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Brain imaging pinpoints neurobiological basis for key symptoms associated with post-traumatic stress disorder

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In a novel brain-imaging study among trauma victims, researchers at NYU Langone Medical Center have linked an opioid receptor in the brain—associated with emotions—to a narrow cluster of trauma symptoms, including sadness, emotional detachment and listlessness. The study, published online today in the journal *JAMA Psychiatry*, holds important implications for targeted, personalized treatment of post-traumatic stress disorder, or PTSD, a psychiatric condition affecting more than 8 million Americans that can cause a wide range of debilitating psychiatric symptoms.

"Our study points toward a more personalized treatment approach for people with a specific symptom profile that's been linked to a particular neurobiological abnormality," says lead author Alexander Neumeister, MD, director of the molecular imaging program in the Departments of Psychiatry and Radiology at NYU School of Medicine, and Co-Director of NYU Langone's Steven and Alexandra Cohen Veterans Center for the Study of Post-Traumatic Stress Disorder and Traumatic Brain Injury. "Understanding more about where and how symptoms of PTSD manifest in the brain is a critical part of research efforts to develop more effective medications and treatment modalities."

The new study confirms a growing body of evidence linking a particular set of symptoms to specific brain circuits and chemicals, and bolsters a shift within the field of psychiatry away from "one-size-fits-all

treatments" and toward more individualized medication regimens that target highly specific neurobiological components. "We know from previous clinical trials that antidepressants, for example, do not work well for dysphoria and the numbing symptoms often found in PTSD," Dr. Neumeister added. "Currently available antidepressants are just not linked specifically enough to the neurobiological basis of these symptoms in PTSD. Going forward, our study will help pave the way toward development of better options."

"People with cancer have a variety of different treatment options available based on the type of cancer that they have," adds Dr. Neumeister. "We aim to do the same thing in psychiatry. We're deconstructing PTSD symptoms, linking them to different brain dysfunction, and then developing treatments that target those symptoms. It's really a revolutionary step forward that has been supported by the National Institute of Mental Health (NIMH) over the past few years in their Research Domain Criteria Project."

The study, funded by the National Institute of Mental Health (NIMH), compared the brain scans of healthy volunteers with those of clinically diagnosed trauma victims with PTSD, major depression, and generalized anxiety disorder whose symptoms ranged from emotional detachment to isolation. Participants received a harmless radioactive tracer that binds to and illuminates a class of opioid receptors, known as kappa, when exposed to high-resolution positron emission tomography (PET). Kappa opioid receptors bind a potent natural opioid known as dynorphin, which is released by the body during times of stress to help relieve dysphoria or numbing.

Chronic exposure to stress, such as the case with PTSD, taxes kappa opioid receptors, however, causing the receptors to retract inside cells, leaving dynorphin without a place to dock. As a result, patients can experience dysphoria, characterized by feelings of hopelessness,

detachment and emotional unease.

Results showed that fewer available kappa opioid receptors in the brain regions believed to govern emotions were associated with more intense feelings of dysphoria, but not feelings of anxious arousal. The findings confirm previous studies in animals linking the opioid-receptor system expressed in these specific brain regions to symptoms of dysphoria. The study also found an association between lower levels of cortisol, a stress hormone, and unavailable kappa opioid receptors, suggesting a new role for cortisol as a biomarker for certain types of PTSD symptoms.

"This is the first brain-imaging study to explore any psychiatric condition using a protein that binds to the kappa opioid receptor system," notes Dr. Neumeister, who says the data support clinical trials under way at NYU Langone and other institutions of new medications that target kappa opioid receptors and other brain systems that can be linked to specific symptoms in trauma survivors. Such medications could be widely available for the treatment of PTSD in the future if ongoing clinical trials yield encouraging results.

This new research study also dovetails with work underway at NYU Langone's Steven and Alexandra Cohen Veterans Center for the Study of Post-Traumatic Stress Disorder and Traumatic Brain Injury, where Dr. Neumeister serves as Co-Director. The center is conducting numerous studies to advance the use of biomarkers to detect PTSD, TBI and other trauma-related illnesses. "Returning veterans are a particularly vulnerable population, so we are hopeful this research will lead to better treatments for them, since they represent an escalating demographic of victims of PTSD," he added. This research was conducted in collaboration with scientists at Yale School of Medicine, the School of Medicine at the University of California, San Diego, and the U.S. Department of Veterans Affairs National Center for Post-Traumatic Stress Disorder.