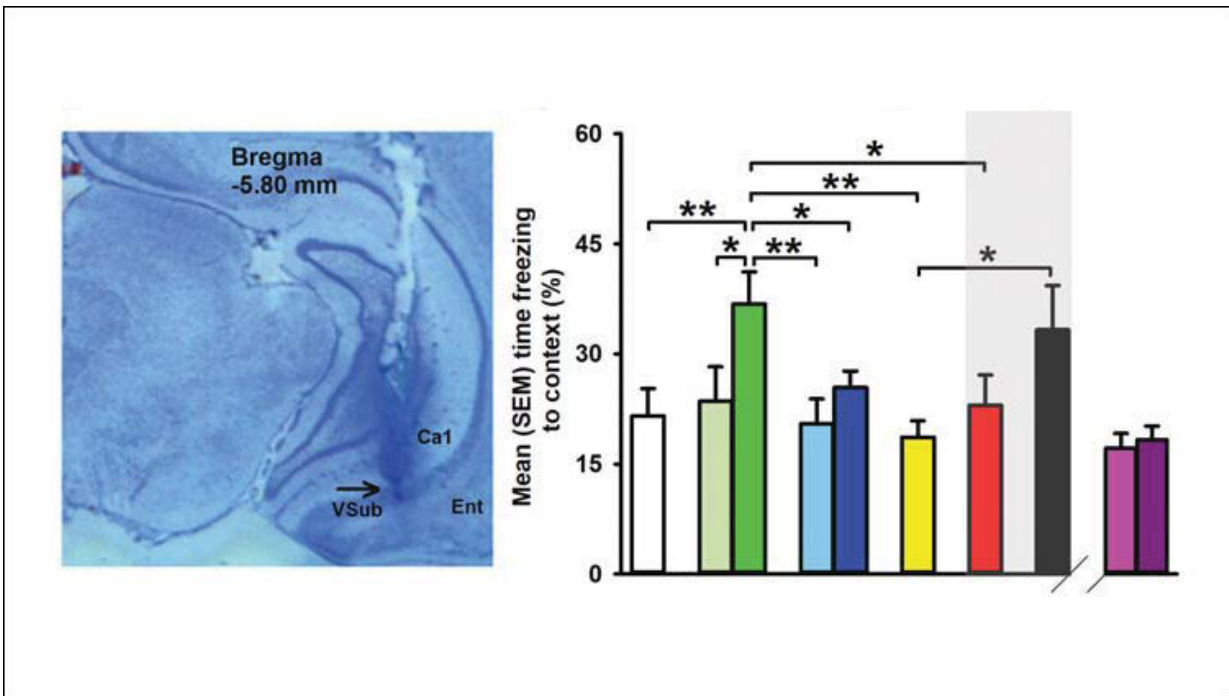


Cannabis study reveals how CBD offsets the psychiatric side-effects of THC

September 30 2019, by Crystal MacKay



Credit: Hudson et al., *JNeurosci* (2019)

Researchers at Western University have shown for the first time the molecular mechanisms at work that cause cannabidiol, or CBD, to block the psychiatric side-effects caused by tetrahydrocannabinol (THC), the main psychoactive chemical in cannabis.

It has been previously shown that strains of cannabis with high levels of

THC and low levels of CBD can cause increased psychiatric effects, including paranoia, anxiety and addictive-behaviours, but why that was occurring was not fully understood.

Steven Laviolette, Ph.D., and his research team used rats to investigate the role of a molecule in the brain's hippocampus called extracellular-signal regulated kinase (ERK) which triggers the neuropsychiatric effects of THC.

"For years we have known that strains of cannabis high in THC and low in CBD were more likely to cause psychiatric side-effects," said Laviolette, a professor at Western's Schulich School of Medicine & Dentistry. "Our findings identify for the first time the molecular mechanisms by which CBD may actually block these THC-related side-effects."

The research, published in the *Journal of Neuroscience* demonstrates that rats that were given THC had higher levels of activated ERK, showed more anxiety behaviours and were more sensitive to fear-based learning. Rats that were given both CBD and THC acted like the control rats: they had normal levels of activated ERK, less anxiety behaviours, and were less sensitive to fear-based learning.

Based on these results, the research team proposes that CBD blocks the ability of THC to overstimulate the ERK pathway in the hippocampus and thus prevent its negative side-effects.

"Our findings have important implications for prescribing cannabis and long-term cannabis use. For example, for individuals more prone to cannabis-related side-effects, it is critical to limit use to strains with high CBD and low THC content," said Laviolette. "More importantly, this discovery opens up a new molecular frontier for developing more effective and safer THC formulations."

Ph.D. Candidate and Vanier Scholar Roger Hudson, lead author on the study, says another interesting finding was that CBD alone had no effect on the ERK pathway. "CBD by itself had no effect," he said. "However, by co-administering CBD and THC, we completely reversed the direction of the change on a molecular level. CBD was also able to reverse the anxiety-like behaviour and addictive-like behaviour caused by the THC."

Laviolette says they will be following up these studies by continuing to identify the specific features of this molecular mechanism. The research team will examine ways to formulate THC with fewer side effects and to improve the efficacy of CBD-derived therapies.

More information: Cannabidiol Counteracts the Psychotropic Side-Effects of Δ -9-Tetrahydrocannabinol in the Ventral Hippocampus Through Bi-Directional Control of ERK1-2 Phosphorylation, *JNeurosci* (2019). [DOI: 10.1523/JNEUROSCI.0708-19.2019](https://doi.org/10.1523/JNEUROSCI.0708-19.2019)

Provided by University of Western Ontario

Citation: Cannabis study reveals how CBD offsets the psychiatric side-effects of THC (2019, September 30) retrieved 19 April 2024 from <https://medicalxpress.com/news/2019-09-secrets-molecular-makeup-cannabis.html>

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