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Neural and behavioral correlates of altered reward and loss processing in depression

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The present thesis focuses on altered reward and loss processing and related associative learning in depression. Therefore, essential components of reward and loss processing in currently and remitted depressed individuals are investigated using functional neuroimaging and behavioral research methods.

Neurobiological alterations during the processing of reward and punishment represent a promising psychophysiological marker of major depression. However, selective reports either focusing on neural alterations during reward or loss conditions dominate the field showing a heterogeneous pattern of brain activation in fronto-striatal regions. Thus, in the first study of this thesis 30 medication-free clinically depressed patients and 28 age-, education-, and sex-matched HC performed an event-related fMRI reward paradigm, which allows the investigation of neural responsivity associated with the processing of reward and loss and the encoding of related PEs. Rewards and losses were presented by monetary gains and losses which were gained or not lost when participant's performed well. Based on findings implicating that anhedonia is associated with learning from positive and negative stimuli, we additionally assessed the relationship between fronto-striatal activation during anticipation and outcome processing and self-reported hedonic capacity. ROI analyses revealed a homogenous pattern of hypoactivity in the NAcc and OFC associated with limited motivational ('wanting') responses to reward- and loss-related incentives in depressed patients compared to HC. We supported these results by our finding that increases in fronto-striatal activity during reward anticipation were associated with hedonic capacity in depressed individuals. During loss anticipation, depressed individuals exhibited decreased activation in the rACC, a prominent region for structural and functional abnormalities in depression. With respect to PE encoding, depressed individuals showed decreased reward-related PE encoding in the amygdala and rACC but increased loss-related PE encoding within the VS. Alterations in PE signaling indicate that depressed individuals show a reduced ability to learn stimulus-reward associations in contrast to an enhanced ability that biases learning of stimulus-loss (Type II punishment) associations. In line with the literature, these results mirror blunted reward and enhanced loss-related associative learning in depression.

In the second study, twenty-three medication-free individuals with rMDD and 23 HC matched for age, sex and education underwent the reward paradigm which was employed in the first study and a computer-based version (ABCD) of the IGT. We were interested in whether behavioral and neural alterations in reward sensitivity still persist although depressed individuals are currently in a remitted state of MDD. Further, we analyzed the association between temperament dimensions measured by the TPQ, behavioral reward sensitivity measured by the IGT, and neural responsivity to reward anticipation and outcome in order to test for the relationship between behaviorally observable and brain-based vulnerability markers of MDD. Compared to HC, patients with rMDD showed enhanced responses to reward incentives associated with activation in fronto-limbic regions, i.e. SFG, hippocampus and amygdala. During reward outcome, rMDD did not significantly differ from HC. Fronto-limbic activity during anticipatory reward processing was found to be related to harm avoidance but not to IGT reward sensitivity although reward sensitivity assessed by IGT performance was marginally reduced in individuals with rMDD. The findings of the second study are of clinical relevance since abnormalities in reward sensitivity in depression might represent a persisting vulnerability marker for depression relapse. Further studies in high-risk samples are needed to evaluate whether reward sensitivity moreover reflects a true vulnerability factor of depression.

Findings on altered reward and loss processing in depression reflect learning mechanisms that seem to account for the pathogenesis and the maintenance of depressive disorder.