

Have we been treating depression the wrong way for decades?

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Have we been treating depression the wrong way for decades?

New analysis questions use of antidepressants, but experts aren't convinced



[Adam Miller](#) · CBC News · Posted: Aug 13, 2022 4:00 AM ET | Last Updated: 8 hours ago



A recent analysis paints a compelling picture that depression isn't caused by a chemical imbalance in the brain. But experts say this is already widely accepted and it's also true that antidepressants can be extremely beneficial to some patients — even if we don't know exactly why. (Shutterstock / Chanintorn.v)

[801](#) comments

This is an excerpt from Second Opinion, a weekly analysis of health and medical science news. If you haven't subscribed yet, you can do that by clicking [here](#).

A new analysis of the cause of depression has seemingly upended what we know about this common condition and challenged the use of antidepressants. But it may also leave patients with more questions than answers as the science evolves.

A systematic umbrella review of 17 studies published in [Molecular Psychology](#) on July 20 looked at the decades-old theory that depression is caused by low serotonin, and found there was "no consistent evidence" of "an association between serotonin and depression."

The theory that depression is caused by a chemical imbalance in the brain has been around since the 1960s. But for years, many experts have doubted this, feeling it oversimplified a complex condition.

SECOND OPINION

2 years into the pandemic, Canada's mental-health system is at a crisis point

"The serotonin theory is very old and has been very popular since the '90s, when the pharmaceutical industry started promoting it," said Dr. Joanna Moncrieff, a psychiatry professor at University College London and lead author of the study.

"But since about 2005, probably a bit before then, there's been sort of rumours that actually the evidence isn't very strong, or it's inconsistent. Some studies are positive, some studies are negative, but no one's really got that evidence together anywhere."

Moncrieff and her team set out to challenge the serotonin theory in a systematic review of available research. They also went a step further in their conclusion by suggesting that antidepressants are ineffective at treating depression — and have largely worked as a placebo.

- **Anxiety, depression, loneliness at highest levels among Canadians since early pandemic: survey**

"Evidence from placebo-controlled trials show that antidepressants are a little bit better than a sugar tablet," she said. "And if that little difference is not to do with rectifying a chemical imbalance, improving low serotonin levels, what is it to do with?"

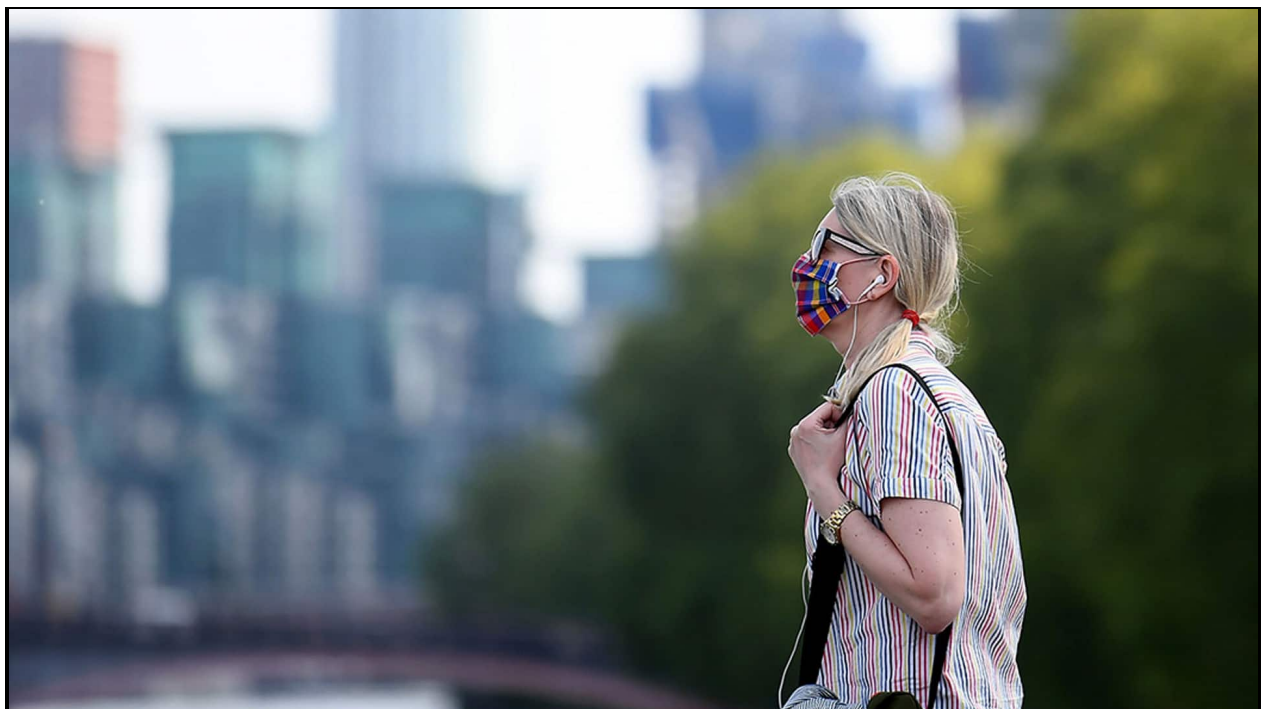
The research paints a compelling picture that depression isn't caused by low serotonin alone. Many experts say this is already widely accepted and that it's also true that antidepressants can be extremely beneficial to some patients — even if we don't know exactly why.

So where does this leave patients and physicians, and could the analysis impact the way we treat depression in the future?

Are antidepressants effective against depression?

Antidepressants are widely believed to affect the behaviour of neurotransmitters, chemical messengers in the brain like serotonin and dopamine, in a way that can alter emotions and mood to help improve the symptoms of depression in some patients.

WATCH | Living alone during pandemic can worsen anxiety, depression:



The ongoing physical distancing precautions because of the COVID-19 pandemic can exacerbate anxiety and depression, especially for people living alone.

People with depression can face a wide range of symptoms, including persistent feelings of sadness and desperation, changes in appetite, sleep deprivation, fatigue, irritability and loss of interest in hobbies and social connections that can impact everyday life.

While it's unclear exactly how antidepressants work at a biological level to alleviate those symptoms, it's clear that they can still be hugely helpful to some patients.

- **Parents, women among Canadians struggling most with mental health during pandemic: surveys**

"It's a typical discovery in medicine — you find a drug that works, but you don't quite know why," said Dr. Phil Cowen, a professor of psychopharmacology at the University of Oxford.

"[The review] is a debunking exercise and in a way, they're criticizing older studies that were hard to do," he said. "These [older] studies, clearly, were very indirect and they're messy, and I don't think anyone thought that they were that great."

Moncrieff's team found that some depressed patients actually had higher serotonin levels in certain areas of the brain, and in some cases the long-term use of antidepressants could actually lower the amount of serotonin — though the findings were "inconsistent."

"I think it makes a huge difference, because how [antidepressants] work actually influences whether they work," she said. "It influences how helpful we think they are."

The findings have caused a major stir in the media and scientific community, with hundreds of news outlets covering the study — quickly landing it in the top five per cent of all research scored by [Altmetric](#), a company that analyzes where published research is shared.

Findings of this perceived magnitude can have a seismic impact on the way we understand and treat a widespread condition like depression, which affects an estimated [one in eight Canadians](#) at some point in their lives.

While the research questions the very nature of what we know about depression, many doctors are hesitant to change the way we treat it.

Antidepressants can be 'lifesaver' for some

Dr. David Juurlink, head of clinical pharmacology at Sunnybrook Health Sciences Centre in Toronto, said he's not surprised by the findings, because the chemical imbalance theory for depression is now widely seen as an "obvious oversimplification" for a complex condition.

"Although I think doctors prescribe serotonin-enhancing antidepressants far too often, in part because of this oversimplification, it's important to acknowledge that they really do improve the well-being of some patients," he said in an email.

"How exactly they do that isn't as clear-cut as we've been led to believe."



A bottle of antidepressants is shown in Miami, Fla. A new analysis suggests depression isn't caused by low serotonin, and that antidepressants are ineffective at treating it. (Joe Raedle/Getty Images)

Dr. David Gratzner, a psychiatrist and attending physician at the Centre for Addiction and Mental Health (CAMH) in Toronto, said he wasn't surprised by the findings — just that they got as much attention as they did.

"This suggestion that depression is all about serotonin all the time hasn't been accepted by psychiatrists for many years, probably many decades," he said, adding that the researchers are "terribly biased" in their assessment of antidepressants.

"Their paper shows things are much more complicated than serotonin — no surprise — and then they turn around and say, 'You see, that's another example of the fact that antidepressants don't really work.' One doesn't necessarily give rise to the other."

- **Antidepressant drugs do work, review on almost 120,000 patients concludes**

Gratzer said he still prescribes antidepressants regularly as a treatment option for depression, and has no plans to stop doing so based on the research.

"That's not going to change. These medications work," he said.

"An antidepressant is not necessarily [recommended] in everyone who has depression — some people might in fact do better with talking therapy — but it is certainly a tool in our tool kit and, to be blunt, it's a lifesaver for some of our patients."

Research calls antidepressants into question

Moncrieff said the research found that another way in which antidepressants may function is by desensitizing the brain to negative emotions associated with depression. In theory, that could also impact other feelings.

She said one of the effects previous studies have reported in patients is "emotional numbing," where they not only don't have unwanted emotions like depression and anxiety, but positive emotions like joy and happiness.

"There may be some people that feel that that's an effect they want. But I think generally, people aren't going to want to be emotionally numbed, not for long periods, anyway, and so I think it totally changes the sorts of decisions people might make about antidepressants," said Moncrieff.

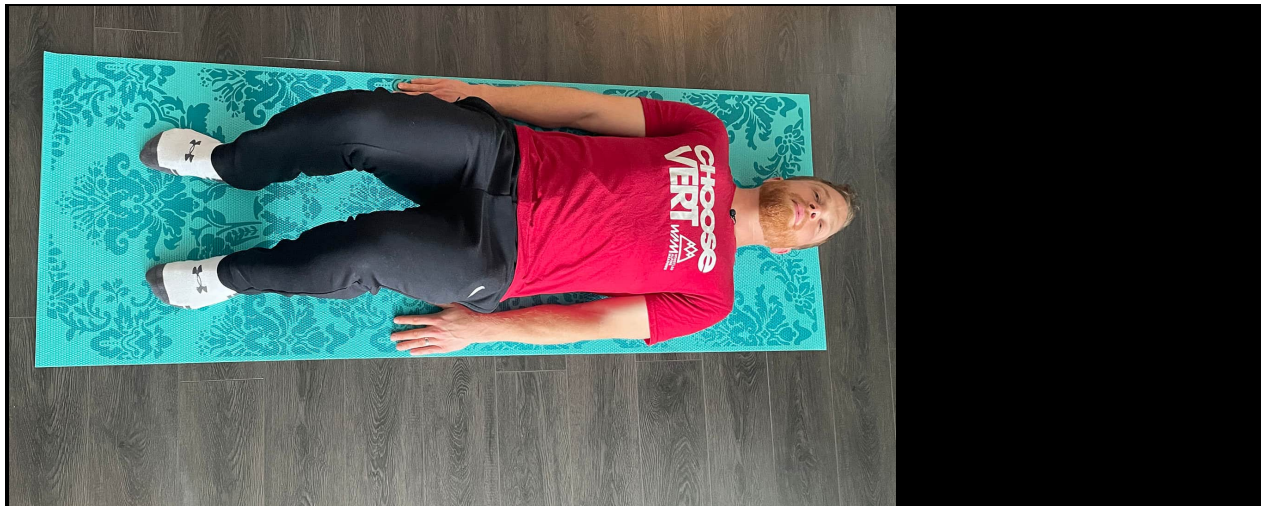
- **Toronto's CAMH gets 1st federal grant to study magic mushrooms as treatment for depression**

Chris Davey, the head of the department of psychiatry at the University of Melbourne, said in an email that undermining the confidence that people with depression have in their treatments can be "very damaging."

"People will stop their medications suddenly, without supervision," he said, "which can cause dramatic deteriorations in their mental health."

Davey said he is concerned that the paper diminished a treatment option that can be incredibly beneficial to some patients, especially when alternatives may not always be available to those at risk of severe depression.

WATCH | Research shows exercise can help alleviate pandemic depression:



A study conducted by B.C. researchers during the COVID-19 pandemic showed how exercise, especially a combination of yoga and high-intensity exercise, helped fight depression – backing up decades of research on how exercise improves mental health.

"This [research] shouldn't make any difference to the treatment of depression. I hope it makes people realize that depression is a very complex condition, and that there are no simple explanations for it," Davey said.

"Everyone should know that improving their diet, exercising more and paying attention to their sleep can be helpful. Everyone should have access to

psychotherapy. And for those people for whom those things don't help, that's when we think about medications."

Gratzer said there are many new areas of research into treatment options for depression that can be beneficial, including novel ways of delivering psychotherapy, emerging medications and discoveries like the use of [ketamine](#).

Ketamine is a general anesthetic first approved in Canada in the 1960s for medical or veterinary surgery, as well as a psychedelic party drug sold on the illicit market. It's also increasingly being used as a fast-acting and effective treatment for depression in low doses, by working to [restore synapses in the brain that are destroyed by stress](#).

- **FIRST PERSON**

[Ketamine-assisted therapy lifted me out of depression. But it remains costly — and controversial](#)

There's "an understanding that certain life experiences might be more connected, and so research is very active. Maybe at the end of the day, we'll understand depression isn't one illness," Gratzer said.

"As is often the case with mental health care, these are early days."

ABOUT THE AUTHOR



[Adam Miller](#)
Senior Writer

Adam Miller is a senior health writer with CBC News. He's covered health, politics and breaking news extensively in Canada for over a decade, in addition to several years reporting on news and current affairs throughout Asia.

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<https://www.cbc.ca/news/health/depression-antidepressants-review-serotonin-1.6548219>

801 comments already, morning of publication. Not a surprise. Nothing scares like mood disorders, especially severe depression. But anxiety can be just as crippling and frightening. Indeed, a solid line of research has always insisted depression and anxiety can be fittingly construed as one disorder. Living with fear is exhausting; living with depression and suicidal tendencies is frightening.

I think there are degrees of honesty at play here, all determined by fear and helplessness. Psychiatrists—and the GP family doctors who do most of the prescribing—love their drugs because they don't know what else to do; they lack any other therapeutic repertoire, and no health authority would pay them to try talk therapy. We all know talk therapy is often not what it is trumped up to be. Moods often “bounce” less high after the initial relief of release and validation. There are placebo effects of a sort with talk therapy too. “Regression to a (mood) mean” can also be what “saves” and uplifts suffering souls.

But we dangerously disrespect profoundly and chronically depressed people if we disbelieve their claims that meds are what keep them alive. A factor not mentioned in the article is the addictive dependency that antidepressants engender such that withdrawal after extended use is typically severe, disturbing, and dangerous, a long extremely difficult process many cannot endure. Drugs are drugs whether it is someone in a white coat dispensing them or a tattooed, ponytailed, pothead, scruffy meth-head local dealer.

Once some kind of “peace” and “safety” has been obtained, by whatever psychotropic route, for whatever causative reasons, it is understandable if “addicts” (legal or otherwise) refuse to give them up when withdrawal strongly suggests (perhaps mistakenly) that there was, and remains, a neurological basis to their mood problems.

All of this does not exonerate SSRI's and other antidepressants. When they (may) work, it is not for the reasons as advertised—serotonin and “chemical imbalances” have long been discredited explanations proffered to take stigma off prescription drugs and add to the placebo effect—with “numbing” itself being a disturbing problem. Other people, especially those with whom we are intimate, depend upon us to be able to feel, discern, and respond “normally.” But when what is “felt” is despair, uncomfortable emotional deadness, and the steady wish to be dead, the depressed may rightly say to us “Sorry, but numbness is the best I can give you. Otherwise, you won't have me at all.”

Adam opines “As is often the case with mental health care, these are early days.” But when we remember how long Science and Big Pharma have been studying the neuropsychological element in mental health—the millions (billions?) of dollars spent—with so many “breakthroughs” being just little-understood chance discoveries from drugs developed for other purposes then repurposed with clever spin for mental illness use--we realize how clueless psychiatry and medical science really are in understanding what it means to be human. TJB