Smokers' genetic background impacts brain opioid receptors, smoking relapse

May 16 2011

Nearly everyone who has tried to quit smoking says it's incredibly difficult, and the struggle is due in part to genetic factors. Now, a new study from the Raymond and Ruth Perelman School of Medicine at the University of Pennsylvania sheds light on how one specific genetic risk for smoking relapse may work: Some of the difficulties may be due to how many receptors, called "mu opioid" receptors, a smoker has in his or her brain. The results, published online this week in the *Proceedings of the National Academy of Sciences*, may lead to the development of new treatments that target these receptors and help smokers increase their chances of success when they try to quit.

“For the first time we’ve identified a mechanism that explains why people with a particular genetic background may be more prone to relapse when they try to quit smoking,” says senior author Caryn Lerman, PhD, the Mary W. Calkins Professor of Psychiatry and Interim Director of the Abramson Cancer Center at the University of Pennsylvania. “These smokers have a greater number of mu opioid receptors that respond to brain chemicals such as beta-endorphin which are released by nicotine. And having more available receptors of this type appears to be related to finding nicotine more rewarding. We’ve connected the dots between the genes, the brain, and the behavior.”

Lerman and colleagues used positron emission tomography (PET) to measure the amount of mu opioid receptors in the brains of smokers. They found that the amount of receptors in the areas of the brain associated with rewards and emotions was related to an individual’s

genotype. Specifically, smokers who have two copies of the common "wild-type" version of the mu opioid receptor gene had significantly more receptors available, compared to smokers who inherited at least one genetic variant of the mu opioid receptor gene.

When the study participants reported the degree of satisfaction gained from either a normal cigarette or one that lacked nicotine, there was no difference associated with the individuals' genotype. However, there was an association between greater reported reward and more receptor expression in people who carried at least one copy of the genetic variant.

Because individuals who have two wild-type copies of the mu opioid receptor gene have more receptor available in their brain, they may benefit most from drugs that block the receptor's activity.

"Although opioid medications have been tested for use for smoking cessation, the results have been mixed," Lerman says. "However, if we know more about their brain mu opioid receptor availability, we may be able to predict who will respond to this type of drug." This will be the subject of future research.

Lerman acknowledges that using sophisticated imaging studies on every smoker isn't feasible because of cost and other logistical constraints. However, this study and future studies that build on it may help researchers translate the receptor expression data into ways to guide smokers to success when they aim to quit. For example smokers who have more available mu opioid receptors may be more responsive to mu opioid receptor blocking medications.

Lerman also points out that although the team only looked at the impact of genetics on mu opioid receptor expression and rewards in the context of tobacco addiction, the results may translate to other type of addictive behaviors for which mu opioid receptors play a role.

Provided by University of Pennsylvania