Ruprecht-Karls-Universität Heidelberg
Medizinische Fakultät Mannheim
Dissertations-Kurzfassung

Neural, behavioral and genetic correlates of learning and memory: Implications for the psychopathology of anxiety and trauma- and stress-related disorders

Autor: Frauke Steiger-White
Institut / Klinik: Zentralinstitut für Seelische Gesundheit Mannheim (ZI)
Doktormutter: Prof. Dr. H. Flor

The present thesis focuses on the role of contextual and cued acquisition processes and their neural, behavioral and genetic correlates in a clinical PTSD sample, a traumatized group, and healthy subjects. With the help of neuroimaging methods, we examined brain regions (the amygdala and the hippocampus) centrally involved in aversive fear learning. In the first study, we investigated context and cued fear acquisition in a clinical sample of PTSD and control subjects. In the second study, we explored the extent to which a genetic risk variant is associated with exaggerated fear responses in a healthy sample.

The results of the first study demonstrate that PTSD patients are less able to differentiate between safe and dangerous contexts according to their differential contingency ratings along with heightened hippocampal activation in comparison to the traumatized subjects and healthy controls. In a second acquisition phase, we demonstrated that PTSD patients, in contrast to the impairment in context acquisition, showed a differential response to the dangerous versus safe cues presented against the background of the respective conditioned contexts. PTSD patients were able to differentiate threat and safety cues to a similar degree as the control groups; which could be related to reduced blocking of cue acquisition by the previously learned context, which was deficient. Impaired context conditioning in PTSD may result in better learning (less “blocking”) of later aversive encounters (new cue fear conditioning) compared to controls. In the second cue conditioning study, we demonstrated in a healthy sample (N=116) that a genetic risk variant of the NPS receptor for hyperarousal (and exaggerated fear responses) significantly influences the amygdala activation during fear acquisition and is associated with elevated level of nocturnal cortisol. Additionally, our risk allele carriers of NPS showed diminished inferior frontal gyrus activation in early learning stages. These findings might be an explanation for sleeping disturbances (such as nightmares or generally interrupted sleep) that are often reported in anxiety disorders or PTSD. NPS could especially play a role in PTSD patients where the hyperarousal subtype of PTSD is pronounced.

The two studies that comprise this thesis provide evidence for associative learning processes, more specifically impaired context learning as well as a shift towards cue learning, as putative mechanistic underpinnings for the etiology of PTSD. Moreover, genetic factors such as NPS, can influence specific domains such as arousal, by enhanced fear learning processes associated with enhanced amygdalar activation and elevated nocturnal cortisol levels.