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Dysregulation of motivation: evidence for a biological vulnerability factor of bipolar I disorder

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Objectives: To date, it is unclear whether abnormalities in motivation and reward processing observed in bipolar I disorder represent a biological vulnerability factor, scars of prior episodes or might be better ascribed to current mood states, medication or comorbidity. To define the status of motivational processing as a vulnerability factor, neural mechanisms related to motivation were examined in euthymic bipolar patients and unaffected first-degree relatives of bipolar patients. Further, it was investigated how previous episodes influence sensitivity to positive and negative feedback relevant for motivation.

Methods: To determine whether altered motivational processing represents a vulnerability factor of bipolar disorder, two samples, the first consisting of 19 euthymic bipolar patients and 19 matched controls, the second including 22 relatives and 22 matched controls were examined. Motivational processing was assessed with a probabilistic reversal learning task during event-related functional magnetic resonance imaging (fMRI). Data were analysed using a region-of-interest approach restricting analysis to medial and lateral orbitofrontal cortex, amygdala, anterior cingulate cortex and striatum. In addition, 23 euthymic patients with bipolar I disorder, 19 remitted patients with major depression and 19 healthy persons underwent a task, which discriminates whether persons learn better from negative or positive feedback. Here, multiple hierarchical regression analyses were applied with number of past depressive and manic episodes, residual mood symptoms, affective quality of the last episode, time in remission, medication, illness severity and age as predictors.

Results: Increased activation in response to reward and reversal of reward contingencies was observed in left medial orbitofrontal cortex in patients and right medial orbitofrontal cortex in relatives. Further, activation of amygdala in response to reversal of reward contingencies was increased in patients and relatives. In response to reward, activation of amygdala was increased in relatives only, but there was a significant negative correlation between medication and amygdala activation in patients. Further, findings revealed that for both sensitivity to positive and negative feedback, the quality of the last affective episode was the only significant predictor. Bipolar disorder patients, who last experienced a manic episode learned well from positive but not negative feedback, whereas bipolar disorder patients, who last experienced a depressive episode showed the opposite pattern.

Conclusions: Results identify increased activation of medial orbitofrontal cortex and amygdala, related to heightened reward sensitivity and deficient prediction error signal as vulnerability factor of bipolar disorder. In addition, we identified differences in response to positive and negative consequences that carry over into the euthymic state and were related to the polarity of the preceding episode. These results shed new light on previous inconsistent data in euthymic bipolar disorder patients, support a role of altered motivational processing in the risk architecture of bipolar I disorder and could also guide tailored treatment.