B01 - FINDING THE GOOD IN THE BAD: FEAR EXTINCTION RECONCEPTUALIZED AS AN APPETITIVE LEARNING PROCESS

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since 2012

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since 2014

The project investigates whether extinction can be understood as a prediction error-based reward learning process where the positive experience that an expected threat (e.g., a shock) does not occur (the extinction prediction error) is mediated by phasic dopamine release from mesoaccumbal neurons. Phasic optogenetic activation and inhibition of dopamine neuron activity at the time of threat omission in mice are complemented by systemic pharmacological manipulations in combination with computational modeling of behavioral and fMRI data in humans.

B02 - CORTICAL MECHANISMS OF ADAPTIVE FEAR EXTINCTION UNDERLYING STRESS RESILIENCE

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B02 investigates whether extinction of fear of complex conditioned stimuli involves primary sensory cortices. It specifically focuses on dynamic intra-cortical excitability regulation during extinction via inhibitory interneurons in the auditory cortex. Having identified the relevant interneuron types, A02 will go on to perturb the identified elements of the micro-circuitry using optogenetics, to demonstrate their causal role in extinction. Finally, B04 will investigate the sensitivity of these mechanisms to stressors, and the possibility to manipulate these mechanisms to protect animals against stressor-induced extinction deficits.

B03 - FEAR NETWORK INTERACTIONS UNDERLYING RESILIENCE TO STRESS

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B03 investigates how interactions between the amygdala, hippocampus, prefrontal cortex and nucleus accumbens shape resilience to stress. To this end, we will record neural activity in all four structures simultaneously in mice before, during and after exposure to a chronic stressor. We will examine whether functional connectivity between these structures is associated with resilience to stress-induced impairments of social, cognitive and emotional functioning. Optogenetic manipulations will also be performed to test the causal contribution of these network interactions to resilient behavior.

B04 - LIPID SIGNALING BY ANANDAMIDE AND THE BLISS OF RESILIENCE: GENETIC MODELS AT CELLULAR AND NEURAL-NETWORK LEVELS

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B04 will investigate the role of anandamide signaling in resilience. Anandamide is an endocannabinoid and ligand of the cannabinoid CR1 receptor, implicated in fear extinction, relief from anxiety and HPA axis down-regulation. It is expected that anandamide signaling at the time of stressor exposure facilitates stress response regulation by its effects on neuronal excitability as well as large-scale network function. B04 will genetically enhance anandamide signaling at precise time points during stressor exposure in selected neurons of the network and investigate its effect on excitability, network function, and resilience

B05 - REGULATION OF NEURAL EXCITABILITY AND NEURAL-NETWORK FUNCTION IN RESILIENCE – A MULTIMODAL AND (BACK-) TRANSLATIONAL APPROACH

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NITSCH, ROBERT| PROF. DR. MED. DR. PHIL.
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since 2009

Using neuronavigated transcranial magnetic stimulation over human dorsomedial prefrontal cortex (as a probe) in combination with simultaneous EEG (as a read-out), B05 will determine the excitability and cortico-cortical functional connectivity of this cortex area, pursuing the hypothesis that adaptive stress response during differential fear conditioning and excitability changes are linked to distinct functional cortical connectivity signatures and resilient outcome. Both, in mice and humans, B5 will conduct state-of-the-art functional connectivity measures, and a back-translation of human stimulus activation paradigms to the mouse. Finally, causal optogenetic manipulations will be developed.