

New theory may explain cause of depression and improve treatments

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A new area in depression research suggests dysfunction in mitochondria—the main source of energy for cells—could lead to major depression. Published in *Frontiers in Neuroscience*, this new insight to long-held theories on the causes of depression could lead to the

development of novel and more effective antidepressant drugs.

Depression is a highly prevalent disorder affecting up to 20% of the population. It is commonly thought to be caused by a chemical imbalance in the brain, yet the specific biological mechanisms which lead to [depression](#) are not fully understood.

"Until now, most theories about the biological causes of depression have focused on the idea that depression is caused by an imbalance in neurotransmitters like serotonin," says Dr. Lisa E. Kalynchuk, co-author of the review from the University of Victoria, Canada.

"However, antidepressants can increase serotonin levels almost immediately, yet take weeks to have a therapeutic effect on the symptoms of depression. This suggests serotonin is unlikely to be the root cause of depression."

Most antidepressant drugs used today are the same as those developed more than 50 years ago. In addition to the delayed onset of effective symptom relief, antidepressants only work in around half of patients—and often have adverse side effects.

The team recognized the necessity for new and more effective treatments for depression. However, before new drugs can be developed, it is necessary to first understand the cellular causes of depression.

"Despite extensive research efforts, there is still a fundamental lack of understanding about the specific biological changes that give rise to depressive symptoms," explains Kalynchuk.

To better understand how depression arises, the researchers looked for specific causes within the brain cells. This led them to a small organelle found within brain cells called mitochondria. Mitochondria are the main

source of energy for cells, but they also help to regulate brain function.

"Animal models showed that depression is associated with the decreased generation of new cells in the hippocampus—a region of the adult [brain](#) known to regulate emotion, mood, cognition and stress," says Kalynchuk.

"As these are all implicated in depression, this originally led us to think that depression was caused by the deficiency in new cell generation. However, this theory does not explain all the research findings because [depressive symptoms](#) can occur in the absence of this deficiency.

"What we do know that this process is metabolically demanding and requires a lot of energy. This led us to suspect mitochondria as the root cause of depression, as they provide energy for [cells](#)."

The researchers believe the dysfunction of mitochondria can lead to a cascade of effects which result in depression. This idea offers new opportunity for the development of new [antidepressant drugs](#) which can normalize [mitochondria](#) function.

"This would be a completely novel approach that has little to do with what current anti-depressants are doing," says Kalynchuk. "It will take time to fully explore these ideas, but we hope it will open doors to new areas of research in the depression field and lead to the development of more effective antidepressant medication."

More information: Josh Allen et al, Mitochondria and Mood: Mitochondrial Dysfunction as a Key Player in the Manifestation of Depression, *Frontiers in Neuroscience* (2018). [DOI: 10.3389/fnins.2018.00386](#)

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