Researchers may have found test for depression

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Researchers from the University of Illinois at Chicago College of Medicine have discovered that a change in the location of a protein in the brain could serve as a biomarker for depression, allowing a simple, rapid, laboratory test to identify patients with depression and to determine whether a particular antidepressant therapy will provide a successful response. The research is published in the March 12 issue of the *Journal of Neuroscience*.

"This test could serve to predict the efficacy of antidepressant therapy quickly, within four to five days, sparing patients the agony of waiting a month or more to find out if they are on the correct therapeutic regimen," said Mark Rasenick, UIC distinguished university professor of physiology and biophysics and psychiatry.

Despite decades of research, the biological basis of depression is unknown, and the molecular and cellular targets of antidepressant treatment remain elusive, although it is likely that these drugs have one or more primary targets.

Rasenick said the discovery could help millions who suffer from undiagnosed depression or receive unsuccessful treatment.

"We discovered that in depressed individuals a signaling protein is located in specific areas of the cell membrane called lipid rafts," he said. This protein, called Gs alpha, activates adenylyl cyclase, a link in signal transduction, and is responsible for the action of neurotransmitters such

as serotonin.

"These 'rafts' are thick, viscous, almost gluey areas, that either facilitate or impede communication between membrane molecules," Rasenick said. "When Gs alpha is caught in these lipid raft domains, its ability to couple with and activate adenylyl cyclase is markedly reduced. Antidepressants help to move the Gs alpha out of these rafts and facilitate the action of certain neurotransmitters."

Previous research in both rats and cultured brain cells by Rasenick and his colleagues, as well as others, has shown that Gs alpha changed its location in response to antidepressants, moving out of the lipid rafts to areas of the membrane that allow more efficient communication among membrane components responsible for neurotransmitter action. Further, antidepressant and antipsychotic drugs have been shown to concentrate in these lipid rafts.

"This new study shows that in depressed humans, Gs alpha protein is confined in lipid rafts, where it's less likely to mediate the action of neurotransmitters, and that antidepressants have the opposite effect," Rasenick said.

"In simple language -- we may be able to tell you if you are depressed and more importantly, whether you are responding to the chosen antidepressant therapy."

The new study may also explain why antidepressants take so long to work and why chemically dissimilar compounds have similar effects.

In their study, Rasenick and colleagues compared brain samples from depressed people who had committed suicide with controls who had no history of psychiatric disorders. They found that while the total amount of Gs alpha was the same in the depressed and non-depressed, the

depressed have a greater proportion of Gs alpha confined to lipid rafts. The localization of other G proteins was not different.

Rasenick and his colleagues have begun further studies to confirm and expand these findings.

Source: University of Illinois at Chicago