

Metabolite may play a role in nicotine addiction

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A substance that scientists identify to screen people for nicotine use may also play a role in smokers becoming addicted to tobacco.

"When you smoke, nicotine is converted into a metabolite called cotinine," explained South Dakota State University Psychology Professor Brady Phelps. Even those who inhale [secondhand smoke](#) can test positive for cotinine. The metabolite is measured in urine, saliva and blood.

"Cotinine remains in the body much longer than nicotine," Phelps said. The half-life—the amount of time it takes for half of the substance to leave a person's system—is about 15 hours for cotinine, but approximately two hours for nicotine, according to Mayo Medical Laboratories.

Phelps and Associate Professor Tyler M. Miller worked with Professor Shafiqur Rahman of the Department of Pharmaceutical Sciences to study how cotinine affects the behavior of flat worms called planarians. Pharmacology Professor Scott M. Rawls of the Center for Substance Abuse Research at Temple University was also part of the research team.

"Preliminary evidence suggests that nicotine dependence may involve more than just nicotine," Phelps said. "Cotinine may be amplifying or contributing to the addictive properties of nicotine." Study results were published online in March and will appear in print in the June 2019 issue of *Neuroscience Letters*.

Six undergraduate students worked on the project, which was supported by the SDSU Research and Scholarship Support Fund.

"Planarians are commonly used as an [animal model](#) to study the effects of a drug with addiction potential," Phelps explained. "If given a choice, these aquatic worms prefer a dark environment—they display behavior described as being very light phobic or a negative phototaxis response."

To test the addictive nature of this nicotine metabolite, the researchers

immersed the aquatic worms in solutions containing three levels of cotinine under light for 10 minutes. The concentration levels mirrored those used to assess the worms' responses to nicotine in a study which Rawls conducted.

Pairing light with drug exposure has the potential to change the planarian's behavior, a technique called conditioned place preference. If the light phobic behavior is reversed and the worms have acquired a preference for an environment paired with light, this is evidence of a conditioned place preference, Phelps explained.

The conditioned place preference has been used in many other [animal species](#), including mammals, and is one way to assess a compound's rewarding or addictive properties. With very few exceptions, drugs that establish a conditioned place preference will also serve as a reward for drug-self-administration, another widely used technique to assess addiction potential.

The study showed planarians exposed to cotinine, regardless of the level, spent significantly more time in the light than those in the control group. "This is the first demonstration that cotinine will establish a conditioned place preference in planarians," Phelps said. "There may be more to nicotine dependence than just [nicotine](#)—cotinine may be a contributing factor." However, he cautioned, "These data are preliminary and must be followed up on with other studies."

More information: Brady J. Phelps et al. Preliminary evidence from planarians that cotinine establishes a conditioned place preference, *Neuroscience Letters* (2019). [DOI: 10.1016/j.neulet.2019.03.024](https://doi.org/10.1016/j.neulet.2019.03.024)

Provided by South Dakota State University

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