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Deficient inhibitory control as an outcome of childhood trauma

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ABSTRACT

Childhood trauma has been linked to the development and severity of psychiatric disorders as well as deficits in cognitive functioning. This study aimed to investigate the performance of bipolar disorder (BD) patients and healthy controls (HC), with or without a history of childhood trauma, on a parametric Go/No–Go (PGNG) task measuring important aspects of executive functions, namely attention and inhibitory control. Two hundred and thirty-three individuals with BD and 90 HC completed diagnostic interview, childhood trauma questionnaire (CTQ), symptom severity scales, and a PGNG task. Four comparison groups were created using a 1.0 standard deviation cut-off of the mean of the HC total CTQ score: BD-trauma, BD-normative, HC-trauma and HC-normative. We assessed interactions between diagnosis and trauma on Go/No–Go levels of interest by using a two-way multivariate analysis of covariance. Results showed a significant main effect of trauma on inhibitory control accuracy, as the trauma group exhibited significantly poorer accuracy on inhibition trials compared to the normative group. There was also a main effect of diagnosis on response time. These findings suggest that early trauma might adversely impact the development of cognitive systems and brain circuits that support inhibitory aspects of executive functioning in individuals with a history of trauma.

1. Introduction

Traumatic experiences, including abuse and neglect, encountered early in life are major risk factors for the development and severity of psychiatric disorders later in life (Agid et al., 2000; Caspi et al., 2003). In particular, childhood trauma is associated with susceptibility to bipolar disorder (BD) (Etain et al., 2010), a more severe BD course, adverse impact on clinical characteristics such as age of illness onset, number of mood episodes and worse overall functioning (Leverich et al., 2002; Larsson et al., 2013). Most interventions related to trauma involve psychosocial and Cognitive Behavioral Therapy (CBT), which heavily rely on cognitive processes (Bisson et al., 2007). However, we still have not clearly identified the specific cognitive deficits associated with childhood trauma that may hinder intervention outcomes in healthy or mentally-ill individuals.

Bipolar disorder is a severe and chronic psychiatric disorder that is associated with increased morbidity and mortality (Angst et al., 2002), including significant cognitive difficulties and associated negative impact upon everyday functioning (Ryan et al., 2013). Significant difficulties in cognitive functioning in BD have been well-documented in the literature, including processing speed, attention, executive functioning, memory, and fine motor skills (van Gorp et al., 1998; Robinson et al., 2006), and exist even among individuals in the euthymic state (Zubieta et al., 2001; Thompson et al., 2005; Langenecker et al., 2010).

Recent studies have started to clarify the association between childhood trauma, mental illness, and altered neural and cognitive development. There is growing evidence that exposure to sexual abuse is related to poorer verbal and visual memory performance (Savitz et al., 2007; Savitz et al., 2008) and reduced cognitive flexibility (Savitz et al., 2008) in BD. Even in healthy populations, physical abuse and emotional neglect encountered early in life have been linked to memory and executive deficits in adulthood (Majer et al., 2010; Spann et al., 2012), deviations in negative affect and cognitive control (Rogosch et al., 1995), as well as increased depression, smoking and alcohol abuse (Goldstein et al., 2013). Russo et al. (2014) investigated the effect of sex and childhood trauma on affective processing in bipolar disorder patients and found that females reported both a higher number of different types of childhood trauma compared to males with greater severity of emotional abuse, sexual abuse, and emotional neglect and tended to a more conservative cognitive style; whereas male

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bipolar patients who reported emotional abuse tended to a more risk taking behavior compared to female bipolar patients. While the neural mechanisms underlying the cognitive sequelae of trauma are still unclear, it has been shown that acute stress is implicated in the reduction of white matter in dorsolateral prefrontal cortex, which could potentially be a mediating factor of executive dysfunction (Qin et al., 2009). Neuro-imaging studies have also indicated that childhood trauma may alter brain volume in first-episode psychosis population, with findings of decreased volume in hippocampal/amygdalar regions that are important for memory and emotional processing (Hoy et al., 2012). Similar results were obtained in a recent study with healthy individuals (Samplin et al., 2013) where childhood emotional abuse correlated with higher levels of subclinical psychopathology in healthy adults, and moreover, with reduced volume in the hippocampus in males. While we know that executive functioning difficulties are present in both adult and child BD (Clark et al., 2002; Martinez-Aran et al., 2004; Frangou et al., 2005; Bearden et al., 2007; Langenecker et al., 2010), and that BD is associated with early childhood trauma (Leverich et al., 2002; Larsson et al., 2013), less is known about the impact of trauma on specific aspects of executive functions such a attention and inhibitory control, which are key components of goal-oriented behavior and self-regulation. We are also lacking a model explaining how early trauma may exacerbate already deficient cognitive and affective systems in mentally ill individuals. To date, even for the few studies trying to address this complex relationship it has been a challenge to include both patients and demographically matched healthy controls in the same study to examine effects of trauma on executive functions.

Therefore, the present study aimed to investigate the relation between early childhood trauma and attention and inhibitory functioning concurrently in adult patients with BD and healthy controls with or without a history of childhood trauma. To this goal, we adopted a task that has been well-validated and enabled us to measure both selective attention and inhibitory control, the Parametric Go/No–Go task (Langenecker et al., 2007b). By including four groups (BD-trauma, BD-normative, HC-trauma and HC-normative), this afforded us the unique opportunity to disentangle the effects of trauma from the effects of trauma in interaction with mental illness. Based on the existing literature linking cognitive problems to early trauma in healthy population (Savitz et al., 2007; Majer et al., 2010; Spann et al., 2012), we predicted that the HC group with a trauma history would perform worse than the HC-normative group in terms of inhibitory control accuracy. Moreover, because of the evidence that childhood trauma affects cognitive functions (Savitz et al., 2007; Majer et al., 2010; Spann et al., 2012) and that BD patients exhibit reduced inhibitory control relative to HC (Savitz et al., 2008; Langenecker et al., 2010; Passarotti et al., 2010; Ryan et al., 2013) we predicted that the compounding effects of trauma and BD may lead to the most severe inhibition deficits. Hence, we expected that the BD group with a trauma history would exhibit the most severe deficits in inhibitory control relative to the other three groups. With regard to the less challenging attention task, we predicted that the BD groups would perform more poorly from the HCs in terms of accuracy and reaction time (RT) given that difficulties in attention and processing speed have been well documented in individuals with BD (van Gorp et al., 1998; Robinson et al., 2006).

2. Method

2.1. Participants

Study participants were recruited from the Prechter Bipolar Repository between October 2005 and December 2011 at the University of Michigan for a study of phenotypic and biological outcomes of bipolar disorder (for description, see Langenecker et al. (2010)). Of the 586 participants recruited for the longitudinal cohort, 233 individuals with confirmed BD (191 BD Type I, 42 BD Type II) and 90 healthy controls (HC) were included in the present study. The BD and HC samples were matched on age, education, and verbal intelligence using the Wechsler Vocabulary score (Wechsler, 1999). Four comparison groups were created using a 1.0 standard deviation cut-off of the mean of the healthy controls' Childhood Trauma Questionnaire (Bernstein and Fink, 1998) (CTQ) Total Score ($M=35.76$ ($SD=9.60$); cut-off score$=45.35$). Those below the cut-off score of 45.35 were labeled normative group whereas those participants with a score equal to/or above 45.35 were labeled trauma group: BD trauma (n$=117$), BD normative ($n=116$), HC trauma ($n=17$), and HC normative ($n=73$). As expected, the distribution of the presence of childhood trauma differed for HC and BD. Within the HC group, 81.1% were below our cut-off score, whereas 18.9% were above our cut-off score. In contrast, within the BD group, 49.8% were below our cut-off score, whereas 50.2% were above our cut-off score.

Recruitment of participants occurred through an outpatient specialty psychiatry clinic, an inpatient psychiatric unit, and advertisements on the web and in the newspaper. All participants gave informed consent prior to participation. Participants were evaluated with Diagnostic Interview for Genetic Studies (Nurenberger et al., 1994; DIGS), neuropsychological testing, life event and symptom questionnaires, Hamilton Depression Rating Scale (Hamilton, 1960) (HDRS), and Young Mania Rating Scale (Young et al., 1978) (YMRS). Final diagnoses were determined through a best estimate process and confirmed by two of the current study authors who are MD/PhD clinicians. Participants with BD were excluded from the study if they had a history of schizophrenia or schizoaffective disorder, active or current substance dependence, or a medical illness specifically associated with mood symptoms (including but not limited to: terminal cancers, Cushing's disease, or stroke). HC participants were not eligible to participate if they had a history of any DSM-IV axis I disorder, active and current substance use disorder diagnosis, any medical illness specifically associated with mood symptoms, or any first-degree family member who had been diagnosed or hospitalized for mental illness. This study was approved by the University of Michigan Institution Review Board (IRBMED: HUM00000606).

Table 1 contains demographic characteristics of the BD and HC groups. As expected, based on study design, there were no significant differences between BD and HC groups for age, $F(3)=1.41$, $p=.23$, education, $F(3)=2.00$, $p=0.11$, Wechsler Vocabulary, $F(3)=1.91$, $p=0.12$, or gender, $\chi^2(3, N=323)=4.462$, $p=0.216$.

Clinical information was collected during the baseline DIGS interview. Clinical variables of interest include years with BD illness, medication loading (based on current medications and using a medication classification procedure reported in Hassel et al., 2008, see analysis section below), cumulative number of total mood episodes (including hypomania), cumulative number of episodes of mania and depression, number of psychiatric hospitalizations, age of BD illness onset, age of first manic episode, age of first depressive episode, and length of BD illness. There was a significant difference between the groups on the HDRS, $F(3, 322)=53.3$, $p=<.001$, and YMRS, $F(3, 319)=18.3$ $p=<.001$, with both BD groups having higher scores than the HC groups. There was also a significant difference between the BD groups on the HDRS, $t(231)=-3.45$, $p=0.001$, YMRS, $t(228)=-2.01$, $p=0.046$, and total number of mania episodes, $t(226)=-2.47$, $p=0.014$, with the BD trauma group having higher scores than the BD normative group. There was a significant difference for age at onset of first mood episode, $t(230)=2.19$, $p=0.029$, as those BD with trauma had a younger age at onset. A significant difference was also found for years of illness, $t(230)=-2.76$, $p=0.006$, as the BD trauma group had greater years of illness compared to the BD normative group. No other differences in clinical variables were found between the BD groups.

2.2. Measures

All participants completed the Childhood Trauma Questionnaire (CTQ) (Bernstein and Fink, 1998) which is a brief, retrospective self-report questionnaire designed to assess five types of negative childhood experiences including emotional neglect, emotional abuse, physical neglect, physical abuse, and sexual abuse. Each item is rated on a 1–5 scale, ranging from never true when you were growing up to very often true when you were growing up. Scores ranged from 5 to 25 for each type of negative childhood experience. The CTQ has demonstrated test–retest reliabilities ranging from.79 to.86 over an average of four months as well as internal consistency reliability coefficients ranging from a median of 0.66 to a median of 0.92 across samples (Bernstein and Fink, 1998). Furthermore, Scher et al. (2001) explored the factor structure and reliability of the CTQ in a racially mixed community sample of men and woman and results showed acceptable internal consistency for the entire measure. Mean CTQ total scores for each group are included in Table 1.

The Parametric Go/No–Go task (PGNG) (Langenecker et al., 2005; Langenecker et al., 2007a; Langenecker et al., 2007b; Votruba and Langenecker, 2013) was used to assess attention and inhibitory control. The design was based upon an original Go/No-Go task developed by Garavan, Ross and Stein (Garavan et al., 1999), derived from the work of Luria (Luria et al., 1973). Whereas the original Go/No-Go task consisted of two targets (i.e., the letters "x" and "y" presented among other letters of the alphabet), the PGNG has the added advantage of including three levels of