A fast-acting antidepressant appears within reach

May 1 2014

For someone with depression in the midst of a crisis, there is no time to waste. Yet time is exactly what currently-available antidepressants require to take effect—often on the order of weeks.

A new study suggests a fast-acting antidepressant may be on the horizon. In mice, the drug produces evidence of a mood lift within 24 hours and then continues working for sustained relief.

"What makes this study unique and exciting is that in the same drug we seem to have both of the properties you want in an antidepressant—both rapid and sustained effects," said Jeffery Talbot, Ph.D., director of the Research Center on Substance Abuse and Depression at Roseman University of Health Sciences and one of the study's lead investigators.

Though many drugs are currently available to treat people with depression, existing drugs do not work quickly, and they do not work for everyone. "Many people with depression simply don't respond to available medications," said Talbot. "There's still a real need for new antidepressants."

The drug, referred to by Talbot as its coded name MI-4 and better known among scientists as Ro-25-6981, has been shown by previous researchers to cause a rapid antidepressant effect in animals by blocking one of the brain's signaling chemicals. But until now, researchers were not aware of the full spectrum of its antidepressant properties.

The new study bolsters the evidence for MI-4's rapid effect and adds an exciting twist: MI-4 also works in the long term. Moreover, it may accomplish its long-term effects through a three-pronged approach known as triple reuptake inhibition, which refers to a drug's ability to simultaneously increase the levels of three key chemicals in the brain that are known to affect mood and feelings of pleasure—dopamine, norepinephrine and serotonin. Most depression drugs only target one of these chemicals, which may explain why they are not effective in all patients.

The researchers found MI-4 via "virtual screening," a method that uses computer modeling to find drugs that are likely to interact with particular receptors in the brain. "From looking at its structure, one would never have guessed that this drug interacts with the same monoamine transporter proteins as does Paxil or cocaine, but it does. That speaks to the 'needle in a haystack' detection power of the virtual screening methodology," said Christopher Surratt, Ph.D., a professor of pharmacology working on this aspect of the study at Duquesne University.

Following the virtual screening, the researchers tested MI-4's effects in cell cultures and then in mice. In addition to providing new evidence of its antidepressant properties, the study shows MI-4 would be unlikely to become addictive.

Depression is one of the most common mental illnesses in the world, affecting about 20 million people in the United States. Causing persistent sadness and loss of energy, it can take an enormous toll on a person's ability to work or have healthy personal relationships and is a leading cause of suicide.

Antidepressants are some of the most commonly prescribed medications, with 264 million prescriptions written for antidepressants in 2011

totaling more than $11 billion in sales.

More information: Jeffery Talbot will present the findings during the Experimental Biology 2014 meeting on Wednesday, April 30 at the Pharmacology and Experimental Therapeutics poster session in Sails Pavilion, San Diego Convention Center.

Provided by Federation of American Societies for Experimental Biology