

How genetics shape our addictions: Genes predict the brain's reaction to smoking

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Have you ever wondered why some people find it so much easier to stop smoking than others? New research shows that vulnerability to smoking addiction is shaped by our genes.

A study from the Montreal Neurological Institute and Hospital - The Neuro, McGill University shows that people with genetically fast [nicotine](#) metabolism have a significantly greater brain response to [smoking](#) cues than those with slow nicotine metabolism. Previous research shows that greater reactivity to smoking cues predicts decreased success at smoking cessation and that environmental cues promote increased nicotine intake in animals and humans. This new finding that nicotine metabolism rates affect the brain's response to smoking may lead the way for tailoring smoking cessation programs based on individual genetics.

Smoking cues, such as the sight of cigarettes or smokers, affect smoking behavior and are linked to relapse and cigarette use. Nicotine metabolism, by a [liver enzyme](#), also influences smoking behavior. Variations in the gene that codes for this enzyme determine slow or fast rates of metabolism and therefore, the level of nicotine in the blood that reaches the brain. In the study smokers were screened for their nicotine metabolism rates and their enzyme [genotype](#). Participants were aged 18 – 35 and smoked 5-25 cigarettes daily for a minimum of 2 years. People with the slowest and fastest metabolism had their brain response to visual smoking cues measured using functional MRI. Fast metabolizers had significantly greater response to visual cigarette cues than slow

metabolizers in [brain areas](#) linked to memory, motivation and reward, namely the [amygdala](#), hippocampus, striatum, insula, and cingulate cortex.

"The finding that nicotine metabolism rate has an impact on the brain's response to smoking cues supports our hypothesis that individuals with fast nicotine metabolism rates would have a greater [brain response](#) to smoking cues because of close coupling in everyday life between exposure to cigarettes and surges in blood nicotine concentration. In other words they learn to associate cigarette smoking with the nicotine surge," says clinician-scientist Dr. Alain Dagher, lead investigator at The Neuro. "In contrast, individuals with slow metabolism rates, who have relatively constant nicotine blood levels throughout the day, are less likely to develop conditioned responses to cues. For them, smoking is not associated with brief nicotine surges, so they are smoking for other reasons. Possibilities include maintenance of constant brain nicotine levels for cognitive enhancement (ie, improved attention, memory), or relief of stress or anxiety. "

Future research could focus on improving smoking cessation methods by tailoring treatments for different types of smokers. One possibility is to measure the rate of nicotine metabolism as part of the therapeutic decision-making process. For example, targeting cue-induced relapse risk may not help those with slow nicotine metabolism, who are more likely to benefit from long-acting cholinergic drugs such as the nicotine patch, consistent with previous clinical trials. Conversely the use of non-nicotine based therapies aimed at reducing craving may help fast metabolizers, as demonstrated for bupropion, an anti-depressant that has been used for [smoking cessation](#).

Provided by McGill University

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