UKE Paper of the Month June 2013

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Single dose of L-dopa makes extinction memories context-independent and prevents the return of fear

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ABSTRACT: Traumatic events can engender persistent excessive fear responses to trauma reminders that may return even after successful treatment. Extinction, the laboratory analog of behavior therapy, does not erase conditioned fear memories but generates competing, fear-inhibitory "extinction memories" that, however, are tied to the context in which extinction occurred. Accordingly, a dominance of fear over extinction memory expression-and, thus, return of fear-is often observed if extinguished fear stimuli are encountered outside the extinction (therapy) context. We show that postextinction administration of the dopamine precursor L-dopa makes extinction memories context-independent, thus strongly reducing the return of fear in both mice and humans. Reduced fear is accompanied by decreased amygdala and enhanced ventromedial prefrontal cortex activation in both species. In humans, ventromedial prefrontal cortex activity is predicted by enhanced resting-state functional coupling of the area with the dopaminergic midbrain during the postextinction consolidation phase. Our data suggest that dopamine-dependent boosting of extinction memory consolidation is a promising avenue to improving anxiety therapy

STATEMENT: *This paper represents interdisciplinary neuroscientific work in animals and humans that opens a unique avenue for improving the psychotherapy of anxiety disorders.*

BACKGROUND: The studies in humans were performed at the Institute of Systems Neuroscience in the Emmy-Noether Group of Prof. Raffael Kalisch and were part of the PhD thesis of the Pharmacist Dr. Jan Haaker. In a translational approach, Dr. Fabio Morellini (Experimental Neuropediatrics, Center for Molecular Neurobiology Hamburg) conducted a part of the corresponding animal studies. These laboratories have a strong interest of memory and learning processes in the domain of neuroscience. The group of Raffael Kalisch works on neuronal processes underlying fear and extinction learning in humans and Fabio Morellini investigates neurophysiological mechanisms underlying cognitive functions in mice.