Researchers looking for genetic predictors for suicide

September 9 2009

Every 16 minutes, an American commits suicide. It's the 11th leading cause of death in this country, a fact being widely noted during National Suicide Prevention Week Sept. 6-12. And now researchers at the University of Alabama at Birmingham (UAB) are looking deep inside the brain for ways to determine the reasons people commit suicide - and identify those most likely to attempt it.

Monsheel Sodhi, Ph.D., an assistant professor in the UAB Department of Psychiatry and Behavioral Neurobiology, says it is generally perceived that suicide tends to run in families. Genes, which are the blueprint for a cell's formation, use proteins to carry out their instructions. Sodhi is examining the role of specific proteins in the brain to develop a test that potentially could identify those at highest risk so they could be steered to therapy.

Funded by a grant from the American Foundation for Suicide Prevention (AFSP), Sodhi is investigating a protein called the serotonin 2C receptor. Scientists refer to it as a signaling protein, one of several that are responsible for the proper functioning of serotonin, a chemical in the brain that regulates feelings of well-being and happiness. Serotonin 2C interacts with anti-depressant drugs such as Prozac, which are thought to treat depression by boosting serotonin signalling.

"Most people who attempt or complete suicide have an underlying psychiatric illness, such as depression, bipolar disorder or schizophrenia," said Sodhi. "An imbalance in serotonin is one factor

thought to contribute to such illnesses. The imbalance might be caused by low production of serotonin or inability of cells to receive it or even a problem in the pathways in which serotonin signals travel."

That leads Sodhi to a second type of protein called ADAR, which seems to inhibit the activity of the serotonin 2C protein when serotonin is absent. Simply put, too much ADAR leads to too little serotonin 2C signaling.

"It appears that the ADARs switch serotonin 2C partially off in critical brain regions, perhaps altering the brain's ability to interpret messages of happiness, pleasure and well-being," Sodhi said. "That could contribute to psychiatric disorders such as depression, which most often is the underlying cause of suicide."

The AFSP grant is enabling Sodhi to study serotonin 2C and ADAR proteins in post-mortem brain tissue. Sodhi is working with a team of scientists at the National Institutes of Health who have collected brain tissue from 500 people, divided into three groups. The first is a control group of some 200 people who never attempted suicide and had no diagnosis of a psychiatric disorder. A second group comprises people with a psychiatric disorder who did not commit suicide, and the third comprises people who committed suicide.

"We're looking at altered levels of ADARs and serotonin 2C by measuring changes in messenger RNA," said Sodhi. "If we find mutations in the ADARs that seem to correspond with an increased likelihood of suicide, this information could lead to the development of diagnostic tests that could predict those patients who are most at risk for suicide and those who would respond well to particular therapies."

Simply knowing more about the role of ADARs and serotonin 2C in the development of mental illness could also boost suicide-prevention

efforts. Untreated mental illness is a major cause of [suicide](), and Sodhi says that identifying a dysfunctional gene or protein provides scientists with new targets for the development of better drug treatments.

Source: University of Alabama at Birmingham ([news]() : [web]())