may point the way toward new treatments for PTSD, a severe anxiety disorder which is estimated to afflict as many as one in eight returning Iraq and Afghanistan War veterans.

"The HDAC inhibitors are **already being used** in clinical trials, but in relation to other neurological diseases, like Alzheimer's and Huntington's," says **Igor Ponomarev**, a research assistant professor in the College of Pharmacy and the Waggoner Center. "They've never been tested in PTSD. The results of this study suggest that they should be."

PTSD occurs as a result of exposure to severe stress—from battle, for example, or a natural disaster—and its symptoms,

including flashbacks, an excessive startle response, depression, anxiety, and insomnia, can persist over long periods of time.

Researchers believe that PTSD occurs when the brain's system for regulating stress overloads to the point where it can no longer revert to a normal state, even after the cause of the stress disappears. Particularly affected is the amygdala, which is one of the critical structures in the brain related to learning and memory, and in particular to fear-related learning and memory.

Those suffering from PTSD can end up with an amygdala that is on high alert for mild stressors and stimuli that are evocative of the original source of the stress.

Ponomarev and co-author **R. Adron Harris**, professor of neurobiology, used a rat model of PTSD to trace these broad changes in the amygdala down to the level of gene expression.

"What we found were that genes that are known to be involved in excitation and inhibition changed their expression three weeks after stress," says Ponomarev. "The overall result is an amygdala that's unable to normally respond to stressors."

One of the most potentially useful findings of the study is that severe stress—like the kind that produces PTSD—can result in the increased expression of certain genetic elements that had, until recently, been dismissed by neuroscientists as "junk DNA."

These particular DNA sequences may prove significant, says Ponomarev, because they seem to be involved in, or indicative of, a process known as "**chromatin remodeling**," which helps determine which genes are or are not expressed in a given cell. It's precisely this process that seems to be responsive to the HDAC inhibitors.

"It's a hot area in neuropsychiatric disorders," he says, "because there are some pharmacological compounds that can block or promote chromatin remodeling. It's possible to imagine that some of the long-term changes in gene expression, which we've seen result from severe stress, could be reversed or modulated by the drugs."

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