A team of scientists has developed a new technique to better understand the effects of nicotine on the brain. In a study published in Nature Methods, the investigators described the creation of a novel light-activated nicotine compound, which will allow scientists to better study
receptors that play a key role in nicotine addiction.

"Investigators are now able to study the neurotransmitter receptor for nicotine in ways not previously possible," said co-corresponding author Ryan M. Drenan, PhD, associate professor of Pharmacology. "Scientists interested in studying nicotine dependence or acetylcholine—the neurotransmitter that normally binds to 'nicotine receptors'—now have a fantastic tool that, when properly employed, may enable us to uncover fundamental principles of cholinergic transmission."

Matthew C. Arvin, PharmD, a graduate student in Drenan's laboratory, was a co-first author of the study, which was conducted in collaboration with investigators at the Howard Hughes Medical Institute's Janelia Research Campus.

Photoactivatable versions of drugs, which can be activated by brief flashes of light, are an important tool used in pharmacological research to study processes in cells and to model drug behavior. Until recently, however, scientists lacked the ability to develop compounds for many drugs, including a class with a so-called "tertiary nitrogen," which includes nicotine.

In the current study, the team of scientists developed a new chemical method for preparing derivatives of such previously "uncageable" drugs—and applied the strategy to nicotine. After developing a photoactivatable nicotine, called PA-Nic, they utilized the compound to study nicotinic acetylcholine receptors.

"We used the probe to reveal new details about how chronic nicotine exposure changes the activity and location of these receptors, paving the way for a new approach to studying nicotine dependence," Drenan said.

The new strategy will be essential for studies of acetylcholine
transmission and nicotine dependence, but the approach could also be applied to other drugs that have a tertiary nitrogen, according to the authors. For example, the study demonstrates the creation of photoactivatable versions of the opioid fentanyl and the antidepressant escitalopram, among others.

"This could lead to novel research in many aspects of neurobiology that impact human health, including mood disorders or the opioid epidemic," Drenan said.


Provided by Northwestern University


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