

Temperament and Behavior in Toddlers of Mothers with Bipolar Disorder: A Preliminary Investigation of a Population at High Familial Risk for Psychopathology

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Abstract

Objective: There are no published studies examining concurrent associations between temperament and behavior during toddlerhood in offspring of parents with bipolar disorder (OBD), a population at high familial risk for psychopathology. Better understanding of early determinants contributing to well-being or mental illness in this high-risk population has the potential to aid in the identification of problem domains to be targeted clinically, and facilitate the development of early intervention and prevention initiatives for an appropriate subgroup of children at the youngest possible age.

Methods: A total of 30 offspring of mothers with BD (mean age = 25.4 ± 4.9 months) participated in this study at Emory University. The mothers completed the Early Childhood Behavior Questionnaire (ECBQ) and the Child Behavior Checklist (CBCL).

Results: The results of the correlational analyses indicated that the broad temperament dimension Negative Affectivity and the individual ECBQ scales Sadness and Shyness were positively associated with the broad CBCL dimension Internalizing Problems, whereas Sociability was negatively associated with Internalizing Problems. In addition, the temperament scales Soothability and Frustration were negatively and positively associated with Internalizing Problems, respectively. All ECBQ scales included in the broad temperament dimension Effortful Control, except for Cuddliness, were significantly negatively associated with the broad CBCL dimension Externalizing Problems. A significant sex difference was found for the ECBQ scale Positive Anticipation and the CBCL scale Sleep Problems, with a higher mean rank score for girls than for boys.

Conclusions: This is the first systematic investigation of temperament and behavior and concurrent associations between these two domains in toddlers of mothers with BD. The present findings provide a platform for future investigations of the contribution of temperament and early behavior to potential well-being or mental illness in OBD.

Introduction

THE IDENTIFICATION OF EARLY DETERMINANTS contributing to well-being or mental illness in young children at familial risk for psychopathology is a high priority research domain. Better understanding of predictive factors and precursors of future psychopathology in this vulnerable population has the potential to contribute to the early identification of children at greatest risk, and facilitate the development and delivery of targeted, novel, and preventive interventions for an appropriate subgroup of children at the youngest possible age. This line of work can also identify problem domains to be targeted clinically in early interventions,

and promote resilience and reduce risk by “reprogramming” adaptive systems that have been derailed from the course of normal development. In this context, the examination of temperament and behavior in toddlers of mothers with bipolar disorder (BD) represents an important area of investigation.

Numerous approaches have been employed in the conceptualization of temperament. In the present study, Rothbart’s theoretical model provided a framework for the examination of the relationship between temperament and behavior from a reactivity-regulation perspective. In this model, temperament is defined as biologically based individual differences in emotional, motor, and attentional reactivity, as measured by the latency, intensity, and recovery of

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Funding: This research was supported in part by National Institute of Mental Health (NIMH) Mentored Patient-Oriented Research Career Development Award K23MH096042-03 (D.I.S.).

response, and self-regulation (Rothbart and Derryberry 1981). Very few studies have investigated temperament in young offspring of parents with BD (OBD).

One study reported that OBD (6–18 years of age; $n=53$) have decreased levels of energy and motor activity, and increased approach behavior and regularity of sleeping pattern compared to population means (Chang et al. 2003). The same study indicated that compared with healthy OBD, children with psychiatric disorders in the cohort demonstrated decreased flexibility, decreased ability to persevere in tasks without distractions, and less positive affect. Another study indicated that compared with healthy controls, OBD (8–18 years of age; $n=31$) had increased activity level and decreased task orientation (Singh et al. 2008). Also, in this investigation, compared with OBD without mood disorders, OBD with mood disorders showed a decrease in the following characteristics: novelty seeking, flexibility to adapt to new situations, ability to follow the same sleeping pattern, and ability to persevere on tasks. Furthermore, a study of OBD with psychopathology compared with OBD without psychopathology and healthy controls reported a positive association between: 1) emotionality and lifetime psychopathology, and 2) emotionality and increased risk for a psychiatric illness in general, and a mood disorder in particular (Duffy et al. 2007). This study sample had a wide age range (8–25 years of age; $n=75$) and was not limited to child offspring of parents with BD. Another study found that high emotionality significantly increased the risk of psychopathology and mood disorders in OBD (mean age = 21.6/no age range reported; $n=221$) (Doucette et al. 2013). A single investigation has focused on temperament in very young OBD (2–6 years of age; $n=34$) by examining laboratory-observed behavioral disinhibition, which represents an extreme tendency to seek out novelty, approach unfamiliar stimuli, and display disinhibition of speech and action in unfamiliar settings (Hirshfeld-Becker et al. 2006). The findings indicated significantly higher levels of behavioral disinhibition in OBD than in offspring of parents with other psychiatric illnesses; these results support the hypothesis that behavioral disinhibition might represent an early marker of risk for BD.

It has been well documented that temperament in early childhood is a precursor to later behavioral problems and psychopathology. Dimensions associated with “difficult temperament” (e.g., emotionality, adaptability, approach/withdrawal, impulsivity) predict both internalizing and externalizing problems. For example, activity level predicts externalizing problems (Teglasi and MacMahon 1990) and shyness and fearfulness predict internalizing problems (Goldsmith and Lemery 2000). In addition, some studies in BD have focused on the relationship between temperament and psychopathology, and provided evidence that temperament may be predictive of later psychopathology (McKinnon et al. 2013). Also, a pilot investigation of concurrent associations between temperament and behavior in OBD with and at high risk for developing BD indicated that this might be a promising research approach, with the goal of identifying problem domains to be targeted clinically in early interventions and children at greatest risk (Simeonova et al. 2005).

There are no published studies examining associations between temperament and behavior during toddlerhood in OBD. The present study aims to investigate this relationship. Early childhood is an important developmental period, because significant neurobiological and social-emotional maturational processes take place. If temperament and behavioral problems are significantly associated in toddlerhood, the period before 36 months of age may provide an important opportunity for preventive efforts in

OBD. The older the child, the more likely it is that temperament will be obscured by overlap with newly emergent behaviors (e.g., onset of symptoms, behavioral problems, and psychopathology). Examining the premorbid relationship between temperament and behavior as early as possible in development provides a research strategy with potential direct clinical relevance. The early identification of temperament traits that may serve as protective factors or risk markers for later BD and their behavioral correlates has significant implications for identification of children at greatest risk, early intervention, and prevention of psychopathology in this high-risk population.

The purpose of this investigation is to characterize temperament and behavior in toddlers of mothers with BD, and to examine concurrent associations between temperament and behavior in this population. The Early Childhood Behavior Questionnaire (ECBQ) (Putnam et al. 2006) was used to assess temperament and the Child Behavior Checklist (CBCL) (Achenbach and Rescorla 2000) was used to assess behavioral problems. Based on previous research, it was hypothesized that the temperament dimensions Negative Affectivity, Sadness, and Shyness would be positively associated with Internalizing Problems, whereas Sociability would be negatively associated with Internalizing Problems. Also, Effortful Control, Inhibitory Control, Attention Shifting, and Attention Focusing would be negatively associated with Externalizing Problems. Because clinicians and researchers are often expected to evaluate and link children’s problems to diagnostic categories to facilitate clinical care, a secondary purpose of the present study is to examine the relationship between temperament and DSM-oriented diagnostic categories. It was predicted that Effortful Control and Inhibitory Control would be negatively associated with the CBCL DSM-oriented scales Attention Deficit/Hyperactivity Problems (ADHP) and Oppositional Defiant Problems (ODP), and that Attention Shifting and Attention Focusing would be negatively associated with the CBCL DSM-oriented scale ADHP. Moreover, given research evidence of sex differences in temperament and behavior (Olino et al. 2013), this study also aims to explore offspring sex as a variable of interest.

Methods

Participants

Young children of women participating in a longitudinal study of the perinatal course of BD at the Emory Women’s Mental Health Program (WMHP) were screened for study participation. Inclusion criteria were: 1) Maternal lifetime diagnosis of bipolar I or II disorder as determined by the Structured Clinical Interview for Axis I DSM-IV Disorders (SCID-I) (First et al. 2002); and 2) maternal completion of the ECBQ and the CBCL. Exclusion criteria were: 1) Active substance use disorder within the past 6 months; 2) positive urine drug screen; and 3) primary maternal lifetime diagnosis of schizophrenia or other psychotic disorders. The Emory University Institutional Review Board approved this study, and the mothers provided written informed consent. Mothers concurrently completed the ECBQ and CBCL measures about their child.

Measures

The ECBQ was used to assess temperament according to maternal report. This parent-report measure consists of 201 items evaluating 18 domains of temperament in children between the ages of 18 and 36 months. Parents are asked to rate the frequency

of temperament-related domains observed over the previous 2 weeks on a scale from 1 (never) to 7 (always). Factor analysis revealed a three factor structure of the ECBQ: Negative Affectivity including eight scales (Discomfort, Fear, Motor Activation, Sadness, Perceptual Sensitivity, Shyness, Soothability, and Frustration), Surgency-Extraversion including five scales (Impulsivity, Activity Level, High-intensity Pleasure, Sociability, and Positive Anticipation), and Effortful Control including five scales (Inhibitory Control, Attention Shifting, Low-intensity Pleasure, Cuddliness, and Attention Focusing). Detailed description of the dimensions of temperament contained in the ECBQ is presented in Table 1.

The parent-report CBCL for ages 1.5–5 years was used to assess behavioral problems of toddlers. The measure includes 99 behavioral/emotional problem items rated as 0 (not true), 1 (somewhat or sometimes true), or 2 (very or often true). The CBCL scales contained in the measure are: Emotionally Reactive, Anxious/Depressed, Somatic Complaints, Withdrawn/Depressed, Sleep Problems, Attention Problems, and Aggressive Behavior. The CBCL also consists of two broadband dimensions, Internalizing Problems (Emotionally Reactive, Anxious/Depressed, Somatic Complaints, and Withdrawn/Depressed) and Externalizing Problems (Attention Problems and Aggressive Behavior), and a Total Problems score. In addition, the CBCL yields five DSM-oriented scales (Affective Problems, Anxiety Problems, Pervasive Developmental Problems, Attention Deficit/Hyperactivity Problems, and Oppositional Defiant Problems). The cutpoint for the normal range for the seven syndrome scales and the five DSM-oriented scales is a *T* score < 65, borderline is from 65 to 69, and the clinical range is ≥ 70. For Internalizing, Externalizing, and Total Problems, the cutpoint for the normal range is a *T* score < 60, borderline is from 60 to 63, and the clinical range is ≥ 64.

Data analysis

Distributions were examined and indicated that the data were not normally distributed. Therefore, associations between temperament and behavior were tested with the Spearman’s ρ correlation coefficient. The Mann–Whitney *U* test was performed to test for sex differences in temperament and behavior between girls and boys. Given the preliminary nature of the study and that a specific set of hypothesized associations was examined, an adjustment for multiple comparisons was deemed highly conservative and was not conducted. The statistical significance for all tests was set at $p \leq 0.05$. All analyses were performed using SPSS Version 17.0.

Results

A total of 38 mother–toddler dyads were approached, and 30 were eligible for study participation. Concurrent ECBQ and CBCL data were completed for 30 offspring of mothers with bipolar I ($n = 24$) or II ($n = 6$) disorder, ranging in age from 18 to 36 months. One offspring was included from each mother. The sample consisted of 16 boys and 14 girls, with mean age 25.4 ± 4.9 months at the time of the assessment. The majority (90%) of the toddlers were Caucasian, the median maternal educational level was college graduate, mean maternal age was 33.7 ± 4.6 years, and 94% of the mothers were married or cohabiting at the time of the study.

The means, standard deviations, range for ECBQ and CBCL scores, and frequency of cases with CBCL scores in normal, borderline, and clinical ranges for toddlers of mothers with BD are presented in Table 2.

Temperament scores, as determined by the three broad factors of the ECBQ measure, ranged from a score of 1.77 to a score of 5.78. The mean scores were 2.89, 4.23, and 4.52 for Negative Affectivity, Surgency-Extraversion, and Effortful Control, respectively.

TABLE 1. DESCRIPTION OF DIMENSIONS OF TEMPERAMENT CONTAINED IN THE ECBQ MEASURE

<i>Dimensions of temperament</i>	<i>Definition</i>
Negative Affectivity	Tendency to react to stimuli with discomfort, fear, anger/frustration, and/or sadness, and difficult to soothe
Discomfort	Amount of negative affect related to sensory qualities of stimulation
Fear	Negative affect related to anticipated distress and/or potentially threatening situations
Motor Activation	Repetitive small-motor movements and fidgeting
Sadness	Tearfulness or lowered mood related to personal suffering, or response to other’s suffering
Perceptual Sensitivity	Detection of slight, low-intensity stimuli from the external environment
Shyness	Slow or inhibited approach and/or discomfort in social situations involving novelty or uncertainty
Soothability	Rate of recovery from peak distress, excitement, or general arousal
Frustration	Negative affect related to interruption of ongoing tasks or goal blocking
Surgency-Extraversion	Temperament dimension characterized by high activity level, high-intensity pleasure seeking, impulsivity, low shyness
Impulsivity	Speed of response initiation
Activity Level	Rate and intensity of gross motor activity, including rate and extent of locomotion
High-intensity Pleasure	Pleasure related to situations involving high stimulus intensity, rate, complexity, novelty, and incongruity
Sociability	Seeking and taking pleasure in interactions with others
Positive Anticipation	Excitement about expected pleasurable activities
Effortful Control	Ability to effectively inhibit behavioral responses and mobilize attentional resources to regulate behavior and emotions
Inhibitory Control	The capacity to stop, moderate, or refrain from a behavior under instruction
Attention Shifting	The ability to transfer attentional focus from one activity/task to another
Low-intensity Pleasure	Pleasure related to situations involving low stimulus intensity, rate, complexity, novelty, and incongruity
Cuddliness	Child’s expression of enjoyment in and molding of the body to being held by a caregiver
Attention Focusing	Sustained duration of orienting on an object of attention and resisting distraction

ECBQ, Early Childhood Behavior Questionnaire.

TABLE 2. MEAN SCORES, STANDARD DEVIATIONS, RANGE FOR ECBQ AND CBCL SCORES, AND FREQUENCIES OF CASES IN NORMAL, BORDERLINE, AND CLINICAL RANGE FOR CBCL SCORES FOR TODDLERS OF MOTHERS WITH BIPOLAR DISORDER

	Mean	SD	Range	Normal Range	Borderline Range	Clinical Range
<i>ECBQ Scales</i>						
Negative Affectivity	2.89	0.56	1.77–4.33			
Discomfort	1.79	0.77	0.70–4.20			
Fear	2.22	0.97	1–4.45			
Motor Activation	1.46	0.35	1–2.09			
Sadness	2.38	0.98	0.92–4.25			
Perceptual Sensitivity	3.46	1.04	1.50–5.75			
Shyness	3.12	1.22	0.83–5.25			
Soothability	5.61	0.66	3.70–6.90			
Frustration	3.28	0.97	1.67–5.17			
Surgency-Extraversion	4.23	0.57	3.03–5.26			
Impulsivity	4.50	0.92	1.80–6.10			
Activity Level	4.25	0.79	2.42–5.92			
High-intensity Pleasure	3.71	0.88	2.17–5.42			
Sociability	4.83	1.29	1.75–7.00			
Positive Anticipation	3.84	1.24	1.82–6.00			
Effortful Control	4.52	0.57	3.52–5.78			
Inhibitory Control	3.88	1.09	1.75–5.92			
Attention Shifting	4.53	0.77	2.58–6.42			
Low-intensity Pleasure	4.79	0.82	3.18–6.64			
Cuddliness	4.99	0.83	2.75–6.25			
Attention Focusing	4.39	0.78	3.08–5.75			
<i>CBCL Scales</i>						
Internalizing Problems	45.47	9.37	29–63	28	2	–
Emotionally Reactive	52.77	4.07	50–67	29	1	–
Anxious/Depressed	52.00	3.56	50–63	30	–	–
Somatic Complaints	52.77	4.17	50–62	30	–	–
Withdrawn/Depressed	51.93	2.91	50–60	30	–	–
Externalizing Problems	46.23	7.66	28–60	29	1	–
Attention Problems	52.10	3.82	50–62	30	–	–
Aggressive Behavior	51.70	2.87	50–63	30	–	–
Sleep Problems	54.33	5.57	50–70	29	–	1
Total Problems	45.40	8.32	28–59	30	–	–
DSM – Affective Problems	52.20	2.85	50–60	30	–	–
DSM – Anxiety Problems	52.20	4.97	50–70	28	1	1
DSM – Pervasive Developmental Problems	52.70	4.26	50–68	29	1	–
DSM – Attention Deficit/Hyperactivity Problems	52.36	3.53	50–60	30	–	–
DSM – Oppositional Defiant Problems	52.90	4.26	50–67	29	1	–

ECBQ, Early Childhood Behavior Questionnaire; CBCL, Child Behavior Checklist; DSM, *Diagnostic and Statistical Manual of Mental Disorders*.

The behavioral profile for the study sample of toddlers, as assessed by CBCL individual and composite scales, and CBCL DSM-oriented scales, was characterized by one case within the clinical range for Sleep Problems (mean = 54.33, SD = 5.57), and three cases within the borderline range for Internalizing Problems (mean = 45.47, SD = 9.37) and Externalizing Problems (mean = 46.23, SD = 7.66) (see Table 2). Also, three cases fell within the borderline range for the DSM-oriented scales Anxiety Problems (mean = 52.20, SD = 4.97), Pervasive Developmental Problems (mean = 52.70, SD = 4.26), and Oppositional Defiant Problems (mean = 52.90, SD = 4.26), and one case fell within the clinical range for the scale Anxiety Problems. 100% of cases, however, fell within the normal range for parent-reported Total Problems (mean = 45.40, SD = 8.32).

The results of the correlational analyses between ECBQ and CBCL scores are presented in Table 3. Consistent with the hy-

potheses, the broad temperament dimension Negative Affectivity and the individual ECBQ scales Sadness and Shyness were positively associated with Internalizing Problems, whereas Sociability was negatively associated with Internalizing Problems. In addition, the temperament scales Soothability and Frustration were negatively and positively associated with Internalizing Problems, respectively. All ECBQ scales included in the broad dimension Effortful Control, except for Cuddliness, were significantly negatively associated with Externalizing Problems. As predicted, the correlational analyses confirmed a negative association between Inhibitory Control and the DSM-oriented scales ADHP and ODP, and between Attention Focusing and ADHP. In addition, a number of individual ECBQ scales were significantly correlated with CBCL individual and DSM-oriented scales (see Table 3).

The Mann-Whitney *U* test showed that there was a statistically significant sex difference for the ECBQ scale Positive Anticipation,

TABLE 3. CORRELATIONS BETWEEN ECBQ AND CBCL SCORES FOR TODDLERS OF MOTHERS WITH BIPOLAR DISORDER

	ER	A/D	SC	W/D	AP	AB	SP	IP	EP	TP	D-AP	D-ANP	D-PDP	D-ADHP	D-ODP
Negative Affectivity	0.35	0.41*	0.32	0.51*	-0.15	0.15	0.29	0.42*	0.04	0.34	0.29	0.30	0.61**	-0.16	0.28
Discomfort	0.25	0.10	0.32	0.28	-0.25	-0.08	0.10	0.22	-0.15	0.11	-0.05	0.14	0.38*	-0.26	0.12
Fear	0.34	0.17	0.22	0.46**	-0.28	0.02	0.05	0.24	-0.15	0.12	0.12	-0.02	0.51**	-0.25	0.18
Motor Activation	0.27	0.07	0.34	0.28	0.22	0.24	0.18	0.29	0.18	0.23	-0.06	0.05	0.27	0.34	-0.01
Sadness	0.16	0.52**	0.35	0.29	0.14	0.08	0.28	0.40*	0.03	0.28	0.21	0.24	0.33	0.14	-0.07
Perceptual Sensitivity	0.20	0.01	0.06	0.14	-0.30	-0.12	0.17	0.08	-0.21	-0.01	-0.06	0.19	0.25	-0.37*	0.12
Shyness	0.32	0.47*	0.29	0.47**	-0.14	0.28	0.30	0.44*	0.19	0.43*	0.42*	0.39*	0.51**	-0.08	0.39*
Soothability	-0.49**	-0.29	-0.35	-0.23	-0.16	-0.31	-0.25	-0.51**	-0.31	-0.45*	-0.22	-0.35	-0.32	-0.12	-0.40*
Frustration	0.47**	0.54**	0.31	0.32	0.11	0.37*	0.49**	0.57**	0.30	0.54**	0.45*	0.51**	0.53**	0.01	0.42*
Surgency-Extraversion	-0.13	-0.25	0.05	0.03	0.03	-0.17	0.16	-0.23	-0.07	-0.13	-0.36	-0.10	-0.10	0.04	0.06
Impulsivity	-0.19	-0.27	0.08	-0.29	0.24	-0.06	0.04	-0.21	0.09	-0.16	-0.22	-0.18	-0.46*	0.30	-0.15
Activity Level	0.29	-0.06	0.15	0.26	0.20	0.24	0.13	0.26	0.34	0.29	-0.06	0.18	0.42*	0.29	0.34
High-intensity Pleasure	0.11	-0.16	0.23	0.33	-0.04	0.02	0.01	0.02	0.05	0.02	-0.25	-0.05	0.26	-0.01	0.18
Sociability	-0.52**	-0.34	-0.26	-0.21	-0.25	-0.33	-0.12	-0.55**	-0.30	-0.38*	-0.47**	-0.17	-0.34	-0.21	-0.18
Positive Anticipation	0.01	-0.05	-0.07	0.02	0.01	-0.19	0.35	-0.09	-0.17	-0.03	-0.06	-0.06	-0.09	-0.08	0.01
Effortful Control	-0.03	-0.22	-0.07	-0.09	-0.32	-0.58**	-0.21	-0.30	-0.65**	-0.46*	-0.31	-0.20	-0.06	-0.34	-0.46**
Inhibitory Control	-0.13	-0.11	0.05	-0.02	-0.32	-0.53*	-0.13	0.17	-0.60**	-0.39*	-0.10	-0.30	-0.15	-0.39*	-0.43*
Attention Shifting	0.01	-0.17	-0.24	-0.06	-0.19	-0.51*	-0.28	-0.24	-0.44*	-0.36	-0.20	-0.11	0.04	-0.34	-0.24
Low-intensity Pleasure	0.04	-0.14	0.10	0.06	-0.20	-0.34	-0.01	-0.18	-0.41*	-0.23	-0.23	-0.05	0.09	-0.16	-0.27
Cuddliness	-0.09	-0.11	-0.22	-0.19	-0.17	-0.17	0.02	-0.26	-0.21	-0.17	-0.32	0.03	-0.09	-0.06	-0.15
Attention Focusing	0.04	-0.07	-0.05	-0.22	-0.38*	-0.31	-0.29	-0.15	-0.44*	-0.33	-0.12	-0.09	-0.13	-0.42*	-0.24

* $p \leq 0.05$; ** $p \leq 0.01$.

ER, Emotionally Reactive; A/D, Anxious/Depressed; SC, Somatic Complaints; W/D, Withdrawn/Depressed; AP, Attention Problems; AB, Aggressive Behavior; SP, Sleep Problems; IP, Internalizing Problems; EP, Externalizing Problems; TP, Total Problems; D-AP, DSM-Affective Problems; D-ANP, DSM-Anxiety Problems; D-PDP, DSM-Pervasive Developmental Problems; D-ADHP, DSM-Attention Deficit/Hyperactivity Problems; D-ODP, DSM-Oppositional Defiant Problems; ECBQ, Early Childhood Behavior Questionnaire; CBCL, Child Behavior Checklist; DSM, *Diagnostic and Statistical Manual of Mental Disorders*.

$U=36.5$, $p=0.002$, and the CBCL scale Sleep Problems, $U=62.5$, $p=0.033$, with a higher mean rank score for girls than for boys. There were no other significant sex differences.

Discussion

This is the first systematic investigation of temperament and behavior and concurrent associations between these two domains in toddlers of mothers with BD, a population at high familial risk for psychopathology. The major findings are consistent with the hypotheses and with the limited number of studies focused on temperament in OBD. The correlational analyses confirmed concurrent relationships between temperament and behavior. The results are in line with prior research in children indicating concurrent and longitudinal associations between high levels of Negative Affectivity and high levels of internalizing problems, and between low levels of Effortful Control and high levels of externalizing problems (Eisenberg et al. 2005). Furthermore, the strongest correlations between temperament and behavior encompassed the ECBQ scales Frustration, Soothability, Sociability, Effortful Control, and Inhibitory Control. This, combined with the finding of seven cases of CBCL scores in the borderline range and two in the clinical range, might suggest that young OBD with these temperament traits might be at increased risk for development of behavioral problems over time and should be monitored closely. It is possible that these temperament traits might serve as potential target for early identification of emerging emotional difficulties and early intervention efforts to delay/prevent the onset and progression of mood disorders and comorbid conditions in this population. This has critical implications for clinical practice with OBD. Knowledge about temperament traits may contribute to tailoring/amending existing psychosocial interventions to meet the individual needs of the child and the family, and aid in developing novel psychosocial interventions for this population.

How can the present findings combined with research on temperament-based interventions benefit clinicians, OBD, and parents with BD more effectively parent youth to prevent the development of clinically significant psychiatric symptoms? Research indicates that child temperament interacts with parenting practices. Children with difficult temperament have worse externalizing symptoms in response to negative discipline and have fewer externalizing symptoms and aggression in response to positive parenting (Van Zeijl et al. 2007). Moreover, research evidence of a bidirectional relationship between child temperament and parenting in toddlerhood (Braungart-Rieker et al. 1997) and middle childhood (Lengua and Kovacs 2005) shows that child negative emotionality evokes inconsistent discipline, and inconsistent parenting increases child negative emotionality. Such findings can be used by clinicians to assist parents with BD to identify their parenting patterns with OBD high in negative emotionality, and teach temperament-based strategies to break the negative cycle between parent and child. Also, McClowry and colleagues (2008) outline helpful guidelines for the development and adaptation of temperament-based interventions examined through the lens of self-regulation, which could be beneficial for clinical practice with OBD.

From a developmental perspective, the present findings of concurrent significant associations between specific ECBQ scales in the broad temperament dimension Negative Affectivity and Effortful Control with internalizing and externalizing problems, respectively, appear to be a downward extension of research in pediatric BD. The results provide novel evidence for the role of negative affect and impaired attentional resources in a high-risk

population of toddlers of mothers with BD. Specifically, pediatric BD studies have shown that emotionally demanding environments, in particular those characterized by frustration (Rich et al. 2005), are a critical factor in eliciting attentional deficits and that compared with controls, BD youth were more upset by frustration-inducing conditions and exhibited greater emotional reactivity (Rich et al. 2010). Attentional performance in children with BD was impaired only in the setting of negative emotions (Rich et al. 2005). The current study is the first report in the literature to provide evidence for the importance of negative affect and attentional deficits at a much earlier developmental stage in toddlers at risk for development of mood disorders and other comorbid conditions.

The present findings suggest that early in development, OBD already demonstrate subtle temperament trait markers (e.g., decreased frustration tolerance, inhibitory control, soothability) that may be linked to the emergence of later psychopathology or adaptive functioning. This indicates that perhaps difficult temperament characteristics early in development may serve as global indicators of risk across a spectrum of internalizing and externalizing problems. The ECBQ scale Frustration was significantly correlated with a broad number of CBCL scales. Combined with the abovementioned findings regarding frustration in pediatric BD, it is possible that frustration might be a trait-related vulnerability marker (and one of multiple risk factors) in unaffected OBD. Another ECBQ scale that was significantly associated with a number of CBCL scales was Shyness. This might suggest that shy, inhibited, and anxious OBD may be at increased risk for the development of behavioral problems. This is in line with the notion of anxiety as an early predictor of later psychopathology in OBD (Simeonova et al. 2009; Duffy 2012; Duffy et al. 2013) and it deserves further research attention.

Also, it is important to note that in the study sample of 30 toddlers, there were 7 cases with CBCL scores in the borderline range (Scales: Internalizing Problems, Emotionally Reactive, Externalizing Problems and DSM-oriented scales Anxiety Problems, Pervasive Developmental Problems, and Oppositional Defiant Problems), and 2 cases with CBCL scores in the clinical range (Scales: Sleep Problems and DSM-oriented scale Anxiety Problems). Although this finding should be interpreted with caution, because of its descriptive nature, it provides some evidence for the emergence of very early behavioral problems is OBD. For example, studies have shown the existence of a CBCL-juvenile BD phenotype as defined by a profile of T scores > 70 on the scales Anxious/Depressed, Aggression, and Attention Problems (Mick et al. 2003; Faraone et al. 2005). More research is needed, but the CBCL might have the potential to be used as an early predictive screening tool in OBD.

Given that this is the first study to examine temperament and behavior in toddlers of mother with BD, direct comparison with previous studies is not possible. The overall findings, nevertheless, are consistent with the limited number of studies of temperament in OBD, which support the relationship between temperament and symptoms of mania, depression, and overall psychopathology. Also, a retrospective study of early childhood temperament in infancy and toddlerhood in children with BD found that several characteristics of difficult temperament (emotional intensity, negative mood, irregular rhythms in toddlerhood, experiencing distress during separation in infancy) were associated with current symptoms of mania and depression (West et al. 2008).

The present study also found a significant sex difference in the ECBQ scale Positive Anticipation and the CBCL scale Sleep Problems, with a higher mean rank score for girls than for boys. The

findings are consistent with results from a study with a normal sample of 1.5–3-year-old children indicating higher scores for females than for males on the scale Positive Anticipation (Putnam et al. 2006). Also, studies utilizing the CBCL with toddlers from the general population (Kott and Verhulst 1991) and with autism spectrum disorder (Hartley and Sikora 2009) show that girls have more sleep problems than boys. It is possible that the finding of a sex difference in sleep problems reflects a normative trend. On the other hand, given that sleep dysregulation is a core feature of mood psychopathology in pediatric and adult populations, it is also possible that this is an early indicator of emerging difficulties. Given the small sample size, however, the results should be viewed as exploratory and interpreted with caution.

The current investigation lends support to the notion that there is continuity over time in temperament traits as one of many precursors/risk factors contributing to the development of emerging psychopathology in high-risk children. Although the study of temperament in child offspring of parents with BD is a small literature at present, the current findings are in line with investigations reporting results from different age groups. What emerges is a unique picture of the developmental trajectory of temperament traits of OBD characterized by global impairments in flexibility, frustration tolerance, inhibitory control, soothability, ability to follow daily rhythm patterns, and negative affectivity. This literature underscores the importance of investigating temperament longitudinally and across developmental stages.

Limitations

Some limitations need to be considered in interpreting the study findings. Criticism has been voiced about the current approach, because of a contamination problem caused by item-content overlap in the assessment of temperament and behavior. Studies have reported, however, that even after removal of the threat to validity presented by overlap in measures, there continue to be significant, interpretable relationships between temperament and behavior (Lengua et al. 1998) and temperament and behavior problems represent unique constructs as evidenced by research utilizing expert ratings and factor analyses approach (Lemery et al. 2002). Also, because of the small number of toddlers studied, it was not possible to examine potential differences in temperament and behavior between OBD subgroups based on maternal diagnosis (BD I vs. BD II). Furthermore, the toddler assessments were completed by an affected mother with BD. Research has cautioned that mothers' evaluations of their children's behavior is influenced by their own mental state, therefore raising questions about the validity of child behavior reports by mothers who are currently emotionally distressed (Najman et al. 2000). Conversely, evidence suggests that maternal symptoms (e.g., depression) do not bias maternal child behavior reports significantly. They provide useful information on current child functioning (Rice et al. 2007) and have high predictive validity in predicting a new-onset mood disorder in high-risk offspring (Lewis et al. 2012). The maternal mood state during the evaluation of the toddlers, however, was not addressed, which is a limitation of this study. Also, given the preliminary nature of this investigation and that a specific set of hypothesized associations was examined, an adjustment for multiple comparisons was deemed highly conservative and was not conducted. This needs to be kept in mind when interpreting the study findings. In addition, the lack of comparison group of offspring of parents without psychopathology or a psychiatric control group is a limitation. This restricts the generalizability of findings and the interpretation with regard to specificity.

Conclusions

Taken together, the present findings provide a platform for future investigations of the contribution of temperament and early behavior to potential well-being or mental illness in OBD, a population at high familial risk for psychopathology. Future research would benefit from investigating whether temperament profiles and behavior can be used as global or specific resilience or vulnerability markers, to predict the onset, progression, severity, treatment response, and other clinical features of emerging psychopathology, or, conversely, predict positive adjustment in OBD. Examining the usefulness of temperament profiles for characterization of the developmental trajectory of the prodrome of mood disorders and comorbid conditions, and comparing OBD with healthy control offspring and another clinical group (e.g., offspring of depressed mothers) represents another viable research direction. Also, future studies would benefit from a longitudinal research design and examination of the relationship between temperament and other significant domains starting in infancy and toddlerhood to enhance early intervention and prevention efforts. Finally, integrating laboratory-based methods of assessment (e.g., mother–infant interaction, observational studies) to capture temperament and behavior, and examining relationships with relevant neurobiological and psychophysiological measures, would further enhance this line of investigation.

Clinical Significance

The present study has significant implications for clinical practice. The results indicate that young OBD with temperament traits characterized by impairments in flexibility, frustration tolerance, inhibitory control, soothability, ability to follow daily rhythm patterns, and negative affectivity might be at an increased risk for development of behavioral and emotional problems over time and should be monitored closely. The identification of specific problem domains can facilitate the development and delivery of targeted, novel, early intervention, and prevention approaches for an appropriate subgroup of children and their families at the youngest possible age. More specifically, the study findings indicate that temperament-based interventions grounded in a self- and reactivity-regulation perspective might be warranted. This can ultimately promote resilience and reduce risk in OBD, a population at high familial risk for psychopathology.

Disclosures

Dr. Simeonova receives research support from the National Institutes of Health (NIH) and the Brain and Behavior Research Foundation (Formerly NARSAD). Dr. Attalla, Ms. Nguyen, Ms. Stagnar, and Ms. Knight have no conflicts of interest to report. Dr. Craighead is a board member of Hugarheill, an Icelandic company dedicated to the prevention of depression, receives book royalties from John Wiley & Sons, and has received research support from Brock Family Fund, the Fuqua Family Foundation, the NIH, and the George West Foundation. Dr. Stowe has received research support from GlaxoSmithKline (GSK), the NIH, Pfizer, and Wyeth, and has served on speakers or advisory boards for Bristol-Myers Squibb (BMS), GSK, Eli Lilly, Pfizer, and Wyeth, and has received honoraria from GSK, Eli Lilly, Pfizer, and Wyeth. Dr. Newport has received research support from Brain & Behavior Research Foundation, GSK, Janssen, Eli Lilly, the NIH, and Wyeth, and has served on speakers' or advisory boards and received honoraria for AstraZeneca, GSK, Eli Lilly, and Pfizer. No coauthor or any family member holds equity positions in pharmaceuticals or biomedical corporations.

References

- Achenbach TM, Rescorla LA: Manual for the ASEBA Preschool Forms and Profiles. Burlington, VT: University of Vermont; 2000.
- Braungart-Rieker J, Garwood MM, Stifter CA: Compliance and non-compliance: The roles of maternal control and child temperament. *J Appl Dev Psychol* 18:411–428, 1997.
- Chang KD, Blasey CM, Ketter TA, Steiner H: Temperament characteristics of child and adolescent bipolar offspring. *J Affect Disord* 77:11–19, 2003.
- Doucette S, Horrock J, Grof P, Keown–Stoneman C, Duffy A: Attachment and temperament profiles among the offspring of a parent with bipolar disorder. *J Affect Disord* 150:522–526, 2013.
- Duffy A: The nature of the association between childhood ADHD and the development of bipolar disorder: A review of prospective high-risk studies. *Am J Psychiatry* 169:1247–1255, 2012.
- Duffy A, Alda M, Trinneer A, Demidenko N, Grof P, Goodyer IM: Temperament, life events, and psychopathology among the offspring of bipolar parents. *Eur Child Adolesc Psychiatry* 16:222–228, 2007.
- Duffy A, Horrock J, Doucette S, Keown–Stoneman C, McCloskey S, Grof P: Childhood anxiety: An early predictor of mood disorders in offspring of bipolar parents. *J Affect Disord* 150:363–369, 2013.
- Eisenberg N, Sadovsky A, Spinrad TL, Fabes RA, Losoya SH, Valiente C, Reiser M, Cumberland A, Shepard SA: The relations of problem behavior status to children's negative emotionality, effortful control, and impulsivity: Concurrent relations and prediction of change. *Dev Psychol* 41:193–211, 2005.
- Faraone SV, Althoff RR, Hudziak JJ, Monuteaux M, Biederman J: The CBCL predicts DSM bipolar disorder in children: A receiver operating characteristics curve analysis. *Bipolar Disord* 7:518–524, 2005.
- First MB, Spitzer RL, Gibbon M, Williams J: Structured Clinical Interview for the DSM-IV Axis I Disorders – Patient Edition, Version November 2002. New York: New York State Psychiatric Institute, Biometrics Research Department; 2002.
- Goldsmith HH, Lemery KS: Linking temperamental fearfulness and anxiety symptoms: A behavioral-genetic perspective. *Biol Psychiatry* 48:1199–1209, 2000.
- Hartley SL, Sikora DM: Sex differences in autism spectrum disorder: An examination of developmental functioning, autistic symptoms, and coexisting behavior problems in toddlers. *J Autism Dev Disord* 39:1715–1722, 2009.
- Hirshfeld–Becker DR, Biederman J, Henin A, Faraone SV, Cayton GA, Rosenbaum JF: Laboratory-observed behavioral disinhibition in the young offspring of parents with bipolar disorder: A high-risk pilot study. *Am J Psychiatry* 163:265–271, 2006.
- Kott HM, Verhulst FC: Prevalence of problem behavior in Dutch children aged 2–3. *Acta Psychiatr Scand Suppl* 367:1–37, 1991.
- Lemery KS, Essex MJ, Smider NA: Revealing the relation between temperament and behavior problem symptoms by eliminating measurement confounding: Expert ratings and factor analyses. *Child Dev* 73:867–882, 2002.
- Lengua LJ, Kovac EA: Bidirectional associations between temperament and parenting and the prediction of adjustment problems in middle childhood. *J Appl Dev Psychol* 26:21–38, 2005.
- Lengua LJ, West SG, Sandler IN: Temperament as a predictor of symptomatology in children: Addressing contaminations of measures. *Child Dev* 69:164–181, 1998.
- Lewis KJ, Mars B, Lewis G, Rice F, Sellers R, Thapar AK, Craddock N, Collishaw S, Thapar A: Do parents know best? Parent-reported vs. child-reported depression symptoms as predictors of future child mood disorder in a high-risk sample. *J Affect Disord* 141:233–236, 2012.
- McClowry SG, Rodriguez ET, Koslowitz R: Temperament-based intervention: Re-examining Goodness of Fit. *Eur J Dev Sci* 2: 120–135, 2008.
- McKinnon MC, Cusi AM, MacQueen GM: Psychological factors that may confer risk for bipolar disorder. *Cogn Neuropsychiatry* 18:115–128, 2013.
- Mick E, Biederman J, Pandina G, Faraone SV: A preliminary meta-analysis of the Child Behavior Checklist in pediatric bipolar disorder. *Biol Psychiatry* 53:1021–1027, 2003.
- Najman JM, Williams GM, Nikles J, Spence S, Bor W, O'Callaghan M, Le Brocque R, Andersen MJ: Mothers' mental illness and child behavior problems: Cause-effect association or observation bias? *J Am Acad Child Adolesc Psychiatry* 39:592–602, 2000.
- Olino TM, Durbin CE, Klein DN, Hayden EP, Dyson MW: Gender differences in young children's temperament traits: comparisons across observational and parent-report methods. *J Pers* 81:119–129, 2013.
- Putnam SP, Gartstein MA, Rothbart MK: Measurement of fine-grained aspects of toddler temperament: The Early Childhood Behavior Questionnaire. *Infant Behav Dev* 29:386–401, 2006.
- Rice F, Lifford KJ, Thomas HV, Thapar A: Mental health and functional outcomes of maternal and adolescent reports of adolescent depressive symptoms. *J Am Acad Child Adolesc Psychiatry* 46: 1162–1170, 2007.
- Rich BA, Holyrod T, Carver FW, Onelio LM, Mendoza JK, Cornwell BR, Fox NA, Pine DS, Coppola R, Leibenluft E: A preliminary study of the neural mechanisms of frustration in pediatric bipolar disorder using magnetoencephalography. *Depress Anxiety* 27:276–286, 2010.
- Rich BA, Schmajuk M, Perez–Edgar KE, Pine DS, Fox NA, Leibenluft E: The impact of reward, punishment, and frustration on attention in pediatric bipolar disorder. *Biol Psychiatry* 58:532–539, 2005.
- Rothbart MK, Derryberry D: Development of individual differences in temperament. In: *Advances in Developmental Psychology*, edited by M.E. Lamb, A.L. Brown. Hillsdale, NJ Erlbaum, 37–86, 1981.
- Simeonova DI, Baumer FM, Steiner H, Chang KD: Temperament characteristics and behavioral problems in bipolar offspring. Abstract presented at the 158th Annual Meeting of the American Psychiatric Association, Atlanta, Georgia, 2005.
- Simeonova DI, Jackson V, Attalla A, Karchemskiy A, Howe M, Adleman N, Chang K: Subcortical volumetric correlates of anxiety in familial pediatric bipolar disorder: A preliminary investigation. *Psychiatry Res* 173:113–120, 2009.
- Singh MK, DelBello MP, Strakowski SM: Temperament in child offspring of parents with bipolar disorder. *J Child Adolesc Psychopharmacol* 18:589–593, 2008.
- Teglasi H, MacMahon BH: Temperament and common problem behaviors of children. *J Appl Dev Psychol* 11:331–349, 1990.
- Van Zeijl J, Mesman J, Stolk MN, Alink LR, van Ijzendoorn MH, Bakermans–Kranenburg MJ, Juffer F, Koot HM: Differential susceptibility to discipline: The moderating effect of child temperament on the association between maternal discipline and early childhood externalizing problems. *J Fam Psychol* 21:626–636, 2007.
- West AE, Schenkel LS, Pavuluri MN: Early childhood temperament in pediatric bipolar disorder and attention deficit hyperactivity disorder. *J Clin Psychol* 64:402–421, 2008.

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