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Depression diversity: Brain studies reveal big differences among individuals

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Depressed people may have far fewer of the receptors for some of the brain's "feel good" stress-response chemicals than non-depressed people, new University of Michigan Depression Center research shows.

And even among depressed people, the numbers of these receptors can vary greatly. What's more, the number of receptors a depressed person has appears to be linked with the severity of their symptoms - and the chances that they'll feel better after taking a medication.

These preliminary findings, presented Tuesday at the American Psychiatric Association's annual meeting in Washington, D.C., amplify a growing understanding of depression as a condition that affects different people in different ways, and is solidly rooted in genetic and molecular factors that are unique to each individual.

The lead U-M researcher, Jon-Kar Zubieta, M.D., Ph.D., says these new results bolster what other researchers have been finding in recent years.

"There's a substantial amount of biological difference even among people who have major depression, which is just as important as the biological differences between people with depression and people without," he says. "The more we can understand about these differences, the better we can address treatment to the individual and have the greatest effect on symptoms."

At the APA meeting, Zubieta presented data from positron emission

tomography, or PET, scans of the brains of patients who met the criteria for major depression but had not yet received treatment for it. Those scans were compared with scans of the brains of non-depressed comparison volunteers.

In one group of depressed and non-depressed volunteers, the scans were made using a tracer that can reveal the location and concentration of a particular type of receptor. Called the 5HT1a receptor, it allows brain cells to receive signals from serotonin, a chemical neurotransmitter produced by the brain.

Serotonin levels in the brain are linked to depression, but the importance of 5HT1a receptor concentrations in the brains of depressed people has been cloudy. That's why Zubieta's team chose to scan only people who had not yet received antidepressant medications, since some such medications may actually encourage the brain's cells to make more serotonin receptors - and masking the actual level of receptors that the person has naturally.

In the study, 5HT1a receptor concentrations were markedly lower in depressed people compared with non-depressed people, in both the left and right hippocampus region of the brain.

But even among depressed people, the lower a person's the 5HT1 receptor levels were, the worse he or she scored on assessments of their ability to function day-to-day - and they less likely he or she was to get relief from symptoms when the researchers prescribed them a common antidepressant.

This finding of individual variation may help explain why in current depression treatment, some patients find great relief from a medication that doesn't help other equally depressed patients, says Zubieta, who is the Phil F. Jenkins Research Professor of Depression in the U-M

Department of Psychiatry. He also holds positions in the U-M Nuclear Medicine division, and the Molecular & Behavioral Neuroscience Institute.

The other group of depressed volunteers - both depressed and non-depressed -- received PET scans with a tracer that allowed the researchers to see the mu-opioid receptors in their brains. These receptors are the gateway for signals sent by chemicals called endogenous opioids -- the brain's natural "painkillers" - which are involved in stress response including response to pain.

Another name for the neurotransmitters that bind to mu-opioid receptors is endorphins, which have become known as a "feel good" chemical involved in reinforcing rewarding experiences. Illicit drugs such as heroin also act upon mu-opioid receptors, creating the "high" sensation and probably playing a role in the addiction process.

In this group of depressed and non-depressed volunteers, the researchers studied the distribution of the mu-opioid receptors and looked at how active the receptors were when the volunteers were asked to summon a sad memory or scenario to mind.

Depressed volunteers had lower concentrations of mu-opioid receptors to begin with. But when they underwent the "sadness challenge", those receptors were much more active than the receptors in non-depressed people. And, just as with the serotonin 5HT1a receptors, the fewer mu-opioid receptors a person had, the less well they responded to an antidepressant medication.

Source: University of Michigan