Safety Can be Learned - and Helps Combat Depression

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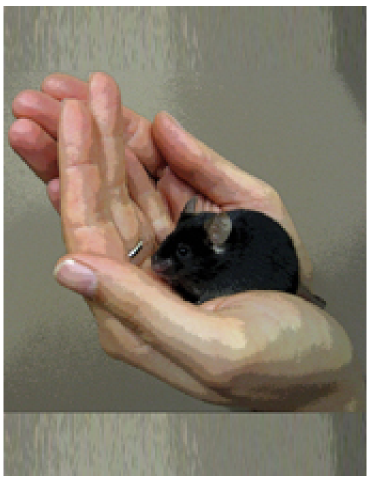

In safe hands: a new animal model demonstrates that "learned safety" can have an anti-depressive effect.

(PhysOrg.com) -- Learning a feeling of safety activates cellular and molecular processes that act against depression. This has been analysed using a new animal model that helps examine and explain the relevant cell biology processes more effectively. The findings now published in the journal *Neuron* show that "learned safety" can have an anti-depressive effect comparable to pharmacological antidepressants but that this effect is controlled by other molecular processes. The project supported by the Austrian Science Fund FWF was carried out by the Howard Hughes Medical Institute at Columbia University in the U.S.

Fear is good. It protects us from all kinds of danger and is therefore both part of our instinct and can also be learned. However, fear can also become aggravating or even chronic and cause various psychological conditions such as depression. To investigate learned fear, fear-reducing behaviour - learned safety - has now been studied in animals, conditioning them to associate specific stimuli with a feeling of safety, which consequently reduces learned fear. It was precisely this experimental model that Dr. Daniela D. Pollak used as project manager in Prof. Eric Kandel's group. This was how she analysed cellular and molecular processes in relation to learned safety.

Using Safety to Fight Depression

The findings from this work, which were recently published in the journal Neuron, were amazingly clear, as Dr. Pollak explains: "Three key conclusions can be drawn from the work of our team. Firstly, learned safety is an animal model for behavioural therapy for depression, resulting in similar effects to treatment using pharmacological antidepressants. Secondly, the animal model therefore also lends itself to analysing cellular and molecular interactions between anti-depressive medication and behavioural treatments for depression. And thirdly, learned safety leads to cell biology reactions such as those caused by antidepressants but uses different molecular mechanisms."

Specifically, Dr. Pollak's team was able to observe the following cellular and molecular processes in relation to learned safety:
It was shown that learned safety has a positive effect on newly created cells in a specific region of the hippocampus (dentate gyrus) in the brain. This was because significantly more new cells survived there when they had previously experienced a stimulus through learned safety. This effect on cell survival could be traced to increased expression of the protein BDNF (brain-derived neurotrophic factor), which is also triggered by learned safety. However, in order to be effective, the

stimulus for the cells, as shown by Dr. Pollak's work, needed to take place in a particular phase after creation of new cells.

Effects on the activity of various key genes were also observed. Learned safety reduces the activity of genes from the dopaminergic and neuropeptide systems in the amygdale. Interestingly, however, no effect was observed on the serotonin-dependent system, which is a key target for medication-based treatment of depression.

Two Approaches - One Goal

Overall, these findings lead Dr. Pollak to believe the existence of at least two different neurotransmitter systems for the anti-depressant effects of learned safety. These lead to neuronal modifications that are similar to those caused by antidepressants. Yet - as the lack of an effect on the serotonin-dependent system suggests - this is done through other cellular processes.

The publication of this work also marks a turning point in Dr. Pollak's career. Armed with two officially recognised scholarships from Austria (a Max Kade Fellowship from the Austrian Academy of Sciences and an Erwin Schrödinger Fellowship from the FWF), she had the opportunity in the last three years to make key contributions to neurophysiology on the team headed by Nobel prize winner Eric Kandel. She will now be pursuing this personal passion in future in research at the Institute of Physiology at the Medical University of Vienna.

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