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# A FAAH Better Thing for Cannabis Users: New Insights May Aid Development of Treatments for Cannabis Use Disorder

Reports new study in Biological Psychiatry

**Philadelphia, PA, October 25, 2016 –** A <u>new paper</u> in <u>Biological Psychiatry</u> reports that chronic cannabis users have reduced levels of an enzyme called fatty acid amide hydrolase (FAAH). The enzyme has been considered for treatment for cannabis dependence because it breaks down substances made in the brain that have cannabis-like effects, called endocannabinoids, rendering them inactive.

"This exciting study sheds new light on cannabis dependence," said John Krystal, Editor of *Biological Psychiatry*. The study provides clues that may help develop treatments for cannabis use disorder for which none currently exist, due in part to our poor understanding of how cannabis affects brain systems.

In the study, first author Isabelle Boileau and colleagues from the Centre for Addiction and Mental Health in Toronto, Canada used a new positron emission tomography radiotracer, [¹¹C]CURB, to measure FAAH levels in 10 active cannabis users, who had been using cannabis for an average of 18 years but were on recent withdrawal for the study, and 22 control subjects. They also analyzed blood, urine, and hair samples for traces of cannabinoids.

FAAH levels were reduced by 14–20% in chronic cannabis users compared with people who did not use cannabis. The low FAAH levels were associated with higher levels of cannabinoids in blood and urine, suggesting FAAH levels correlate with chronic and recent cannabis use.

Cannabis produces its key effects by stimulating CB1 cannabinoid receptors, the target of endocannabinoids. Together the data of the new study suggest that among chronic users, the enhanced stimulation of CB1 receptors by cannabis ingestion, which is known to downregulate CB1 receptors could, during acute cessation, lead to a suppression of FAAH activity in an attempt to restore "normal" CB1 stimulation by endogenous cannabinoids.

According to Krystal, the findings raise the possibility that normalizing cannabinoid CB1 receptor activity might play a role in reducing cannabis use and problems with impulse control in users.

The finding that heavy almost-daily cannabis use downregulates levels of FAAH after overnight cessation from cannabis use may explain the relative absence of withdrawal symptoms in very early abstinence, says Boileau, "and suggests that strategies aimed at keeping levels of this enzyme down might help reduce cannabis withdrawal symptoms."

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## **Notes for editors**

The article is "Fatty Acid Amide Hydrolase Binding in Brain of Cannabis Users: Imaging With the Novel Radiotracer [11C]CURB," by Isabelle Boileau, Esmaeil Mansouri, Belinda Williams, Bernard Le Foll, Pablo Rusjan, Romina Mizrahi, Rachel F. Tyndale, Marilyn A. Huestis, Doris E. Payer, Alan A. Wilson, Sylvain Houle, Stephen J. Kish, and Junchao Tong (doi:10.1016/j.biopsych.2016.04.012). It appears in *Biological Psychiatry*, volume 80, issue 9 (2016), published by <u>Elsevier</u>.

Copies of this paper are available to credentialed journalists upon request; please contact Rhiannon Bugno at +1 214 648 0880 or <a href="mailto:biol.psych@utsouthwestern.edu">biol.psych@utsouthwestern.edu</a>. Journalists wishing to interview the authors may contact Isabelle Boileau at <a href="mailto:isabelle.boileau@camh.ca">isabelle.boileau@camh.ca</a>.

The authors' affiliations, and disclosures of financial and conflicts of interests are available in the article.

John H. Krystal, M.D., is Chairman of the Department of Psychiatry at the Yale University School of Medicine, Chief of Psychiatry at Yale-New Haven Hospital, and a research psychiatrist at the VA Connecticut Healthcare System. His disclosures of financial and conflicts of interests are available <a href="here">here</a>.

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The journal publishes novel results of original research which represent an important new lead or significant impact on the field, particularly those addressing genetic and environmental risk factors, neural circuitry and neurochemistry, and important new therapeutic approaches. Reviews and commentaries that focus on topics of current research and interest are also encouraged.

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