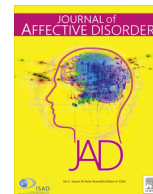




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Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Accuracy of emotion labeling in children of parents diagnosed with bipolar disorder

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ARTICLE INFO

Article history:

Received 16 June 2015

Received in revised form

20 December 2015

Accepted 12 January 2016

Available online 20 January 2016

Keywords:

Bipolar offspring

High-risk offspring

Emotion labeling

Endophenotype

ABSTRACT

Background: Emotion labeling deficits have been posited as an endophenotype for bipolar disorder (BD) as they have been observed in both patients and their first-degree relatives. It remains unclear whether these deficits exist secondary to the development of psychiatric symptoms or whether they can be attributed to risk for psychopathology. To explore this, we investigated emotion processing in symptomatic and asymptomatic high-risk bipolar offspring (HRO) and healthy children of healthy parents (HCO).

Methods: Symptomatic ($n=18$, age: 13.8 ± 2.6 years, 44% female) and asymptomatic ($n=12$, age: 12.8 ± 3.0 years, 42% female) HRO and age- and sex-matched HCO ($n=20$, age: 13.3 ± 2.5 years, 45% female) performed an emotion-labeling task. Total number of errors, emotion category and intensity of emotion error scores were compared. Correlations between total error scores and symptom severity were also investigated.

Results: Compared to HCO, both HRO groups made more errors on the adult face task ($p_{\text{cor}}=0.014$). The HRO group were 2.3 times [90%CI:0.9–6.3] more likely and 4.3 times [90%CI:1.3–14.3] more likely to make errors on sad and angry faces, respectively. With the exception of sad face type errors, we observed no significant differences in error patterns between symptomatic and asymptomatic HRO, and no correlations between symptom severity and total number of errors.

Limitations: This study was cross-sectional in design, limiting our ability to infer trajectories or heritability of these deficits.

Conclusions: This study provides further support for emotion labeling deficits as a candidate endophenotype for BD. Our study also suggests these deficits are not attributable to the presence of psychiatric symptoms.

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1. Introduction

Successful social cognition results from appropriate perception, inference, and judgment of interpersonal and environmental cues. In order to be successful, one must develop: a set of skills that allows for the accurate identification of social cues, a bank of experience that allows for the inference of an appropriate response,

Abbreviations: ADHD, Attention Deficit Hyperactivity Disorder; BD, Bipolar Disorder; CDI, Child Depression Inventory; CPRS, Conner's Parent Rating Scale; DAN-VA, Diagnostic Analysis of Non-Verbal Accuracy; GAD, General Anxiety Disorder; HRO, High-Risk Offspring; HCO, Healthy Control Offspring; K-SADS-PL, Kiddie Schedule for Affective Disorders present and lifetime; MASC, Multidimensional Anxiety Scale for Children; MDD, Major Depressive Disorder; PAHRO, Partially-Affected High-Risk Offspring; SCID, Structured Clinical Interview for DSM-IV; UAHRO, Unaffected High-Risk Offspring; WASI, Wechsler Abbreviated Scale for Intelligence

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cognitive flexibility to shift between attentional demands, and an ability to monitor and regulate ones own intrinsic emotional state. Individuals with BD have been observed to have impairments in social cognition in one or more these aspects (Delvecchio et al., 2012; Ferrier et al., 1999; Malhi et al., 2005; Martínez-Arán et al., 2004; Murphy et al., 1999, 2001; Samamé et al., 2012; Summers et al., 2006; Townsend and Altshuler, 2012; van Gorp et al., 1998; Van Rheenen and Rossell, 2013). Individuals diagnosed with BD report having trouble initiating and maintaining interpersonal relationships, and difficulty coping in social situations. Social cognitive impairments have also been observed to worsen with increased illness burden and increased number of mood episodes (Judd et al., 2005; Morriss et al., 2007; Robinson and Nicol Ferrier, 2006; Scott et al., 2000).

An integral part of successful psychosocial functioning is the perception of social cues, and/or in its most basic form, the accurate identification of emotion. Most consistently, adults with BD

have shown deficits in emotion face labeling irrespective of mood state (Getz et al., 2003; Kohler et al., 2011; Lembke and Ketter, 2002; Samamé et al., 2012). Children diagnosed with BD have also shown deficits in social cognition, suggesting these impairments are not just a consequence of illness burden, but rather precede or exist at the onset of the disorder. Children diagnosed with BD have been observed to perform worse on emotional face labeling tasks, as compared to matched healthy controls (Brotman et al., 2008a, 2010; Guyer et al., 2007; McClure et al., 2003, 2005; Rich et al., 2008a, 2008b, 2006; Schenkel et al., 2007; Wegbreit et al., 2015).

Children of parents diagnosed with BD are at much greater risk of developing BD, as well as a variety of other psychiatric disorders (Birmaher et al., 2010, 2009; Chang et al., 2000; Dean et al., 2010; Henin et al., 2005; Hillegers et al., 2005; Nurnberger et al., 2011). For this reason, these children have been termed high-risk offspring (HRO). Additionally, those offspring who develop childhood anxiety, ADHD or unipolar depression appear to be at the highest risk for developing a diagnosis of BD later in life (Brückl et al., 2007; Chang et al., 2006; Johnson et al., 2000). However, of the few studies that have investigated emotion labeling deficits in HRO populations, either purely asymptomatic (Ladouceur et al., 2013) or combined symptomatic (often anxiety and/or ADHD) offspring samples were recruited (Brotman et al., 2008a, 2008b; Olsavsky et al., 2012; Roberts et al., 2013; Whitney et al., 2013). In these previous studies, HRO were reported to be less accurate in overall emotional face labeling (Brotman et al., 2008a) and required greater intensity of emotion to accurately identify emotional face stimuli compared to healthy peers (Brotman et al., 2008b). While Olsavsky and colleagues found comparable subjective fear ratings to happy and fearful faces, both the unaffected HRO and a BD group showed right amygdala hyperactivity during this rating compared to a healthy control group (Olsavsky et al., 2012). Similarly, Ladouceur and colleagues found no significant differences in accuracy or reaction times, they did find increased recruitment of prefrontal emotion processing regions to emotional face distracters in an unaffected HRO group during an affective working memory task (Ladouceur et al., 2013). Whitney et al. was the first to report on an entirely symptomatic HRO sample (requiring past or present mood symptoms) and found no significant group differences in total error scores in HRO on the DANVA task (Whitney et al., 2013). The authors suggested this may be due to psychopathology or that their healthy control population had higher error rates than previous reports in children of the same age (Whitney et al., 2013). Finally a study done by Roberts et al. reported increased accuracy for fearful face stimuli in a predominately asymptomatic HRO group during an affective go/no-go task (Roberts et al., 2013). They also found a lack of recruitment of prefrontal emotion processing regions, namely the inferior frontal gyrus, while trying to inhibit response to fearful faces in the HRO group compared to a healthy control group (Roberts et al., 2013). These studies and others provide evidence that emotion labeling impairments may precede the onset of psychopathology, and may gradually worsen over time, particularly with the development of symptoms (Bella et al., 2011; Reichart et al., 2007). Future studies should aim to clarify the contribution of psychopathology to the presence of these deficits.

The Diagnostic Analysis of Non-Verbal Accuracy (DANVA) (Nowicki and Duke, 1989) task is a well validated, computerized, emotion labeling task that has recently been highlighted as an accurate measure of social and emotional skills in youth (Humphrey et al., 2011; Nowicki and Carton, 1993; Nowicki and Duke, 1994; Pitterman and Nowicki, 2004). The task was designed to measure a child's ability to accurately identify basic emotions (happiness, sadness, anger and fear) under more normative social conditions (Nowicki and Duke, 1989, 1994). That is, unlike other standardized face labeling paradigms, such as those based on the

Ekman faces (Ekman and Friesen, 1977), the DANVA includes information such as hair, clothing and environment within each stimulus, thereby better representing social conditions (Nowicki and Duke, 1994). Error patterns on the DANVA have been shown to distinguish at-risk bipolar (Brotman et al., 2008a) and depressed (Jacobs et al., 2011) offspring from healthy controls, as well as across childhood psychopathologies (Cadesky et al., 2000; Easter et al., 2005; Guyer et al., 2007). More specifically, Cadesky and colleagues distinguished children diagnosed with conduct problems as being more likely to misinterpret emotions as angry compared to ADHD and healthy children (Cadesky et al., 2000). Guyer and colleagues reported increased emotion labeling errors in children diagnosed with BD compared to a variety of other childhood diagnoses including anxiety, depression, ADHD and conduct disorder (Guyer et al., 2007).

Altogether, emotion-labeling deficits have been found in both BD patients and those at-risk for BD, making it a candidate endophenotype for BD (previously reviewed by Brotman et al., 2008a, 2008b; Olsavsky et al., 2012). While previous work has shown these deficits to occur in at-risk individuals, these findings have not been well validated and it remains unclear how the contribution of risk or developmental psychopathology impact these deficits. In the present study, we investigated the contribution of risk and the development of psychopathology on emotion labeling deficits in HRO. We did this by recruiting high-risk bipolar offspring, with and without psychiatric symptoms, and asked them to perform the DANVA assessment tool in order to assess their emotion-labeling abilities. Specifically, we examined error patterns related to total scores, emotion type and intensity of emotion expression in order to identify error patterns that may differentiate symptomatic and asymptomatic high-risk offspring. We predicted that (1) we would validate previous findings of increased total number of errors in HRO populations compared to healthy control offspring (HCO), and (2) that error scores would differentiate HRO based on the presence or absence of psychiatric symptoms.

2. Methods

2.1. Participants

Subjects included high-risk bipolar offspring (HRO, $n=30$), and age- and sex-matched healthy offspring of healthy parents (HCO, $n=20$) (see Table 1. for demographic and clinical information). All children were between 8–16 years of age. This study was approved by the Hamilton Integrated Research Ethics Board. Parents and their children gave written consent and assent, respectively. For this study, HRO were defined as having at least one biological parent diagnosed with BD (type I or II). These offspring were not excluded for having a diagnosis or meeting subthreshold criteria for psychiatric conditions including depression, anxiety and/or ADHD. This information was used to further separate the HRO group into partially symptomatic ($n=18$) or asymptomatic ($n=12$). HRO were excluded if they met criteria for BD any type. HCO were defined as being free of any psychiatric symptoms, as well as no family history of any psychiatric illness in any first-degree relatives. Exclusion criteria for all participants included the presence of any pervasive developmental disorders, autism spectrum disorder, schizophrenia, any current substance use disorder, any neurological condition, or an IQ less than 70.

2.2. Psychological assessments

The Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime version (K-SADS-PL) (Kaufman et al., 1997)

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