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Emotional Reactivity in Posttraumatic Stress Disorder: Behavioural and Neurobiological Correlates of Underlying Mechanisms and the Role of Emotional Memory Modification

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The symptom pattern of posttraumatic stress disorder (PTSD) comprises four clusters: “involuntary distressing memories”, “persistent avoidance of stimuli related to the traumatic event”, “negative alterations in cognition and mood”, and “in arousal and reactivity” (DSM 5, American Psychological Association). Increasing evidence points towards enhanced emotional reactivity as an underlying mechanism of the latter mentioned symptom pattern in individuals with PTSD. From a process oriented perspective, enhanced emotional reactivity has been linked to aberrant fear conditioning processes: Classical fear conditioning paradigms comprise the association of a neutral cue with an aversive event (danger cue) while another cue (safety cue) is never followed by an aversive event. Although the picture is not clear yet, complex alterations in the context of fear processing have been observed in PTSD: While overall enhanced reactivity to both cues has been found, also difficulties in the ability to differentiate between the conditioned danger and safety cue was examined. Additionally, studies point to slower and/ or reduced fear extinction. It is important to note that the diagnostic criteria of PTSD state that emotional responses in PTSD tend to spread to a variety of stimuli, resembling the traumatic event, which is referred to as overgeneralization. However, as mentioned before, classical fear conditioning paradigms are restricted to two conditioned cues and thus, cannot investigate the transfer of emotional responses to other cues. Therefore, extending the classic paradigms by including a range of cues is important to ensure a better understanding of the respective pathomechanism. On a neurobiological level, enhanced emotional reactivity has been associated with elevated cardiovascular activity and decreased neuronal activity in prefrontal regions, while simultaneously activity of limbic regions has been found to be increased. This pattern is referred to as decreased top-down regulation. Thus, aberrant neurobiological emotional processing in PTSD points to difficulties in regulating emotional states and thus, alterations in emotional reactivity. Importantly, heart rate variability (HRV) is stated to be a biomarker of emotion regulation, since a high HRV has been associated with one’s regulatory capacity. Importantly, HRV has been found to be lower in PTSD. Yet, the relation between HRV and the neuronal response pattern associated with autonomic functioning has not been studied in PTSD. Investigating both parameters simultaneously is hypothesized to help gain a better understanding of PTSD patients’ capacity to regulate emotional responses. Altogether, emotion overreactivity is a key facet of PTSD. Therefore, one aim of therapeutical attempts is to attenuate strong emotional memory. Interestingly, upcoming evidence from experimental research points to a promising technique, which might provide the opportunity to modify consolidated memory permanently and thus, may be beneficial with respect to therapy. That is, upon retrieval of consolidated memories, these memories must once again stabilize, in order to persist. This process of re-stabilization is known as reconsolidation. Herein, pharmacological, as well as behavioral intervention protocols have been shown to successfully attenuate prior learned emotional responses, when applied during reconsolidation. However, studies are sparse in testing whether therapeutical interventions in combination with reconsolidation provide a beneficial effect on emotional memories. Altogether, the present thesis investigated underlying mechanisms of heightened emotional reactivity in PTSD. Moreover, an experimental approach aiming at attenuating a newly formed aversive emotional memory was tested, to provide further insights into processes that may contribute to overcome strong negative emotional states.

In the first study, alterations in the acquisition and generalization of fear were examined. A recently introduced fear conditioning and generalization paradigm was studied in 30 PTSD individuals, 30 healthy trauma exposed and 30 non-trauma exposed healthy control participants. The paradigm covers a range of stimuli parametrically varying in their similarity and thus, forming a continuum between the danger

and safety cue. This allows the testing of fear transfer to stimuli that resemble the danger cue. Hints towards altered emotional reactivity, here, alterations in generalization was found with respect to reaction times while evaluating the risk of an aversive event associated with generalization stimuli in PTSD: PTSD patients were slower in judging the risk related to stimuli of moderate similarity to the danger cue. Additionally, PTSD subjects overall subjectively expected more risk irrespective of the stimulus type across all experimental phases. Importantly, while explicit risk perception was linked to PTSD, implicit measures of overgeneralization were related to traumatization per se.

In a second study, neurophysiological underpinnings of emotion regulation have been addressed. Specifically, the combination of HRV and its' neuronal response pattern (central autonomic network, CAN) was assessed in 57 PTSD individuals and 41 healthy control subjects during resting state functional magnetic resonance imaging (fMRI). PTSD patients were characterized by lower HRV compared to controls. Moreover, PTSD subjects exhibited a widespread connectivity pattern between key nodes of the CAN and multiple cortical and subcortical areas compared to controls. Importantly, while CAN connectivity was related to HRV in controls, this association was not found to be significant in PTSD. These data were interpreted in the frame of increased emotional reactivity and a decoupling of central and autonomic functioning in PTSD.

In a third study, we investigated whether pharmacological and behavioral interventions applied during memory reconsolidation can attenuate a prior acquired fear memory. A differential fear conditioning paradigm was studied in 80 female healthy individuals: Two stimuli (CS+) were associated with an aversive event, while one (CS-) was never followed by an aversive event. Pharmacological (propranolol) and behavioural (reappraisal, multimodal sensory stimulation) intervention protocols were applied upon memory reactivation of one of the two CS+ (reconsolidation disruption) and contrasted to a placebo control condition. Effects on memory were tested during extinction and reinstatement testing. Differential effects regarding the reactivated and non-reactivated CS+ have only been observed in the propranolol condition. Specifically, fear memory was stronger in response to the non-reactivated CS+ compared to the placebo group. None of the behavioural interventions did attenuate fear memory. Yet, an increasing number of studies point towards difficulties in triggering reconsolidation processes. Findings are discussed with respect to boundary conditions.

In sum, the first two studies extended prior investigations on emotional reactivity in PTSD. Results showed that PTSD individuals exhibited altered emotional reactivity to safe stimuli resembling the danger cue, as indexed by alterations in the generalization of fear with respect to the certainty of stimulus evaluation. Together with increased subjective risk perception and alterations in baseline responding and fear learning, these findings provide further evidence for a correlate of altered emotional reactivity in PTSD. Moreover, study II hints towards a psychophysiological-neuronal profile, contributing to emotion regulation difficulties in PTSD. Thus, while PTSD individuals exhibited lower resting HRV, the latter was not associated with the central autonomic network, pointing to a desynchronized pattern. Both studies implicate the importance of emotional (over-) reactivity in PTSD in contributing to the defined symptom pattern of PTSD. However, an attempt to experimentally target emotional memories did not show a beneficial effect by combining reconsolidation with either a pharmacological agent (propranolol) or behavioural therapeutical techniques on a prior established fear memory. Future research should focus on the combination of the mentioned investigation on emotion reactivity and regulation in PTSD. This would provide a broader picture of the complex interplay between both concepts and their associated behavioural und psychobiological profile. Possible implications for PTSD psychotherapy include strategies that reduce uncertainty in save situations. Although more fundamental research is needed to investigate boundary conditions for reconsolidation to occur, a better understanding of the respective mechanism may help to improve therapeutical strategies.