Unexpected experimental results indicate nicotine creates a chronic drug memory in the brain

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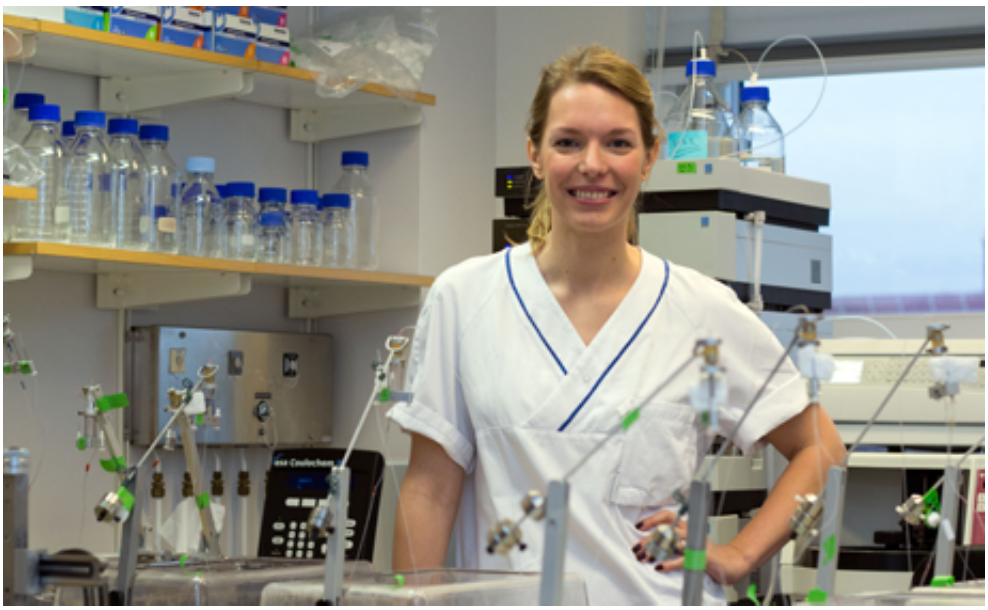

Credit: University of Gothenburg

In a recent study involving nicotine-addicted rats, the first period of nicotine abstinence proceeded as expected. The surprise came after three months, when the lab rats suddenly became fearless and sought out well-lighted areas that prey animals normally avoid. At the same time, signaling in the brain's reward system changed, as shown by a study at Sahlgrenska Academy.

"This indicates very long-lasting changes caused by nicotine that were previously unknown. The nicotine appears to create a cascade of effects that only get worse and worse over time," says Julia Morud Lekholm, researcher in addiction biology at the Institute of Neuroscience and Physiology.

The experiment was done another two times. The researchers wanted to make sure that the unexpected results were not an isolated case. In total, 108 animals were tested, of which half received nicotine and half a salt solution over a three-week period. The outcome was the same every time.

"The nicotine treated animals spend much more time in these more frightening areas compared with those that only received salt solution injections. We don't see this right after the nicotine treatment, only after three or more months into abstinence. So then the animals have not received any nicotine for three months, and suddenly they demonstrate an increased spontaneous impulsiveness, which is very strange," says Julia Morud Lekholm.

Strong impact

"What's interesting is that at the same time, we also begin to see changes in the GABAergic system in the brain, which is the system that normally slows the brain's signaling," she continues.

After another four months, the GABA system in the studied region of the rats' brains was so strongly affected that it had been completely reversed. Instead of dampening the nerve cell signaling, it increased it.

In other words, the results indicated a highly activated system, and an extensive risk of relapsing into smoking if human progression is similar to the rats, for example.

"Of course, rats and people are very different, but in terms of the type of brain circuit that we study, the brain's reward system, we are very much alike. Also in terms of risk-taking behavior, it's possible to translate to humans to some extent. Having poor impulse control isn't good for life in general, of course. One can end up in many bad situations and this may also have effects on the consumption of other drugs later in life," says Julia Morud Lekholm.

Lifelong struggle

Even if the time aspects are not directly transferable to humans, she believes the changed signaling in the brain to some extent explains part of the difficulties and long-lasting problems many who want to quit smoking, or using tobacco have.

"It's a life-long struggle. We understand this when we look at animals who after such a long abstinence from nicotine still have a lot of changes in their reward system. Therefore, more efforts should absolutely be made on this kind of research to try to find new therapies, because it's extremely hard for people to be able to withstand the urge for longer time periods," says Julia Morud Lekholm.

More information: The thesis is available online: gupea.ub.gu.se/handle/2077/48662

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