Depressed females have over-active glutamate receptor gene

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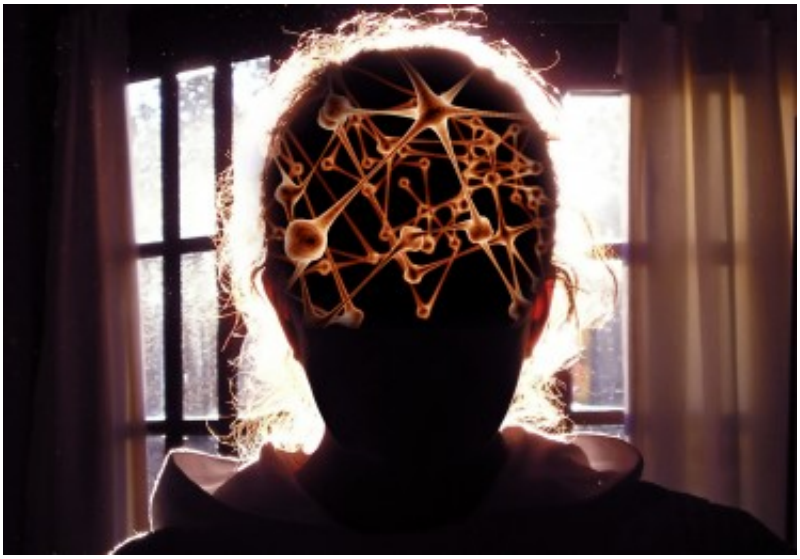

Numerous genes that regulate the activity of a neurotransmitter in the brain have been found to be abundant in brain tissue of depressed females. This could be an underlying cause of the higher incidence of suicide among women, according to research at the University of Illinois at Chicago.

Studying postmortem tissue from brains of psychiatric patients, Monsheel Sodhi, assistant professor of pharmacy practice at UIC, noted that female patients with depression had abnormally high expression

levels of many genes that regulate the glutamate system, which is widely distributed in the brain.

Glutamate is the major excitatory neurotransmitter in the brain. Schizophrenia, epilepsy, autism and Alzheimer's disease have all been linked to abnormalities of the glutamate system.

Gender plays a role in depression and suicide, Sodhi said. Women are two to three times more likely to attempt suicide, but men are four times more likely to die by suicide. The risk of suicide is associated with changes in several neurotransmitter systems.

Sodhi and her colleagues were intrigued by recent studies that found that a low dose of the drug ketamine, which alters glutamate system activity, can rapidly eliminate depression in two-thirds of patients who do not respond to conventional antidepressants. Conventional antidepressants target the monoamine systems, which secrete the neurotransmitters dopamine, serotonin or norepinephrine.

In the new study, published in the journal *Molecular Psychiatry*, Sodhi and her coworkers analyzed brain tissue from people who had suffered from depression. Both females and males were compared to subjects who had never experienced psychiatric illness. Many of the depressed patients, she said, had died by suicide.

Females with depression, Sodhi discovered, had the highest levels of expression of several glutamate receptor genes, perhaps making them more prone to depression. In addition, three of these genes were found to be elevated in both male and female patients who had died by suicide.

"Our data indicate that females with major depression who are at high risk of suicide may have the greatest antidepressant benefit from drugs that act on the glutamate system, such as ketamine," Sodhi said. The

study also suggests new glutamate receptor targets for development of treatments for depression and identifies biochemical markers that could be used to assess suicide risk, she said.

More than 41,000 people die by suicide each year in the United States, according to the Centers for Disease Control and Prevention. It is the second-leading cause of death in people aged 15 to 34 years. Suicide claims a life every 14 minutes in the U.S., and the frequency is escalating. Over 90 percent of the people who take their lives suffer from mental illness, predominantly depression.

Only one-third of patients receiving conventional treatments achieve substantial remission of their depression, which may take several weeks or longer, Sodhi said. This time lag in response to treatment is a problem, she said, due to the high risk of suicide.

Provided by University of Illinois at Chicago