Scientists identify compounds that could thwart post-traumatic stress disorder

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A brain pathway that is stimulated by traumatic or fearful experiences can be disrupted by two compounds that show promise for preventing post-traumatic stress disorder, Indiana University researchers reported.

In a presentation prepared for the Neuroscience 2012 scientific conference in New Orleans Oct. 13 to 17, Anantha Shekhar and colleagues from IU reported the results of experiments with rats using a standard methodology called a conditioned fear test.

The neural signaling activated by fearful experiences—a process that also is involved in learning and in memory formation—begins when the neurotransmitter glutamate activates a receptor called NMDA, resulting in a later protein reaction involving production of nitrous oxide, another chemical messenger in the brain.

The two small molecules tested, known as IC87201 and ZL006, are known to disrupt such nitrous oxide production.

In the experiment, rats treated with either of the two compounds showed significantly less fear response than the untreated rats, the researchers reported.

The results, the researchers said, supported their hypothesis that the NMDA-mediated nitrous oxide production is important in successful formation of fear memories, and disrupting that interaction could potentially offer a means of preventing long-term post-traumatic stress

disorder symptoms

Repeated intense activation of the brain network for fear makes it vulnerable to developing hypersensitivity, said Shekhar, Raymond E. Houk Professor of Psychiatry and director of the Indiana Clinical and Translational Sciences Institute.

"The majority of people who have a traumatic event, perhaps about 80 percent, will have some post-traumatic stress disorder symptoms for a few days. Only about 20 percent will have long-term problems, but currently there is no way to predict who those people will be," Shekhar said.

With that uncertainty, it would be appropriate to administer the treatment to all traumatized patients within a few hours of the incident, such as when a person arrives at an emergency room after an accident or a field hospital after a military incident, he said.

The next steps would be to optimize compounds and begin drug development efforts, Shekhar said.

Shekhar will discuss "Post-trauma disruption of nNOS-PSD95 protein-protein interaction is an effective means to ameliorate conditioned fear," 3 to 4 p.m. Monday, in Hall F-J. Other Indiana University researchers involved in the work were Stephanie D. Fitz, Department of Psychology; Philip L. Johnson, assistant professor of anatomy and cell biology; Andrea G. Hohmann, Linda and Jack Gill Chair of Neuroscience and professor of psychological and brain sciences; Ted Widlanski, professor of chemistry; and Yvonne Y. Lai, Department of Psychological and Brain Sciences.

Provided by Indiana University