

Neuropeptide may aid targeted anxiety therapy

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The targeted control of biochemical processes and neuronal signalling pathways using the messenger substance neuropeptide Y could help in the future treatment of anxiety disorders. This is demonstrated in research findings by the Austrian Science Fund FWF, which were recently published in the scientific journal *Neuropsychopharmacology*.

Palpitations, sweating and sleep problems – most people have already experienced symptoms of anxiety. As a response to danger, [fear](#) is vital for our survival. However, when fear becomes overwhelming or lasts too long, it can result in the development of psychological disorders: "Anxiety disorders are the most common brain diseases and every fifth person will suffer from them in their lifetime," says Ramon Tasan from the Medical University of Innsbruck. Such disorders are currently treated using drugs and behavioural therapies. Yet, a large proportion of patients fail to respond to these approaches and, in many cases, alleviation of symptoms is only temporary. New therapeutic strategies are therefore required. In a project supported by the Austrian Science Fund FWF, Tasan and his team studied the neuronal circuits and biochemical processes that underlie the suppression of [fear responses](#) and erasure of newly acquired fears, and identified new starting points for the development of effective therapeutic strategies and drugs for the treatment of [anxiety disorders](#).

Neuropeptide Y alleviates fear

The focus of the project was on the role of fear control by the body's own neuropeptide Y, a key messenger substance found in the communications network between the neurons in the different regions of the brain. Preliminary studies had shown that neuropeptide Y has a fear-alleviating effect, in particular through the activation of the Y1 docking sites or receptors. "We were then able to identify another receptor as an important node in the brain's communications network for the processing of fear. In the mouse brain, this receptor, which is known as Y2, influences the amygdala pathways, which trigger physical responses like increases in muscle tension, heart frequency and blood pressure in response to fear stimuli. The Y2 receptors thus play a central role in the processing of fear stimuli," says Tasan, summarising the research findings. It was previously assumed that the activation of these receptors inhibits the release of the protective neuropeptide Y and thus intensifies fear. "However, we established that Y2 receptors reproduce the effect of the Y1 receptors and support the suppression of fear and erasure of newly-acquired fears," says Tasan. These findings could represent a crucial turning point in the clinical development of drugs for the treatment of anxiety disorders: Y2 receptors or the neuropeptide Y could offer suitable targets for the development of new drugs.

'Unlearning' fear

The project also provides some important starting points for new behavioural approaches. As part of the project, the scientists examined in the mouse model how fear is acquired and can be erased. "Like humans, mice build up fear memories over the course of their development. This is important from an evolutionary point of view, as it enables the rapid recognition of danger and its avoidance," explains Tasan. "When a fear is erased, the information is stored in a separate extinction memory which, in turn, specifically suppresses the fear memory." Using Pavlovian conditioning, mice learned to identify a particular sound as dangerous in experiments, to store it later in the

extinction memory and in this way cause it to be erased. These effects could be intensified using Y2 receptors.

Hunger erases fear

It emerged here how closely intertwined the neuronal circuits for food intake and fear regulation are: "We discovered that the activation of the Y4 [receptors](#) by the neuropeptide Y influences the feeling of hunger. Animals with no Y4 receptor were slimmer but they also lacked the ability to erase fear," explains Tasan. "We were able to influence this, however, by adapting their food intake: Mice that had not been given any food for 16 hours before the fear erasure process were able to improve their fear management. They had a strongly reduced long-term fear memory but their short-term memory and learning capacity were unaffected."

Overall, the findings of this FWF project, which were recently published in the journal *Neuropsychopharmacology*, open up new possibilities for the development of more targeted drugs and behavioural therapies for anxiety disorders.

More information: R.O. Tasan et al. The role of Neuropeptide Y in fear conditioning and extinction, *Neuropeptides* (2016). [DOI: 10.1016/j.npep.2015.09.007](#)

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