Brain activity after smokers quit predicts chances of relapsing, study suggests

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Caryn Lerman, Ph.D. Credit: Penn Medicine

Quitting smoking sets off a series of changes in the brain that Penn Medicine researchers say may better identify smokers who will start

smoking again—a prediction that goes above and beyond today's clinical or behavioral tools for assessing relapse risk.

Reporting in a new study published this week in the journal *Neuropsychopharmacology*, James Loughead, PhD, associate professor of Psychiatry, and Caryn Lerman, PhD, a professor of Psychiatry and director of Penn's Center for Interdisciplinary Research on Nicotine Addiction, found that smokers who relapsed within seven days from their target quit date had specific disruptions in the brain's working memory system during abstinence that separated them from the group who successfully quit. Such neural activity—mainly a decrease in the part of the brain that supports self-control and a boost in the area that promotes an "introspective" state—could help distinguish successful quitters from those who fail at an earlier stage and serve as a potentially therapeutic target for novel treatments.

"This is the first time abstinence-induced changes in the working memory have been shown to accurately predict relapse in smokers," said senior author Lerman, who also serves as deputy director of Penn's Abramson Cancer Center.

The study's lead author, Loughead, said: "The neural response to quitting even after one day can give us valuable information that could inform new and existing personalized intervention strategies for smokers, which is greatly needed." Indeed, smoking in the U.S. is at an all-time low in adults; however, there are still 42 million Americans who do smoke, including teenagers and young adults.

In the study, researchers used functional magnetic resonance imaging (fMRI) to explore the effects of brief abstinence from smoking on working memory and its associated neural activation in 80 smokers seeking treatment. Participants were between 18 and 65 and reported smoking more than 10 cigarettes a day for more than six months.

Two fMRI sessions occurred: one immediately after a person smoked and one 24 hours after abstinence began. Following smoking cessation counseling, participants set a future target quit date. Seven days after the target quit date, participants completed a monitoring visit, during which smoking behavior was accessed, including a urine test. Past research strongly suggests that if a person is tobacco free after seven days, they will likely remain that way for six months, if not longer, and is therefore highly predictive of long-term quitting success.

Sixty one smokers relapsed and 19 quit successfully for this period, the researchers reported.

Those who relapsed had decreased activity in the left dorsolateral prefrontal cortex, which controls executive functions, like working memory, compared to those who quit. Working memory is an essential cognitive function necessary for staying focused, blocking distractions, and completing tasks. They also had reduced suppression of activation in the posterior cingulate cortex, a central part of the default mode network of the brain, which is more active when people are in a so-called "introspective" or "self-referential" state.

Past studies have shown relationships between these brain networks. A study in *JAMA Psychiatry* from Lerman and colleagues published earlier this year showed how smokers suffering from nicotine withdrawal have more trouble shifting from the default mode network into the executive control network, where people can exert more conscious, self-control over cravings and to focus on quitting for good. However, this new study is the first to use that brain activity to help predict relapse in smokers.

Today, there are clinical and behavioral predictors for relapse, including age, the Fagerstrom Test for Nicotine Dependence and other smoking urges and withdrawal tests, but there is much room for improvement.

In the study, researchers determined predictive values of these two relapse models, as well as a new model that includes the working memory data. Using resampling methods that generate 1,000 replicates of the data from the 80 smokers, they found that incorporating the working memory-related brain activity resulted in an 81 percent correct prediction rate, a significant improvement over current models. Without that data, the prediction values were 73 percent for the model of withdrawal symptoms and demographic/smoking history predictors, and 67 percent for demographic/smoking history predictors only.

While broad implementation of neuroimaging assessment is not currently clinically or economically feasible, these changes in the working memory are potential targets for improved assessment instruments, specifically for early smoking relapse. "In addition...predictive models can identify therapeutic targets for pharmacotherapies or neuroscience-based nonpharmacologic interventions to promote smoking cessation," they write.

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