

Varenicline reduces depressive mood, craving and reward value of cigarettes when smokers attempt to quit, study reports

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Smokers have a higher probability of quitting smoking and a better overall cessation experience when taking varenicline compared to bupropion and to placebo – unmedicated assisted smoking cessation –according to a study published in the journal *JAMA Psychiatry*.

A team led by Paul Cinciripini, Ph.D., professor in the Department of [Behavioral Science](#) at The University of Texas MD Anderson Cancer Center, investigated the relative efficacy of [varenicline](#) and bupropion – both popular anti-smoking drugs on the market – plus intensive counseling to assess the drugs' effects on smoking-cessation and emotional functioning while quitting.

"National surveys show that about 20 percent of adults continue to smoke, but it's disproportionately high among people in low socioeconomic populations and those with mental illness," said Cinciripini. "When smokers try to quit, many are likely to experience a range of nicotine withdrawal symptoms, including [negative mood](#), difficulty concentrating, [irritability](#) and even [depressive symptoms](#) making quitting difficult and increases the chances of relapse."

"Our findings suggest that smokers trying to quit will have a better experience with varenicline as opposed to trying to quit on their own or by taking bupropion," Cinciripini said. "The more we can reduce these negative symptoms associated with quitting the better experience of the

smoker and this may mean that even if they don't quit this time, they will be encouraged to try again."

In this study, funded by the National Institute on Drug Abuse, scientists examined data from 294 smokers who were trying to quit. The participants were randomized into one of three groups; varenicline, bupropion or placebo. QuitRx participants were assessed throughout the 12-week medication portion of the program, and also three and six months after quitting.

The researchers used four different measurements of [abstinence](#) and found that only varenicline significantly improved abstinence rates by all measures at all time periods compared with placebo, which is consistent with results from large phase 3 clinical trials with this medication. Varenicline consistently outperformed bupropion, but unlike the placebo comparisons did not reach statistical significance because of small sample size.

All participants received extensive [smoking cessation](#) counseling via QuitRx and were assessed for nicotine withdrawal and emotional functioning every week during treatment, using the Wisconsin Smoking Withdrawal Scale (WSWS), the Positive and Negative Affect Schedule and the Center for Epidemiologic Studies Depression Scale (CES-D). In the QuitRx program, scientists investigated the effects of medication alone, abstinence alone and the combination of the two on each of these measures, specifically evaluating symptoms of depression, negative affect – a person's mood– and other symptoms of nicotine withdrawal including craving.

Better mood, less anxiety for smokers

When measuring the effects of abstinence alone on emotional functioning, the study found that regardless of which medication the

smoker received, people who were able to abstain from smoking had lower scores for overall negative affect, anxiety and sadness but also showed higher positive affect.

"This is a very interesting finding in that it suggests smoking itself may not be a very good anti-depressant," said Cinciripini, director of MD Anderson's Tobacco Treatment Program. "It also suggests that those who were able to abstain from smoking will ultimately feel better than those who continue to smoke."

The study also found that compared to the non-abstainers, abstainers using either bupropion or varenicline experienced lower levels of sadness, but in terms of overall depressive symptoms the varenicline group fared much better. For those taking varenicline, both abstainers and non-abstainers were less depressed. "This is especially intriguing given the post-marketing data with varenicline that suggests that it may worsen depressive symptoms," said Cinciripini. "More research is needed to look carefully at smokers with current psychiatric illness taking varenicline, since they were not included in this research study."

Suppressing other withdrawal symptoms

Smokers are also subject to other withdrawal symptoms when they try to quit including loss of concentration and craving for tobacco. In this study, both drugs reduced craving relative to placebo, however varenicline showed lower levels of craving even among those who did not quit fully.

Findings also indicate that when compared with bupropion, only varenicline reduced the psychological reward, or pleasure derived from smoking, when measured among those who initially lapsed, while trying to retain abstinence during the program.

Cinciripini noted that this is significant because varenicline which is thought to partially stimulate dopamine – the neurotransmitter associated with reward that lessens overall withdrawal symptoms – also supports another suggested mechanism of action that involves binding the nicotine receptor for a longer period of time.

He explains the net effect of lower withdrawal and psychological reward improves the overall odds of cessation success, which is consistent with other research. "The difference in our study was that this took place against a background of intense counseling suggesting that varenicline can even be of benefit in those situations as well as low counseling intensity environments."

"It is evident from the findings that varenicline is hitting many more affective targets, in comparison to bupropion or placebo, and there is a distinct benefit of these effects on cessation even among those who do not fully abstain," said Cinciripini.

Provided by University of Texas M. D. Anderson Cancer Center

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