L-dopa medication could be helpful in the treatment of phobias and PTSD

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A drug used to treat Parkinson's disease could also help people with phobias or post-traumatic stress disorder (PTSD). Scientists of the Translational Neurosciences (FTN) Research Center at Johannes Gutenberg University Mainz (JGU) are currently exploring the effects of psychotherapy to extinguish fears in combination with L-dopa. This drug does not only help movement disorders, but might also be used to override negative memories.

Professor Raffael Kalisch, head of the Neuroimaging Center (NIC) of the JGU Translational Neurosciences Research Center, and his collaborators at the University of Innsbruck are conducting research in mice and in humans into the psychological and neurobiological mechanisms of anxiety and fear. "Fear reactions are essential to health and survival, but the memories of angst-inducing situations may cause long-term anxiety or phobias," explained Kalisch. In psychotherapy, the 'fear extinction' method is used in exposing people to a threat but without the adverse consequences. Latest research has proven that extinguishing fear also predicts mental health after trauma, suggesting extinction may be an important resilience mechanism.

Fear extinction involves a person being presented with a neutral stimulus, such as a circle on a screen, together with a painful sensation. Soon the person predicts pain in response to the circle on the screen and fear becomes conditioned. Then the person is shown the circle again, but this time without the painful stimulus, so that the person can disassociate the two factors. A person who is afraid of spiders, for example, will in

psychotherapy be confronted with spiders in a way that reassures them that the spider is harmless.

In another research program, Belgian scientists tested the ability to extinguish fear in soldiers later deployed to a war zone and found differences in the soldiers' resilience to traumatic memories. Some experienced post-traumatic stress symptoms following their deployment, whereas those who were able to extinguish fear in the laboratory maintained a good state of mental health. "If you are mentally flexible enough to change the associations that your mind has created, you might be better able to avoid lasting damage," explained Kalisch. In cooperation with other scientists, Kalisch has found first evidence that this process of changing negative associations might involve the brain's systems for reward and pleasure and depend on release of the neurotransmitter dopamine that helps control them.

However, even after successful extinction, old fear associations can return under other stressful circumstances. This might involve the development of PTSD or a relapse after successful psychotherapy. Kalisch has found that L-dopa, a drug to treat Parkinson's disease, can prevent this effect and could therefore possibly be used to prevent relapse in treated PTSD or phobia patients. L-dopa is taken up by the brain and transformed into dopamine that not only controls the brain's reward and pleasure centers and helps regulate movement, but also affects memory formation. The person receiving L-dopa after extinction will thus create a stronger secondary positive memory of the extinction experience and will thus be able to more easily replace the negative memory.

This raises new questions about the role of primary fear memories and secondary prevention by L-dopa. "We would like to be able to enhance the long-term effects of psychotherapy by combining it with L-dopa," said Professor Raffael Kalisch. To this end, he is about to start a clinical

study of people with a spider phobia to determine the effects of L-dopa on therapy outcome. "Manipulating the dopamine system in the brain is a promising avenue to boost primary and secondary preventive strategies based on the extinction procedure," he continued.

More information: Haaker, J. et al. (2013), Single dose of L-dopa makes extinction memories context-independent and prevents the return of fear, *PNAS* Plus - Biological Sciences - Psychological and Cognitive Sciences 110 (26): E2428-36, DOI: 10.1073/pnas.1303061110

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