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Cannabis: Potent Anti-depressant In Low Doses, Worsens Depression At High Doses

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A new neurobiological study has found that a synthetic form of THC, the active ingredient in cannabis, is an effective anti-depressant at low doses. However, at higher doses, the effect reverses itself and can actually worsen depression and other psychiatric conditions like psychosis.

It has been known for many years that depletion of the neurotransmitter serotonin in the brain leads to depression, so SSRI-class anti-depressants like Prozac and Celexa work by enhancing the available concentration of serotonin in the brain. However, this study offers the first evidence that cannabis can also increase serotonin, at least at lower doses.

At higher doses, THC, the active ingredient in cannabis, can actually worsen depression and other psychiatric conditions like psychosis, a new study has found.

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Laboratory animals were injected with the synthetic cannabinoid WIN55,212-2 and then tested with the Forced Swim test -- a test to measure "depression" in animals; the researchers observed an antidepressant effect of cannabinoids paralleled by an increased activity in the neurons that produce serotonin. However, increasing the cannabinoid dose beyond a set point completely undid the benefits, said Dr. Gabriella Gobbi of McGill University.

"Low doses had a potent anti-depressant effect, but when we increased the dose, the serotonin in the rats' brains actually dropped below the level of those in the control group. So we actually demonstrated a double effect: At low doses it increases serotonin, but at higher doses the effect is devastating, completely reversed."

The anti-depressant and intoxicating effects of cannabis are due to its chemical similarity to natural substances in the brain known as "endo-cannabinoids," which are released under conditions of high stress or pain, explained Dr. Gobbi. They interact with the brain through structures called cannabinoid CB1 receptors. This study demonstrates for the first time that these receptors have a direct effect on the cells producing serotonin, which is a neurotransmitter that regulates the mood.

Dr. Gobbi and her colleagues were prompted to explore cannabis' potential as an anti-depressant through anecdotal clinical evidence, she said. "As a psychiatrist, I noticed that several of my patients suffering from depression used to smoke cannabis. And in the scientific literature, we had some evidence that people treated with cannabis for multiple sclerosis or AIDS showed a big improvement in mood disorders. But there were no laboratory studies demonstrating the anti-depressant mechanism of action of cannabis."

Because controlling the dosage of natural cannabis is difficult -- particularly when it is smoked in the form of marijuana joints -- there are perils associated with using it directly as an anti-depressant.

"Excessive cannabis use in people with depression poses high risk of psychosis," said Dr. Gobbi. Instead, she and her colleagues are focusing their research on a new class of drugs which enhance the effects of the brain's natural endo-cannabinoids.

"We know that it's entirely possible to produce drugs which will enhance endo-cannabinoids for the treatment of pain, depression and anxiety," she said.

The study, published in the October 24 issue of The Journal of Neuroscience, was led by Dr. Gabriella Gobbi of McGill University and Le Centre de Recherche Fernand Seguin of Hopital Louis-H. Lafontaine, affiliated with l'Universite de Montreal. First author is Dr. Gobbi's McGill PhD student Francis Bambico, along with Noam Katz and the late Dr. Guy Debonnel* of McGill's Department of Psychiatry.

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