Novel target to help curb smoking addiction

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Neurons that produce the neurotransmitter GABA are identified as a novel target for smoking cessation drugs in mice, according to a study published this week in Molecular Psychiatry. While previous studies have focused exclusively on the neurotransmitter dopamine, these results suggest that it’s the co-activation of dopamine and GABA neurons that plays a vital role in the reinforcing actions of nicotine.
Smoking is the worldwide leading cause of preventable morbidity and mortality, but efficient smoking cessation treatments have yet to be developed due to a lack of understanding of the precise action of nicotine in the brain's reward system.

Uwe Maskos, Philippe Faure and colleagues developed a method to express a specific type of nicotine receptors containing the β2 subunit, shown to play a crucial role in the positive rewarding properties of nicotine, on either dopamine, GABA neurons, or both. The results in mouse models suggest that an increase in activity in GABA interneurons—connector neurons in the brain—contributes to a particular firing pattern, known as burst firing, in dopamine neurons. This firing pattern is believed to be a critical physiological mechanism required for the long-term, habit-forming action of nicotine.

The authors propose that both positive and negative motivational values of smoking are transmitted through dopamine neurons, but it is the combined activity of the dopamine and GABA systems that is necessary for the reinforcing actions of nicotine. The lack of success of present drug therapies for smoking cessation may be due to their exclusive focus on dopamine, whereas these findings provide evidence that GABA neurons may be a more effective target for drug therapies.

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