

Brain chemical may explain why heavy smokers feel sad after quitting

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Heavy smokers may experience sadness after quitting because early withdrawal leads to an increase in the mood-related brain protein monoamine oxidase A (MAO-A), a new study by the Centre for Addiction and Mental Health (CAMH) has shown. This finding, which was published in the *Archives of General Psychiatry*, may also explain why heavy smokers are at high risk for clinical depression.

Using an advanced brain imaging method, a team led by Senior Scientist Dr. Jeffrey Meyer discovered that MAO-A levels in the [brain regions](#) that control mood rose by 25 per cent eight hours after withdrawal from heavy cigarette smoking. These levels were much higher than in a comparison group of non-smoking study participants. All 48 participants filled out questionnaires, and smokers with high brain MAO-A levels during withdrawal also reported greater feelings of sadness.

"Understanding sadness during cigarette withdrawal is important because this sad mood makes it hard for people to quit, especially in the first few days. Also, heavy cigarette smoking is strongly associated with [clinical depression](#)," said Dr. Meyer, who holds a Canada Research Chair in the Neurochemistry of [Major Depression](#). "This is the first time MAO-A, a [brain protein](#) known to be elevated in clinical depression has been studied during cigarette withdrawal."

MAO-A "eats up" chemicals in the brain, such as serotonin, that help maintain a normal mood. When MAO-A levels are higher as in early cigarette withdrawal, it means that this removal process is overly active,

making people feel sad. For this study, MAO-A was detected using a brain imaging technique called positron emission tomography (PET). CAMH has the only PET scanner in the world dedicated solely to mental health and addiction research.

A specific substance in [cigarette smoke](#), called harman, may be responsible for these changes, the researchers note. During active smoking, harman attaches to MAO-A. During early withdrawal in [heavy smokers](#) who had 25 or more cigarettes a day, MAO-A levels rose rapidly to a level beyond that seen in the healthy comparison group.

"This study opens new ways to prevent sad mood during cigarette withdrawal to make it easier to quit smoking. For example, it may be possible to improve the existing cigarette filters that partially screen out harman, or regulate the amount of tryptophan contained in cigarettes, since tryptophan becomes harman when it burns," said Dr. Meyer, who is also head of the Neurochemical Imaging Program in Mood Disorders at CAMH's Research Imaging Centre, and professor of psychiatry at the University of Toronto. "We also identified MAO-A as a target to shut down during the early critical stage of withdrawal with a short course of medication, but this requires further study."

"This finding may explain why heavy smokers are at high risk for clinical depression," says Dr. Anthony Phillips, Scientific Director of the Canadian Institutes of Health Research's (CIHR's) Institute of Neurosciences, Mental Health and Addiction, which funded this study.

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