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Research report

Inefficiency of emotion regulation as vulnerability marker for bipolar disorder: Evidence from healthy individuals with hypomanic personality

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ABSTRACT

Objective: Emotion regulation deficits are a key characteristic of bipolar disorder (BD). In the present study, we asked if deficits in emotion regulation are also a vulnerability marker for BD. To this end, we investigated a healthy group of participants at high-risk for developing BD, defined on the basis of a hypomanic personality trait. We examined the neural correlates of two emotion regulation strategies, reappraisal and distraction.
Method: Twenty-two individuals with higher risk for BD and twenty-four controls were investigated in a functional magnetic resonance imaging paradigm. Participants were presented with negative, positive and neutral pictures and were either required to passively view the images, to down-regulate the emotional response by reappraising the pictures' content, or to perform a distracting arithmetic task.
Results: High-risk individuals showed increased emotional reactivity to negative stimuli, indicated by heightened amygdala activation during passive viewing. High-risk participants were also less successful in down-regulating amygdala activity using reappraisal of negative stimuli. During distraction from positive stimuli, high-risk individuals showed heightened task-related activity in the inferior parietal cortex, suggesting increased distractibility by task-irrelevant positive background stimuli. There were no differences in habitual emotion regulation as assessed by a self-report questionnaire.
Limitations: Generalizability of the present results is limited by the age- and education-homogenous sample and the small sample size.
Conclusions: This is the first study to report neural correlates of increased emotional reactivity and deficient emotion regulation in healthy individuals at risk for BD. These findings suggest inefficient emotion regulation through reappraisal and distraction in individuals with high hypomanic personality who are supposed to be at higher risk to develop bipolar disorder.

1. Introduction

To contribute to aetiological models as well as early diagnosis of mental disorders, the identification of vulnerability markers is an important research goal, which can be achieved by studying healthy individuals at risk for developing the respective mental disorder (Keener and Phillips, 2007). In the present study, we used such a high-risk approach to investigate neural correlates of altered emotional processing as a potential vulnerability marker for bipolar disorder (BD). BD is a severe mental illness that is characterized by extreme poles of emotionality, resulting in significant alterations in emotional processing (Wessa and Linke, 2009). The neural correlates of altered emotional processes are an interesting target, as neural changes might precede behavioral manifestations in a healthy high-risk population. Even in remitted and symptomatic BD patients, neural patterns have been more sensitive to alterations than behavioral measures (Elliott et al., 2004; Wessa et al., 2007).

On a neurobiological level, BD has been associated with hyperactivation of limbic brain structures (e.g., amygdala, insula) and hypoactive cognitive control networks (Houenou et al., 2011; Wessa and Linke, 2009). Reduced engagement of the cognitive control network including dorsal anterior cingulate cortex (dACC), dorsolateral prefrontal cortex (dlPFC), ventrolateral prefrontal cortex (vlPFC), and inferior parietal cortex in BD patients might lead to deficient inhibition of limbic activity and thus to

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persistently increased emotional reactivity (Strakowski et al., 2005). Indeed, significantly increased activation of the amygdala and reduced inhibitory vlPFC activity to negative emotional stimuli have been reported in manic and remitted BD patients (Foland et al., 2008; Houenou et al., 2011). As efficient functioning of the described cognitive control network is highly relevant for successful regulation of emotional responses (Ochsner et al., 2004), inappropriate and inefficient emotion regulation is supposed to be a crucial mechanism in BD (Phillips et al., 2003).

In the present study, we aimed at identifying deficits in emotion regulation and respective neural activation patterns as vulnerability markers for BD. To this end, we investigated a group of healthy individuals at higher risk to develop BD than the normal population and an age- and gender-matched control group. As trait-like tendencies toward manic symptoms and high mood states appear to represent the best predictors of onset of bipolar disorders (Lara et al., 2006; Oedegaard et al., 2009), we selected individuals at high risk to develop bipolar disorder on the basis of a questionnaire assessing hypomanic personality traits (Hypomanic Personality Scale; HPS: Eckblad and Chapman, 1986). High scorers on the HPS are characterized by a chronic mild manic state and mood instability with a subsyndromal change of ups and downs (Eckblad and Chapman, 1986; Hofmann and Meyer, 2006). The HPS has been widely used as an index of hypomanic temperament (Johnson and Carver, 2012) or mania proneness (Piff et al., 2012) as well as a psychometric vulnerability indicator of bipolar disorder (Meyer and Blechert, 2005; Meyer and Deckersbach, 2005). Indeed, hypomanic personality (HP) traits have been shown to predict mania and the onset of bipolar disorder longitudinally, but not psychosis (Blechert and Meyer, 2005; Kwapil et al., 2000). The concept of HP suggests heightened emotional responses (Carver and Johnson, 2009), and indeed, elevated intensity of positive and negative affect (Kwapil et al., 2011) as well as a general excess of positive emotions in response to positive, negative and neutral stimuli (Gruber et al., 2008) have been observed in individuals with HP.

To assess HP individuals' capacity to regulate positive and negative emotions and the underlying neural activation patterns we applied a previously validated emotion regulation task during functional magnetic resonance imaging (fMRI) (Kanske et al., 2011; Kanske et al., 2011). Emotion regulation can be accomplished by using different strategies (Ochsner and Gross, 2005), e.g. by focusing attention away from an emotional stimulus (distraction), or by reinterpreting an emotional situation in order to alter its emotional intensity (reappraisal). These strategies might not be equally impaired in individuals at risk to develop BD. To address this issue, these two emotion regulation strategies were tested in the present experiment.

Based on previous work in healthy individuals, we focused on the analysis of two brain networks: one involved in emotional processing, including amygdala, ventromedial PFC (vmPFC) and subgenual ACC, ventral temporal cortices, and thalamus (Kanske et al., 2011; Phan et al., 2002; Van Dillen et al., 2009) and a second one underlying cognitive control and thus voluntary emotion regulation, comprising orbitofrontal cortex (OFC), dlPFC, dmPFC, dorsal ACC (dACC), parietal cortex and precuneus (Kalisch, 2009; Kanske et al., 2011; Ochsner et al., 2002, 2004; Phan et al., 2005).

In accordance with previous findings for patients with BD (Foland et al., 2008; Wessa et al., 2007) as well as for individuals with HP (Gruber et al., 2008; Kwapil et al., 2011), we hypothesize that HP individuals show heightened emotional reactivity indicated by increased amygdala activity when viewing emotional (positive and negative) stimuli. HP individuals are also hypothesized to display inefficient down-regulation of emotional responses during emotion regulation (reappraisal, distraction), evident in persistently heightened amygdala activation as well as reduced activity in frontal and parietal brain areas, constituting the cognitive control network (Fehr et al., 2007; Kanske et al., 2011; Rickard et al., 2000).

2. Method

2.1. Participants

To select a sufficient number of individuals with HP for an fMRI study, who were willing to participate in the present study and fulfilled the study's inclusion criteria, we screened a total of 1567 individuals (screening sample) with the German version of the HPS (Eckblad and Chapman, 1986); German version: (Meyer et al., 2000). This questionnaire contains 48 true-false items measuring symptoms of a mild manic state (see above) and has good psychometric properties (Eckblad and Chapman, 1986; Meyer et al., 2000). Students were recruited in university lectures and by means of an online questionnaire. According to previous studies on HP (Krumm-Merabet and Meyer, 2005; Kwapil et al., 2000; Meyer and Deckersbach, 2005; Meyer et al., 2000), individuals with a higher risk to develop bipolar disorder were defined as scoring in the upper percentile of the HPS score distribution of the screening sample (HPS score ≥31) resulting in a sample of $N=156$ individuals, principally eligible for inclusion in the high-risk group. However, due to several drop-out reasons, the final study sample of high-risk individuals included only 24 participants. Main drop-out reasons were: contraindication to MRI (e.g., metal implants including orthodontic retainers, agoraphobia); unwillingness to participate in the study despite completion of the screening questionnaires; time constraints; diagnosis of a current Axis-I mental disorder. In line with previous studies (e.g., Krumm-Merabet and Meyer, 2005; Kwapil et al., 2000) we included a gender- and age-matched control group (non-HP) to the high-risk group (HP), which comprised 24 individuals who did not score 0.5 SD above the mean of the HPS score distribution of the screening sample. For statistical analyses, two HP participants had to be excluded due to fMRI motion artifacts and difficulties in understanding task instructions. Accordingly, the final sample for all analyses included 22 HP and 24 non-HP participants. There were no significant group differences in age, gender or education level (Table 1; years of education was 13 for all participants). All individuals were right-handed according to the Edinburgh Handedness Inventory (EHI; (Oldfield, 1971); see Table 1), had normal or corrected-to-normal vision and reported no history of mental disorders as verified by the German version of the Structured Clinical Interview for DSM-IV, SCID-I and -II (First et al., 1997a, 1997b), medical or neurologic illness.

Participants completed the German version of the Emotion Regulation Questionnaire (ERQ) (Gross and John, 2003) with the subscales suppression and reappraisal, as a screening instrument of habitual emotion regulation.

Table 1
Descriptive data of individuals with hypomanic personality traits (HP; $N=22$) and controls (non-HP; $N=24$).

	HP ($N=22$)	Non-HP ($N=24$)	Statistics
Age	20.95 (1.59)	22.29 (2.93)	$t(44)=1.90$; $p=.064$
Sex (female/male)	13/9	14/10	$Chi^2=.003$, $p=.958$
HPS score	34.45 (3.12)	12.63 (4.65)	
Handedness score (EHI)	82.74 (16.97)	84.56 (16.53)	$t(44)=.368$, $p=.715$
ERQ-reappraisal	26.74 (6.38)	26.58 (5.23)	$t(44)=-.105$; $p=.917$
ERQ-suppression	12.55 (4.69)	11.63 (3.59)	$t(44)=-.752$; $p=.456$