MedicalXpress

Researchers uncover new insights into developing rapid-acting antidepressant for treatment-resistant depression

June 12 2014

UT Southwestern Medical Center researchers have generated fresh insights that could aid in the development of rapid-acting antidepressants for treatment-resistant depression.

The researchers found that by blocking NMDA receptors with the drug ketamine, they could elicit rapid antidepressant effects in patients with treatment-resistant depression. Ketamine was developed as an anesthetic, but is better known publicly for its abuse as the party drug Special K. Researchers are now seeking alternatives because ketamine can produce side effects that include hallucinations and the potential for abuse – limiting its utility as an antidepressant.

Therefore, researchers had been investigating a drug called memantine, currently FDA-approved for treating moderate to severe Alzheimer's disease, as a potentially promising therapy for treatment-resistant depression. Memantine acts on the same receptors in the brain as fast-acting ketamine, said Dr. Lisa Monteggia, Professor of Neuroscience. However, recent clinical data suggest that memantine does not exert rapid antidepressant action for reasons that are poorly understood.

"Although, both ketamine and memantine have similar actions when nerve cells are active, under resting conditions, memantine is less effective in blocking nerve cell communication compared to ketamine, This fundamental difference in their action could explain why

memantine has not been effective as a rapid antidepressant" said Dr. Monteggia, who holds the Ginny and John Eulich Professorship in Autism Spectrum Disorders.

The different effects of ketamine and memantine alter signals emanating from NMDA receptors, in particular those that determine antidepressant efficacy. Dr. Monteggia noted that the new findings point a way to blocking NMDA receptors to control depression with fewer side effects.

Dr. Monteggia's lab focuses on the molecular and cellular bases of neural plasticity, the fundamental property of nerve cells to alter their communication, as they pertains to neuropsychiatric disorders, as well as understanding the mechanisms underlying antidepressant efficacy.

Guidelines by the American Psychiatric Association suggest medications are the preferred treatment for moderate to severe depressive symptomatology. About one in 10 people in the U.S. aged 12 and over takes anti-depressant medication, and about 14 percent of those individuals taking antidepressant medication have done so for 10 years or longer.

Antidepressants were the third most common prescription drug taken by Americans of all ages between 2005 and 2008, and the most frequently used prescription drug by people 18 to 44 years old, according to surveys by the Centers for Disease Control. According to the CDC, comparing the 1988-1994 period with the 2005-2008 period, the average rate of antidepressant use in the U.S. among all ages increased nearly 400 percent.

Overall, women are two and a half times more likely to take antidepressant medication as men, with 23 percent of women aged 40 to 59 taking antidepressants – more than in any other group.

The CDC estimates that nearly 8 percent of people over age 12 report being currently depressed, with women reporting higher rates of depression than males in every age group. Women between 40 and 59 years have the highest rates of depression (about 12 percent). Depression generates more than 8 million visits to physician offices, hospital outpatient and emergency departments, and nearly 400,000 in-patient stays, which average 6.5 days.

Provided by UT Southwestern Medical Center