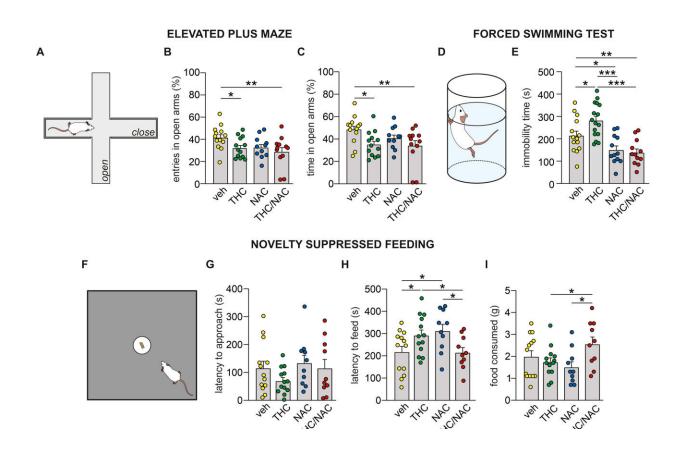


Researchers find potential therapeutic to counteract mental health effects of cannabis

July 29 2024, by Cynthia Fazio



Effects of NAC on anxiety and depressive-like manifestations induced by THC exposure during adolescence. Credit: *Biological Psychiatry Global Open Science* (2024). DOI: 10.1016/j.bpsgos.2024.100361

Researchers at Western have found an over-the-counter natural health product may help counteract the negative effects of heavy cannabis use



among adolescents aged 12 to 17, including depression, anxiety and diminished motivation in adulthood.

In a new paper <u>published</u> in *Biological Psychiatry Global Open Science*, Schulich School of Medicine & Dentistry researchers Marta De Felice and Steven Laviolette demonstrated in animal models that interventions using the antioxidant N-acetylcysteine (NAC) can mitigate the detrimental mental health effects of chronic cannabis use later in life. NAC is available in Canada as an over-the-counter natural health product and is commonly used to treat acetaminophen overdoses.

Their findings also shed light on the mechanisms behind these mental health effects and offer hope for future therapeutic strategies.

Sometimes referred to as "amotivational syndrome," chronic cannabis use in adolescents can result in a lack of motivation, diminished enjoyment from daily activities and other depressive effects. Currently, there is no known intervention strategy available to counteract these negative psychiatric side effects.

The study found that NAC—an amino acid also known for its antioxidant properties and support for respiratory and liver health—effectively counteracts <u>oxidative stress</u>, caused by an imbalance of unstable atoms that can damage cells and antioxidants which can lead a variety of diseases. NAC also reduces high levels of glutamate, an <u>excitatory neurotransmitter</u> which sends chemical signals from neurons to cells.

In this study, researchers tested the effectiveness of NAC in animal models. According to De Felice, lead author and postdoctoral fellow in the department of anatomy and cell biology, the results showed NAC acts as a protective agent by neutralizing oxidative stress and regulating levels of glutamate to preserve the normal function of the part of the



brain known as nucleus accumbens.

"The <u>nucleus accumbens</u> is a region of the brain that regulates <u>mood</u> <u>disorders</u> and addiction and is responsible for motivated behaviors," said De Felice. "That's why testing NAC in this region was so relevant in this study, since it is a crucial area to mediate the effect of drugs being perceived as a reward."

By normalizing the function and activity of this brain region, the researchers believe it potentially prevented the development of the depressive and anxiety phenotype—genes which are responsible for these traits.

Findings from the study also provide a better understanding of how cannabis exposure negatively affects the brain's ability to appropriately respond to motivational cues due to its impact on the oxidative processes and neurotransmitter functions in the region.

"One of the exciting things is that we've identified one of the important mechanisms behind that phenomenon by pinpointing an increase in oxidative stress and glutamate toxicity in the brain," said Laviolette, professor in the department of anatomy and cell biology. "The NAC intervention was very effective in preventing a lot of those effects and it's also considered to be a very safe and accessible supplement."

The researchers hope to move this to a clinical trial within the next couple of years and provide an effective intervention strategy for adolescents to address long-term consequences of cannabis exposure on mental health outcomes.

More information: Marta De Felice et al, The Impacts of Adolescent Cannabinoid Exposure on Striatal Anxiety and Depressive-like Pathophysiology are Prevented by the Antioxidant N-Acetylcysteine,



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Provided by University of Western Ontario

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