

Metabolism may play role in recurrent major depression

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Researchers at University of California San Diego School of Medicine,

in collaboration with Dutch scientists, have found that certain metabolites—small molecules produced by the process of metabolism—may be predictive indicators for persons at risk for recurrent major depressive disorder.

The findings were published in the January 11, 2021 online issue of *Translational Psychiatry*.

"This is evidence for a mitochondrial nexus at the heart of depression," said senior author Robert K. Naviaux, MD, Ph.D., professor of medicine, pediatrics and pathology at UC San Diego School of Medicine. "It's a small study, but it is the first to show the potential of using metabolic markers as predictive clinical indicators of patients at greatest risk—and lower risk—for recurring bouts of major depressive symptoms."

Recurrent major depressive disorder (in lay terms, [clinical depression](#)) is a mood disorder characterized by multiple symptoms in combination: feelings of sadness or hopelessness, anger or frustration, loss of interest, sleep disturbances, anxiety, slowed or difficulty thinking, suicidal thoughts and unexplained physical problems, such as back pain or headaches.

Major depressive disorder (MDD) is among the most common mental illnesses in the United States, with an estimated lifetime prevalence of 20.6 percent, meaning one in five Americans will suffer at least one episode during their lives. For patients who have recurrent MDD (rMDD), the five-year recurrence risk is up to 80 percent.

For their study, Naviaux and colleagues in The Netherlands recruited 68 subjects (45 females, 23 males) with rMDD who were in antidepressant-free remission and 59 age- and gender-matched controls. After collecting blood from patients who were in remission, the patients were

followed prospectively for two-and-a-half years.

Results showed that a metabolic signature found when patients were well could predict which patients were most likely to relapse up to two-and-a-half years in the future. The accuracy of this prediction was more than 90 percent. Analysis of the most predictive chemicals found they belong to certain kinds of lipids (fats that included eicosanoids and sphingolipids) and purines.

Purines are made from molecules, such as ATP and ADP—the major chemicals used for energy storage in cells, but which also play a role in communications used by cells under stress, known as purinergic signaling.

The researchers found that in subjects with rMDD, changes in specific metabolites in six identified metabolic pathways resulted in fundamental alterations of important cellular activities.

"The findings revealed an underlying biochemical signature in remitted rMDD that set diagnosed patients apart from healthy controls," said Naviaux. "These differences are not visible through ordinary clinical assessment, but suggest that the use of metabolomics—the biological study of metabolites—could be a new tool for predicting which patients are most vulnerable to a recurrence of depressive symptoms."

The authors noted that their initial findings require validation in a larger study of at least 198 females and 198 males (99 cases and 99 controls each).

More information: Roel J. T. Mocking et al. Metabolic features of recurrent major depressive disorder in remission, and the risk of future recurrence, *Translational Psychiatry* (2021). [DOI: 10.1038/s41398-020-01182-w](https://doi.org/10.1038/s41398-020-01182-w)

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