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Difficulties in emotional regulation and substance use disorders: A controlled family study of bipolar adolescents

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ABSTRACT

Background: Self-regulatory mechanisms appear etiologically operant in the context of both substance use disorders (SUD) and bipolar disorder (BD), however, little is known about the role of deficits in emotional self-regulation (DESR) as it relates to SUD in context to mood dysregulation. To this end, we examined to what extent DESR was associated with SUD in a high-risk sample of adolescents with and without BD.
Methods: 203 families were assessed with a structured psychiatric interview. Using the Child Behavior Checklist (CBCL), a subject was considered to have DESR when he or she had an average elevation of 1 standard deviation (SD) above the norm on 3 clinical scale T scores (attention, aggression, and anxiety/depression; scores: $60 \times 3 \geq 180$).
Results: Among probands and siblings with CBCL data ($N = 303$), subjects with DESR were more likely to have any SUD, alcohol use disorder, drug use disorder, and cigarette smoking compared to subjects with scores <180 (all p values <0.001), even when correcting for BD. We found no significant differences in the risk of any SUD and cigarette smoking between those with 1SD and 2SD above the mean (all p values >0.05). Subjects with cigarette smoking and SUD had more DESR compared to those without these disorders.
Conclusions: Adolescents with DESR are more likely to smoke cigarettes and have SUD. More work is needed to explore DESR in longitudinal samples.

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1. Introduction

Pediatric-onset bipolar disorder (BD) is thought to occur in approximately 3% of youth (Merikangas et al., 2010) and is associated with substantial impairment and comorbidity (Axelson et al., 2006; Biederman et al., 2005; Carlson et al., 2000; Findling et al., 2001; Geller et al., 2002; Kowatch et al., 2005; McClellan et al., 2007; Wilens et al., 2008). An emerging literature suggests that pediatric-onset BD may be a particularly high risk group for cigarette smoking and SUD (Biederman et al., 1997; Carlson et al., 2000; Delbello et al., 2007; Geller et al., 2008; Goldstein et al., 2008a, b; West et al., 1996; Wilens et al., 1997, 2008; Wills et al., 1995; Young et al., 1995). An excess of SUD has been reported in adolescents with BD or prominent mood lability (Biederman et al., 1997; Carlson et al., 2000; Delbello et al., 2007; Geller et al., 2008; Goldstein et al., 2008a, 2008b; West et al., 1996; Wilens et al., 1997, 2008; Wills et al., 1995; Young et al., 1995). For example, we previously reported that 34% of BD adolescents at a mean age of 14 years already met criteria for SUD compared to 4% of similarly aged control youth (OR = 2.8, $p < 0.004$) and that this association was not accounted for by comorbid conduct disorder (Wilens et al., 2008, 2009). Conversely, BD has also been reported to be over-represented in youth with SUD (Biederman et al., 1997; Weinberg and Glantz, 1999; West et al., 1996; Wilens et al., 1997; Wills et al., 1995; Young et al., 1995). Hence, a bidirectional relationship between pediatric BD and cigarette smoking/SUD exists although the mechanism(s) linking this association remain unclear.

Self-regulatory mechanisms may be an important factor within the context of SUD and youth with BD (Lorberg et al., 2010). One dimensional domain critical in the study of psychopathology and SUD is deficits in emotional self-regulation (DESR). While a myriad of definitions exist for DESR, what appears to be common among them is DESR being defined by affect, emotional lability, reactivity, irritability and lack of self-regulation of such emotions (Althoff et al., 2010a,b; Cheetham et al., 2010). One useful measure of DESR in children is the Child Behavior Checklist (CBCL), one of the most commonly used measures of child psychopathology (Achenbach, 1991). Our group and others have identified a

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unique continuous profile within the empirically derived CBCL consisting of elevated scores (at least 1 standard deviation [SD] above the norm: $60 \times 3 \geq 180$ combined) on three clinical scales: anxiety/depression, attention, and aggression (AAA; Althoff et al., 2010a,b; Biederman et al., 2012). A profile of >2SD elevation in these clinical scales has been referred to as the "Dysregulation Profile" (Althoff et al., 2010a) and is synonymous with more severe DESR.

DESR correlates with psychopathology including disruptive, mood, and anxiety disorders; children with DESR have been found to be at risk for suicidal behavior and psychiatric hospitalization (Althoff et al., 2010a; Biederman et al., 1995; Gratz and Roemer, 2004; Reimherr et al., 2005). DESR has also been purported to be important in pediatric BD (Biederman et al., 1995; Gratz and Roemer, 2004), although DESR is nonspecific to mood disorders. For instance, DESR has been associated variably with attention deficit/hyperactivity disorder (ADHD), conduct and oppositional defiant disorders (Barkley et al., 2008), all of which are frequently comorbid with BD (Wilens et al., 2008). Adults with DESR manifest a lower quality of life, worse social adjustment, elevated traffic accidents and criminality (Surman et al., 2010).

Recent work has also highlighted the role of DESR in cigarette smoking and SUD (Aguilar de Arcos et al., 2008; Cheetham et al., 2010; Dorard et al., 2008; Gonzalez et al., 2008). For instance, Gonzalez et al. (2008) showed DESR to be related to an enhanced motivation to smoke and greater perceived barriers to quitting. DESR has also been shown to be related to the motivation for, and regular use of marijuana (Bonn-Miller et al., 2008; Dorard et al., 2008). Similarly, more DESR has been shown in current opioid abusers (Aguilar de Arcos et al., 2008), present even while patients are in remission. This calls in to question whether DESR represents a stable trait of the patient that may then be subsequently related to the development of SUD. Interestingly, an analysis of 325 at risk infants followed for 19 years showed that a CBCL proxy of DESR did not predict any particular psychiatric disorder, but was associated with SUD, suicidality and poorer overall functioning (Holtmann et al., 2011). Despite these studies, relatively little is known about the relationship of DESR as it relates to SUD in high-risk samples of adolescents with severe affective illness.

Since DESR represents an indicator of very high affective reactivity that is variably related to BD (Althoff et al., 2010a; Biederman et al., 1995; Gratz and Roemer, 2004; Holtmann et al., 2011), it may represent an important dimensional construct that may also be related to a higher risk or earlier-onset of SUD. Given that DESR is measurable from an early age through the use of questionnaires like the CBCL, it may be possible to identify specific youth who, by nature of the DESR, may be at high risk to develop SUD. Such identification has important clinical and scientific implications. Clinically, the identification of specific youth at very high risk for SUD by nature of DESR is critical for prevention of SUD particularly given that psychosocial and pharmacological interventions exist for DESR. Scientifically, the examination of neurocircuitry related to DESR (Leibenluft et al., 2003, 2007) may further our understanding of the etiologies of SUD.

To this end, we used the CBCL to examine DESR in a high-risk sample of BD youth, non-mood disordered controls, and their siblings. We hypothesized that high levels of DESR would be associated with a higher risk for cigarette smoking and SUD. Secondarily, we hypothesized that DESR severity would be associated with the risk for cigarette smoking and SUD: the group with a combined CBCL – AAA score of 1SD above the mean would be associated with a higher risk for SUD than those without DESR, but with a lower risk than those with scores of 2SD above the mean.

2. Materials and methods

The current analyses are based on baseline assessments of our ongoing, case-controlled longitudinal family study of BD adolescents (our sample was evenly split between BPD I and II (51 and 49%, respectively; Wilens et al., 2008). The methods of the study are described in full detail elsewhere (Wilens et al., 2008). Briefly, female and male subjects aged range 10–18 years with BD and without a mood disorder and their first-degree relatives were ascertained from both community and clinical sources. We excluded any youth with major sensorimotor handicaps (paralysis, deafness, blindness), autism, inadequate command of the English language, or a Full Scale IQ less than 70. We excluded controls with any mood disorder including dysthymia or unipolar depression secondary to concerns of "manic switching" from dysthymia or unipolar depression to BD (Strober and Carlson, 1982). Due to the family nature of this study, potential subjects were also excluded if they had been adopted, or if their nuclear family was not available for study. Parents provided written informed consent for their children and children provided written assent to participate. The institutional review board at Massachusetts General Hospital approved this study and a federal certificate of confidentiality was obtained.

A two-stage ascertainment procedure selected subjects. For BD probands, the first stage confirmed the diagnosis of BD by screening all children using a telephone questionnaire with their primary caregiver. The second stage was the structured psychiatric interview as described below. Only subjects who received a positive diagnosis at both stages were included in the sample. We also screened potential non-mood disordered controls in two stages. First, control mothers responded to the telephone questionnaire, then eligible controls meeting study entry criteria were recruited for the study and received the diagnostic assessment with a structured interview. Only subjects classified as not having any mood disorder at both stages were included in the control group. All BD and control probands were assessed using structured psychiatric interviews for the full presence of DSM-IV BD or for the absence of any mood disorder (controls).

2.1. Assessments

All assessments for psychiatric and substance use disorders used DSM-IV-based structured interviews given by raters with bachelor's or master's degrees in psychology who had been extensively trained and supervised by the senior investigators. Raters were blind to the ascertainment status of the probands. Assessments for subjects under 18 years of age relied on the DSM-IV Kiddie Schedule for Affective Disorders-Epidemiologic Version (KSADS-E; Ambrosini, 2000) and for subjects 18 years and older relied on the Structured Clinical Interview for DSM-IV (SCID; First et al., 1997) Interview structure included independent interviews with mothers and direct interviews with probands and controls.

SUD and cigarette smoking were diagnosed on the basis of DSM-IV criteria using the KSADS-E and SCID. To meet a positive diagnosis of cigarette smoking, subjects under 18 needed to endorse any amount of smoking daily, whereas subjects over 18 needed to endorse smoking at least a pack of cigarettes per day. If either parent endorsed full criteria for a psychiatric disorder or SUD during his/her SCID, then the family history of the proband was considered positive.

All cases were presented to a committee composed of board certified child psychiatrists and licensed psychologists. Diagnoses presented for review were considered positive only if the diagnosis would be considered clinically meaningful due to the nature of the symptoms, the associated impairment, and the coherence of the clinical picture. Discrepant reports were reconciled using the

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