Functional Correlates of childhood maltreatment and symptom severity during affective theory of mind tasks in chronic depression

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Among multiple etiological factors of depressive disorders, childhood maltreatment (CM) gains increasing attention as it confers susceptibility for depression and predisposes to chronicity. CM assumedly inhibits social-cognitive development, entailing interactional problems as observed in chronic depression (CD), especially in affective theory of mind (ToM). However, the extent of CM among CD patients varies notably as does the severity of depressive symptoms. We tested whether the extent of CM or depressive symptoms correlates with affective ToM functions in CD patients. Regional brain activation measured by functional magnetic resonance imaging during an affective ToM task was tested for correlation with CM, assessed by the Childhood Trauma Questionnaire (CTQ), and symptom severity, assessed by the Montgomery-Åsberg Depression Rating Scale (MADRS), in 25 unmedicated CD patients (mean age 41.52, SD 11.13). Amygdala activation during affective ToM correlated positively with CTQ total scores, while (para)hippocampal response correlated negatively with MADRS scores. Our findings suggest that differential amygdala activation in affective ToM in CD is substantially modulated by previous CM and not by the pathophysiological equivalents of current depressive symptoms. This illustrates the amygdala's role in the mediation of CM effects. The negative correlation of differential (para)hippocampal activation and depressive symptom severity indicates reduced integration of interactional experiences during depressive states.

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1. Introduction

The individual presentation and course of depressive disorders reflect multifactorial contributions (Beck and Alford, 2009). A chronic course of depression, which corresponds to the DSM-5 diagnosis of persistent depressive disorder (PDD) (American Psychiatric Association, 2013), is characterized by symptoms of a depressive mood most of the day for more days than not and persisting for at least 2 years (McCullough and Clark, in press). Chronic depression (CD) is additionally associated with multiple relapses and a heightened treatment resistance (Keller et al., 1992). As about 65% of chronically depressed patients report a history of childhood maltreatment (CM) (Wiersma et al., 2009) and up to 70% of all CD cases are manifested before the age of 21 years (Cassano et al., 1992), the impact of early life experiences such as experiencing abusive or neglectful parental behaviour is assumed a major contributing factor of CD (Teicher and Samson, 2013). CM increases the lifetime risk for depression (Chapman et al., 2004), accompanied by a strong dose-response relation between frequency of exposure and the extent of depressive

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The main goal of our study was to disentangle the functional effects of adverse early life experiences on social-cognitive functioning in chronic depression from effects caused by current depressive symptoms. We examined if ToM network dysfunctions are more likely associated with CM or reflect a side effect of emotion dysregulation and cognitive disturbances due to current depression severity. Such knowledge about the long-term impact of CM in current states of depression should improve treatments by defining social-cognitive deficits as treatment targets in chronically depressed patients. The distinction between effects of CM and current depressive symptoms is important because for selecting an appropriate therapeutic intervention, especially antidepressant medication vs. specific psychotherapy. To investigate whether the activation of the amygdala and hippocampus during affective ToM generation is differentially influenced by CM and acute depression, we selected a group of chronically depressed patients for our study as they provide various combinations of CM and depressive symptom severity. This variance of CM and depression severity facilitates the examination of the functional effect of both factors during affective mentalizing in one group of patients (McCullough, 2003). Due to the findings concerning amygdalar and hippocampal activation during affective ToM generation and the reported impact of CM and depression, we hypothesized that CM and current depression severity would have distinguishable functional correlates during affective mentalizing, which could be detected in the activation of the amygdala and the hippocampus in a group of CD patients.

In addition, we aimed to probe the effects of CM on functional activation during affective social cognition, which is clearly distinguishable from a stimulus driven automatic response to highly overlearned emotional cues such as facial expressions (Dannowski et al., 2013; Grant et al., 2011; Klein et al., 2014; Siegle et al., 2002; Van Harmelen et al., 2013), as it has been suggested that CM inhibits early development of social-cognitive functions.

2. Materials

2.1. Subjects

We analysed behavioural and functional data of 25 subjects with CD (16 female, mean age 41.52, SD 11.13) who had been free of psychotropic medication for at least 2 weeks. With regard to the reported conjunction between chronicity, multiple relapses and heightened treatment resistance in depression (Keller et al., 1992), we included subjects who met the DSM-IV (American Psychiatric Association, 2000) criteria for a current episode of chronic major depression (with the modification of at least 1 year of depressive symptoms) or recurrent major depressive episodes (≥3 episodes with the preceding episode no more than 2.5 years before the onset of the current episode), assessed by the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID) (First et al., 2002). Our group was a subsample of a bicentric randomized clinical trial exploring the effects of psychotherapy (CBASP, Cognitive Behavioural Analysis System of Psychotherapy) versus medication with selective serotonin reuptake inhibitors (SSRI) (Schrann et al., 2015). For the clinical trial, 60 outpatients were recruited and observed over the course of 8 and 28 weeks, respectively. The main inclusion criterion was a score of at least 18 on the Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979), which was determined before the patients entered the study. Out of the 60 subjects, 34 participated in the additional functional magnetic resonance imaging (fMRI) trial involving two fMRI scan sessions – one before the beginning of the treatment, the second one 8 weeks later. Each fMRI examination comprised four functional paradigms, the ToM task reported in this article, a reward
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