New research shows how the brain adapts to the effects of nicotine

European scientists have shed new light on how the brain adapts to the long-term effects of nicotine and how it reacts when the drug is no longer delivered. A work that brought together researchers from the French National Center for Scientific Research (CNRS) and the Karolinska Institute in Sweden, was published online in the journal Proceedings of the National Academy of Sciences (PNAS). Nicotine is addictive when it interferes with the brain’s reward centers by attaching to nicotinic acetylcholine receptors. These receptors consist of five subunits, and there are 10 types of subunit. They are all activated by the neurotransmitter acetylcholine as well as by nicotine. However, these different types of receptors may have different physiological functions and therefore represent different potential therapeutic targets.

Last year, researchers from the CNRS showed that the beta2 subunit called alpha7, are involved in activating the reward system in the brain after a high dose of nicotine. In this recent study, scientists wanted to find out what happens to these receptors when exposed to nicotine for extended periods of time. For several weeks, they administered nicotine to mice so that the levels of nicotine in their blood plasma were similar to those found in smokers; sufficient to induce symptoms of hunger.
By comparing normal mice with mice lacking the beta2 receptor, researchers discovered how the beta2 and alpha7 receptors work to maintain balance when the brain is exposed to prolonged exposure to nicotine. On the one hand, beta2 receptors are anesthetized and become inactive when exposed to nicotine. On the other hand, it is counterbalanced by the adaptation of neural circuits with alpha7 receptors. 'In short, our data from studies in mice provide evidence of a functional balance between nicotinic receptor subtypes that may also exist in nicotine-treated smokers,' the researchers write.

The results mean that researchers developing drugs to help quit smoking will need to consider both receptors. The findings also have implications for diseases involving nicotinic receptors. "This is especially true of schizophrenia," explains Philippe Faure of the CNRS, one of the authors of the publication. People being treated for this disease smoke significantly more than the general population, and some believe it may be a form of self-medication.

This phenomenon may be due to the action of a compensatory mechanism related to alpha7 receptors. Other diseases that affect nicotinic receptors include Alzheimer’s disease, attention deficit hyperactivity disorder (ADHD), and autism. These disease states are excellent targets for the continued operation of novel nicotine drugs, the researchers conclude.