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CLINICAL OUTCOMES OF LABORATORY-OBSERVED PRESCHOOL BEHAVIORAL DISINHIBITION AT FIVE-YEAR FOLLOW-UP

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Abstract

Objective—"Behavioral disinhibition" refers to a temperamental tendency to exhibit boldness, approach, and spontaneity in unfamiliar situations. We previously found it to be associated with childhood disruptive behavior and mood disorders as well as with parental bipolar disorder. In the present study, our objective was to examine the diagnostic outcome in middle childhood of behavioral disinhibition assessed at preschool-age among offspring at risk for anxiety and mood disorders.

Method—The sample consisted of 284 children including offspring of parents with panic disorder or major depression and comparison offspring of parents without these disorders, who had been assessed with laboratory observations of temperament at ages 21 months-6 years. We reassessed 215 of the children (77%) at 5-year follow-up (mean age 9.6 years) with structured diagnostic interviews.

Results—Compared with non-inhibited, non-disinhibited controls, behaviorally disinhibited children had higher lifetime rates of comorbid mood plus disruptive behavior disorders, and higher current rates of any disruptive behavior disorder and of oppositional defiant disorder.

Conclusion—Behavioral disinhibition appears to be a temperamental antecedent of disruptive behavior disorders and their comorbidity with mood disorders in middle childhood, which may be targeted for preventive intervention.

Keywords

Behavioral disinhibition; disruptive behavior disorders; mood disorders; children; temperament; psychopathology

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Introduction

The ability to identify early in life children at risk for the behavioral and emotional dysregulation evident in disruptive behavior and mood disorders would facilitate the prospective study of etiologic mechanisms and could inform the development of targeted prevention and early intervention protocols. One approach to the identification of potential markers of risk is to focus on temperamental factors that are measurable through standardized laboratory assessments at early ages, when precise diagnosis of psychopathology is difficult. Over the past two decades, our group has focused on two temperamental domains that characterize extremes in the way young children respond to novel people, activities, and settings. The first, "behavioral inhibition to the unfamiliar," is defined as a tendency to react to novelty with restraint, reticence, avoidance or distress (Kagan et al 1988). The second, which we have termed "behavioral disinhibition" (BD), refers to the opposite tendency to react with boldness, approach, and spontaneity (Hirshfeld-Becker et al 2002). Children at the extremes of inhibition or disinhibition show relatively stable typical responses to novelty that likely reflect underlying neurophysiological differences and that may predispose to anxious or frustrated behaviors, respectively (Hirshfeld-Becker et al 2003), whereas children in the middle of the spectrum of approach or avoidance of novelty often vary in their responses from occasion to occasion (Kagan et al 1988).

Behavioral inhibition is hypothesized to reflect a lower threshold to limbic and sympathetic activation, reflected in higher reactivity of the basolateral and central nuclei of the amygdala and their projections to the striatum, hypothalamus, and sympathetic nervous system (Kagan et al 1988;Schwartz et al 2003). In contrast, BD may represent a higher threshold to activation, for which children may compensate through seeking sensation and novelty (Brimer and Levine 1983;Cloninger 1987;Raine et al 1990;Zentall and Meyer 1987). It may also be conceptualized as reflecting high novelty-seeking, rooted in dopaminergic pathways, and low harm-avoidance, rooted in serotonergic and cholinergic pathways (Cloninger 1987;Cloninger et al 1993). Alternatively, it may reflect overactivation of Gray's "behavioral activation system," which mediates appetitive and aggressive behaviors, and underactivation of Gray's "behavioral inhibition system," which increases arousal in response to signals of novelty or threat (Derryberry and Rothbart 1997;Gray 1982;Gray and McNaughton 1996). Although the term "behavioral disinhibition" is used by different investigators to describe different constructs, we use it to mean an automatic reaction to novelty, similar to what Kagan terms "uninhibition" (Kagan et al 1988). Thus, behavioral disinhibition is theoretically distinct from "effortful control" which can be thought of as the capacity for active voluntary inhibition or modulation of conduct or self-regulation (Kochanska et al 1997;Kochanska et al 1996;Rothbart and Ahadi 1994;Rothbart et al 1994) and which is assumed to be rooted in the mid-prefrontal cortex (anterior attention network) (Rothbart et al 1994).

Recently, our group has begun to explore the nature of the risk conferred by BD (Hirshfeld-Becker et al 2003;Hirshfeld-Becker et al 2002;Hirshfeld-Becker et al 2006) using data from a large longitudinal sample of offspring at risk for panic disorder and major depression and comparison offspring of non-clinical parents (Rosenbaum et al 2000). Children from this sample were assessed with laboratory observations of temperament at baseline (either at age 21 months, 4, or 6 years), with diagnostic interviews at mean age 6, and, as reported here, in a subsequent follow-up wave five years after initial recruitment. Our studies and others have suggested that childhood BD may be linked to dysregulatory disorders including attention-deficit hyperactivity disorder (ADHD), other disruptive behaviors, alcohol and substance use disorders, and possibly comorbid mood and disruptive behavior disorders (Hirshfeld-Becker et al 2003). For example, we found that children selected as extremely bold, spontaneous and outgoing in unfamiliar situations in toddlerhood who remained at this extreme at ages 4, 5, and 7 years were significantly more likely than inhibited or non-stably bold children to develop

DSM-III-R oppositional disorder by age 8 (Hirshfeld et al 1992). Likewise, among 216 children of parents with panic disorder and depression and of comparison parents from the present sample, we found that children who exhibited BD in the laboratory in early childhood (age 2–6 years) had elevated rates of disruptive behavior disorder, mood disorder, and comorbid disruptive behavior and mood disorders at mean age 6 (Hirshfeld-Becker et al 2002). Despite their young age, children with BD already had higher rates of placement in special classes, higher ratings of school behavior problems, more problems becoming involved in free-time activities and structuring their free time, lower overall functioning, and higher rates of psychosocial treatment.

Other investigators have connected BD (i.e. approach, stimulation-seeking, and/or behavioral undercontrol) in the preschool years with inattention at age 7 (Rothbart et al 1994), delinquency at ages 10–13 (Tremblay et al 1994), aggression at age 11, (Raine et al 1998) inattention, hyperactivity and antisocial behavior at ages 13–15 (Caspi et al 1995), aggression, danger-seeking and impulsivity at age 18 (Caspi and Silva 1995), and antisocial personality disorder at age 21 (Caspi et al 1996). Studies have also suggested links between BD and alcohol and substance use (Krueger et al 2002;Young et al 2000). However, with few exceptions (Raine et al 1998), these studies did not rely upon standardized laboratory assessments of BD. Moreover, with the exception of our own earlier studies cited above, none of the investigations to date have combined standardized laboratory assessments of BD at preschool-age with structured diagnostic interview assessments of outcome, and none assessed outcome of BD among offspring at risk for psychopathology.

In the present study, our aim was to further explore the risk conferred by preschool-age BD among children at risk for mood and anxiety disorders and comparison children, by examining diagnostic outcomes at 5-year follow-up. We hypothesized that the disinhibited children would show higher rates of disruptive behavior disorders and of comorbid disruptive behavior and mood disorders than their non-disinhibited, non-inhibited peers. To our knowledge, this is the first study to examine longitudinal outcomes of laboratory assessed BD using standard diagnostic interviews in a large controlled sample of children at high risk for mood and anxiety disorders.

Methods and Materials

Subjects

This study is a five-year follow-up of a sample originally recruited between 1993–1998. As described in earlier reports (Biederman et al 2001a;Rosenbaum et al 2000), we recruited three groups: 1) 131 parents treated for panic disorder and their 227 children (of these parents, 113 either had comorbid panic and major depression [N=102] or a spouse with major depression [N=11]); 2) 39 parents with major depression without panic disorder or agoraphobia and their 67 children; and 3) 61 comparison parents without major anxiety or mood disorders and their 119 children. Of these 413 children, 284 were in the age-range at baseline (ages 21 months-6 years) to undergo a laboratory assessment of behavioral inhibition.

Parents with panic disorder and major depression had been recruited from hospital outpatient and HMO settings and advertisements, and were included if they met full DSM–III–R criteria for panic disorder or major depressive disorder on the Structured Clinical Interview for DSM-III-R (SCID; Spitzer et al 1990) and had been treated for these disorders. Parents who were acutely psychotic or suicidal were excluded from the study; however, parents in the panic and depression groups were not excluded on the basis of any comorbid disorders. Comparison parents were recruited through advertisements to hospital personnel and in the community, and were included only if both parents did not meet DSM–III–R criteria on the SCID for any major anxiety (panic disorder, agoraphobia, social phobia or OCD) or mood disorders (major

depressive disorder, bipolar disorder, or dysthymia) and had never received psychiatric treatment. The institutional review board at Massachusetts General Hospital approved this study protocol as well as the follow-up protocol. All parents signed written consent for themselves and their children. Children assented to study procedures.

Assessment of Behavioral Inhibition and Disinhibition

As described previously (Biederman et al 2001b;Rosenbaum et al 2000), children ranging from 21 months to six years of age were assessed for behavioral inhibition at baseline during a single visit to the Harvard Infant Study Laboratory under the direction of Jerome Kagan and Nancy Snidman. Age-specific laboratory observational protocols (for children ages 21 months, 4, or 6 years) were used (Rosenbaum et al 2000). For these assessments, the child came to the laboratory, accompanied by mother, and interacted with unfamiliar toys, adult examiners and activities, and the child's behavior was videotaped and quantified. At age 6, one of the activities was the Matching Familiar Figures Test (MFFT; Kagan 1964), which assesses impulsive versus reflective decision-making style.

Three definitions based on different summary indexes were used to aggregate children's inhibited behaviors, and children were considered behaviorally inhibited if they met criteria for two out of the three definitions: (1) Based on earlier work by Kagan and colleagues, 21-month-olds were categorized as inhibited if they exhibited four or more fears during the course of the battery or were rated as showing "minimal" vocalization or smiling. Older children were rated inhibited if the number of spontaneous comments and smiles they made were in the lowest 20^{th} percentile of comparison children. (2) A 4-point rating of the child's inhibition across the entire battery was made. Children who received ratings of 3 (more inhibited than not) or 4 (extremely inhibited) were considered inhibited. (3) A summary score was derived from a principal factors factor analysis with varimax rotation of all the behavioral variables rated, computed separately for children in each of the three age groups. Children were rated as inhibited if their score fell in the upper 20^{th} percentile for their age group on this summary inhibition score.

In a subsequent re-analysis, children who had shown signs during the laboratory assessments of extreme approach or disinhibition of speech or actions were classified as behaviorally disinhibited (BD; Hirshfeld-Becker et al 2002). For these classifications we were limited by the variables assessed in the behavioral inhibition assessments (see Hirshfeld-Becker et al 2002 for details of the rationale for the variables used). To be classified as BD, 21-month-olds had to show minimal avoidance of unfamiliar stimuli, maximal approach, or maximal vocalization. Four- and six-year-olds had to make more spontaneous comments than 75% of children of non-clinical comparison parents, and 6-year-olds additionally had to show impulsive style on the MFFT or be assigned a global rating of extreme disinhibition.

Three of the 284 children assessed showed signs of both inhibition and disinhibition and therefore could not be clearly classified. Therefore the present follow-up focused on the 281 children who could be rated unequivocally as inhibited, disinhibited, or neither.

Follow-up Assessment Procedures

Follow-up assessments occurred a median of five years after baseline laboratory assessments (mean: 5.4 ± 1.4 years). Psychiatric assessments of the children relied on the DSM-IV based Kiddie Schedule for Affective Disorders and Schizophrenia, Epidemiologic Version (K-SADSE) (Orvaschel and Puig-Antich 1987;Puig-Antich and Ryan 1986). We conducted indirect interviews with the mothers for all subjects and direct interviews with subjects 12 years and older. We considered a disorder positive if DSM-IV diagnostic criteria were unequivocally met in either interview. The proportion of interviews relying on indirect plus direct interviews

versus those relying upon indirect interviews only did not differ between BD and non-BD groups (Pearson χ^2=1.43, p =0.489). We assessed both lifetime and current (past month) rates of disorder. In presenting lifetime rates, we also include diagnoses reported as present in the child's lifetime during the baseline assessment (Biederman et al 2001a). Thus, lifetime rates of disorder include disorders reported either at baseline or follow-up as having been present at any point in the child's life. Socioeconomic Status (SES) was assessed with the Hollingshead Four-Factor Index (Hollingshead 1975).

Mothers and children were assessed by interviewers blind to the child's temperamental status and to all previous information collected about the child and family. Interviewers had undergraduate or master's degrees in psychology and were trained to high levels of inter-rater reliability. They underwent a training program which required them to a) master the diagnostic instruments, b) learn about DSM-IV criteria, c) watch training tapes, d) participate in interviews performed by experienced raters, e) rate several subjects under the supervision of the project coordinator, f) undergo continued supervision of their assessments by senior project staff, and g) audiotape all interviews for later random checking. All interviews were presented for review to a committee of board-certified child and adult psychiatrists and licensed psychologists blind to the subject's ascertainment status, referral source, and all other data, to resolve diagnostic uncertainties. Diagnoses presented for review were considered positive only if a consensus was achieved that criteria were met to a clinically meaningful degree.

We computed kappa coefficients of agreement for all diagnoses by having experienced, board-certified child and adult psychiatrists and licensed clinical psychologists diagnose subjects from audio taped interviews made by the assessment staff. Based on a total of 500 assessment modules from interviews of children and adults, the median kappa coefficient was 0.98. Kappa coefficients for individual diagnoses indicated excellent reliability between ratings by the non-clinician raters and experienced clinicians, ranging from .88 for ADHD to 1.0 for several disorders including conduct disorder (CD) and major depression. Additionally, to estimate the reliability of the diagnostic review process, we examined agreement between individual clinicians and the diagnoses assigned by the review committee. Kappa coefficients for individual diagnoses ranged from .73 for OCD to 1.0 for ADHD, CD, and major depression (median .87).

Statistical Analyses

We first conducted univariate comparisons to determine whether demographic variables differed between groups of children who were and were not reassessed or children with or without BD. We considered a demographic variable a potential confound if univariate tests showed it to be significantly associated (at the conservative level of $p \leq .10$) with both the predictor and the outcome variable. We then used the potential confound as a covariate in the models used to assess the link between BD and child outcome.

For outcomes which were binary variables (e.g. presence or absence of disorder), we used logistic regression and for those which were continuous, we used linear regression. Multiple siblilngs from the same family cannot be considered independent because they share genetic, cultural, and social risk factors. Therefore, we used Huber-White robust estimates of variance so that p-values would be accurately estimated, as implemented in STATA (Stata 1997). We used Wald's test to assess the statistical significance of individual predictors.

For some binary outcomes (e.g. comorbid mood and disruptive behavior disorders), there were strata in which no subjects reported a positive response, yielding a prevalence of zero. This sparse data situation prevented the fitting of a standard logistic model. In these cases, we report p-values as provided by Fisher's Exact test. All tests were two-tailed with alpha set at 0.05.

Results

Attrition and Demographic Characteristics

Of the 281 children assessed for temperament at baseline, 215 were reassessed diagnostically at follow-up (77%). As seen in Table 1, children who were and were not reassessed did not differ on demographic variables (age, sex, SES, intactness of family, race), temperament (BD), or parental diagnoses (presence of parental panic disorder or depression). At follow-up, children ranged in age from 6–15 years (mean, SD: 9.61, 1.92).

As seen in Table 2, children with BD (n=75), behavioral inhibition (n=67), and neither (n=73) showed significant differences in sex, family SES, and presence of parental major depression. Therefore, these variables were covaried in all comparisons in which they were related to the outcome variable (at $p \leq .1$).

Psychiatric Disorders in Offspring

Results center on tests of rates of disorders in behaviorally disinhibited children compared with non-inhibited, non-disinhibited children; results for inhibited children have been presented elsewhere (Hirshfeld-Becker et al in press); they are shown here only for contrast.

As seen in Table 3, children who had BD in early childhood were significantly more likely to develop lifetime presence of a mood and disruptive behavior disorder compared with children without disinhibition or inhibition. The mood disorders included in this category were major depressive disorder, bipolar disorder (I or II), or dysthymia. BD increased the chance of developing this comorbidity, even after parental depression, male gender, and low SES were taken into account. Whereas rates of disruptive behavior disorders, ADHD, and ODD among disinhibited children were higher than those in non-inhibited, non-disinhibited children (odds ratios [with 95% confidence intervals] without potential confounds covaried: OR=2.81[1.33–5.95], OR=2.24[1.02–4.88], OR=2.95[1.23–7.07], respectively), these comparisons did not maintain significance when parental depression, SES, and sex were included in the equations.

When we examined current disorders at five-year follow-up, we found that preschool BD significantly predicted a two-fold increase in disruptive behavior disorders, beyond the rate predicted by parental depression, male gender, and low socioeconomic status. This difference was accounted for by a two-fold increase in the rate of ODD.

Because a small number of children included in the present analysis (n=21) had a parent with bipolar disorder, and because we had previously found BD in children from this sample to be associated with presence of parental bipolar disorder (Hirshfeld-Becker et al 2006), we examined whether covarying parental bipolar disorder would affect our results. The association between child BD and lifetime comorbid mood and disruptive behavior disorder remained robust (OR=7.57 [1.09–52.82], z=2.04, p=0.041). Associations with current disruptive behavior disorders and ODD maintained high odds ratios, but dropped below the threshold of significance (OR=2.57 [0.95–6.94], z=1.87, p=0.062; and OR=3.18 [0.96–10.56], z=1.89, p=0.059, respectively).

To explore whether the timing of the assessment for BD affected rates of disorders at follow-up, we examined the rates of the disorders that were significantly associated with BD within the subgroups of children who had been assessed at the three different ages (21 months, 4 years or 6 years). Although the cell sizes were too small for meaningful statistical comparisons, Table 5 reveals that regardless of the age at which BD was assessed, the raw rates of lifetime comorbid mood plus disruptive behavior disorders, current disruptive behavior disorders, and current ODD were two-to-five times higher among the disinhibited children.

DISCUSSION

This study provides prospective evidence that behavioral disinhibition (BD) measured in early childhood predicted the presence, five years later, of current disruptive behavior disorders in general and oppositional defiant disorder in particular, even after considering the contribution of parental psychopathology and low socioeconomic status. Moreover, the study suggests that preschool BD represents a risk factor for the development of comorbid mood plus disruptive behavior disorder by middle childhood.

Our findings are consistent with results from the initial wave of this study demonstrating that BD was associated with disruptive behavior disorders and their comorbidity with mood disorders at a mean age of six years (Hirshfeld-Becker et al 2002). They are also consistent with other prospective studies finding associations between approach behaviors, stimulation-seeking, or behavioral undercontrol in early childhood and later delinquency (Tremblay et al 1994), aggression (Raine et al 1998), inattention, hyperactivity and antisocial behaviors (Caspi et al 1995;Caspi et al 1996). However, this is the first study to our knowledge to examine prospective outcomes of laboratory-observed preschool BD using diagnoses derived from structured diagnostic interviews in a sample of offspring at risk for psychopathology, as well as the first to examine the risk associated with BD independently from the risk conferred by parental psychopathology.

The finding that BD is a precursor to the comorbidity between mood and disruptive behavior disorders is consistent with the hypothesis that BD may be associated with risk for bipolar disorder. Increasing evidence implicates comorbid mood and behavior disorders or their symptoms as precursors to bipolar disorder (Biederman et al 2000b). ADHD, ODD, conduct disorder, and mood disorders have been observed in the histories of both adults (Sachs et al 1994) and children (Biederman et al 1999;Biederman et al 2000a;Faedda et al 1995;Geller et al 2002;Kessler et al 2001;Wozniak and Biederman 1995;Wozniak et al 2001) with bipolar disorder, as well as in offspring at risk for bipolar disorder (Carlson and Weintraub 1993;Chang et al 2000;Cytryn et al 1982;DelBello and Geller 2001;Duffy et al 2000;Grigoroiu-Serbanescu et al 1989;Radke-Yarrow et al 1992;Zahn-Waxler et al 1988). Evidence from longitudinal studies suggests that early dysregulation of behavior and mood precedes onset of bipolar disorder (Akiskal et al 1995;Carlson and Weintraub 1993;Egeland et al 2003;Kovacs et al 1994) and may in some cases represent the early manifestations of bipolar disorder in children. For example, Carlson and Weintraub (1993) found that children at risk for bipolar disorder had elevated rates of mild to moderate attentional and disruptive behavioral problems at ages 7–16 compared with offspring of controls, and that these problems predicted later affective symptoms. In a test of the hypothesis linking BD to risk for bipolar disorder, we found that children from the present sample whose parents had bipolar disorder had significantly elevated rates of BD (Hirshfeld-Becker et al 2006). It is noteworthy that our present analyses revealed that BD predicted comorbid mood and disruptive behavior disorders even after presence of parental bipolar disorder was taken into account.

Children with BD whose parents did not have bipolar disorder also had significantly increased risk for disruptive behavior plus mood disorders. Therefore, we theorize that BD is a marker of motivational or emotional dysregulation which might predispose a child to develop one of several disorders involving behavioral or motivational dysregulation (Nigg 2000), including ADHD, ODD, conduct disorder, alcohol or substance use disorders, and bipolar disorder (Depue and Iacono 1989;Iacono et al 1999). Continued follow-up of these children as they enter adolescence, the period of greatest risk for these disorders, will clarify whether this is indeed the case.

The disinhibited children in our sample did not show significantly higher current (past month) rates of comorbid mood and disruptive behavior disorders. Because mood disorders are episodic, we would expect a lower number of children to have experienced an episode in the past month than over their lifetime. Only 7% of the disinhibited children were in a current mood episode at the time of the follow-up assessment (and all had a concurrent disruptive behavior disorder). Therefore, even though none of the comparison children had current comorbid mood and disruptive behavior disorders, the difference between disinhibited and comparison children only reached trend significance (p=.058).

It is important to underscore that although BD increased the statistical risk of developing comorbid mood and disruptive behavior disorders, the majority of disinhibited children in our sample did not develop these disorders. Therefore, BD is by no means tautological with this comorbid psychopathology. Instead, our findings suggest that BD may be a temperamental risk factor for the subsequent development of these disorders which is measurable very early in development.

An examination of the raw rates of disorder predicted by BD as assessed at different age points (age 21 months, 4 years, or 6 years) suggested that, regardless of the age at which it was assessed, BD was associated at follow-up with an increase in lifetime comorbid mood plus behavior disorder, current disruptive behavior disorder, and current ODD. This result suggests that BD in early childhood predicts adverse outcome in middle childhood regardless of the age at which it is assessed. Whereas further studies with larger samples are needed to confirm this finding, the result does imply that BD may be a marker of risk even in very young children (21-month-olds).

Our study should be viewed in light of several methodological limitations. Because we assessed BD at only a single time point, we do not know whether the children we studied remained stably disinhibited. Our current results suggest that even based on one assessment, BD in early childhood signals increased risk for future dysfunction. On the other hand, our design limited our ability to assess whether stability of BD across early childhood would increase its predictive association with disruptive behavior and comorbid mood disorders. Future studies that assess BD at two or more time points are needed to address this issue.

Additionally, because of the relatively low base rates of mood disorder in this young at-risk sample, our conclusions about the rates of comorbid mood and disruptive behavior disorders were based on a small number of individuals. Although these differences clearly attained significance, we do not have a precise estimate of the strength of the relationship (odds ratio) given that the 95% confidence interval for the odds ratio was 1.21–58.96.

This study was also limited by reliance upon parental report for lifetime diagnoses in children under age twelve. We did not directly interview younger children about their lifetime diagnoses because children under twelve are limited in their ability to understand questions from structured diagnostic interviews (Breton et al 1995) and to map events in time and have been found to be unreliable in their reports of psychopathology (Edelbrock et al 1985;Schwab-Stone et al 1994). In contrast, maternal reports of psychopathology, have shown high reliability, even over a one-year period (Fallon and Schwab-Stone 1994;Faraone et al 1995). By relying on parent-reports for diagnoses in children 11 and under and combined parent- and child-reports in children 12 and older, we introduced method variance. However, we opted for this approach, because using only the parent reports for children over 11 might result in our missing important information about mood, conduct, and inattention symptoms among adolescents. Moreover, because these methods were used to the same degree with both the BD and non-BD groups, this method variance cannot confound our analyses. Future waves of data collection, in which all children in the sample will be old enough to be directly interviewed about their symptoms

will enable us to confirm our current findings and to explore further hypotheses about the outcome of children with BD. The study was also limited by the homogeneity of the sample, which included a low representation of minority families. Further studies of more ethnically diverse samples are needed to extend the generalizability of findings.

Despite these limitations, our findings suggest that preschool-age BD appears to identify a subset of children at elevated risk to develop comorbid mood and disruptive behavior disorders by middle childhood. Clinically, these results suggest that young children who show signs of BD should be monitored closely for signs of disruptive behavior and mood disorders. They also raise the hypothesis that these children might benefit from early or preventive interventions.

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Table 1

Baseline Characteristics of Children Assessed for Temperament who Did or Did Not Participate in the Follow-Up Study

	Participants (N=215)		**Non-Participants (N=66)**		**Significance**
	Mean	*SD*	*Mean*	*SD*	*Wald* χ^2, *p*
Child's Age at Baseline	4.18	1.29	4.24	1.47	χ^2=3.87, p=0.14
Socioeconomic Status	2.04	0.98	2.15	1.01	χ^2=0.47, p=0.49
	n	*%*	*n*	*%*	*Wald* χ^2, *p*
Child's Sex (% Female)	99	46%	24	36%	χ^2=1.99, p=0.16
Family Intactness (% Intact)	184	86%	57	86%	χ^2=0.020, p=0.88
Race (% Caucasian)	198	92%	62	94%	χ^2=0.17, p=0.68
Panic Disorder in Parent	108	51%	40	61%	χ^2=1.48, p=0.22
Depression in Parent	138	65%	37	57%	χ^2=0.84, p=0.36
Temperament (% BD)	75	35%	26	39%	χ^2=0.45, p=0.50

Note: Socioeconomic status refers to the Hollingshead Four Factor class (ranging from 1, highest, to 5, lowest; see Methods section). Families were considered intact if the child's biological parents were living together and were not divorced or separated.

Abbreviation: BD=behaviorally disinhibited.

Table 2

Demographic Characteristics at Follow-Up of Children with Behavioral Disinhibition (BD), Behavioral Inhibition (BI) and Neither

	Children with BD (N=75)		Children without BD or BI (N=73)		Children with BI (N=67)		Significance
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*F, p*
Child's Age	9.64	1.92	9.89	1.76	9.28	2.07	F=1.66, p=0.19
Socioeconomic Status	2.04†	1.06	1.73	0.85	2.17*	0.96	F=3.46, p=0.034
	n	*%*	*n*	*%*	*n*	*%*	*Wald* χ^2, *p*
Child's Sex (% Female)	27	36%†	37	51%	35	52%	χ^2=4.54, p=0.10
Family Intactness (% Intact)	56	76%	56	78%	51	77%	χ^2=0.090, p=0.96
Race (% Caucasian)	73	97%	69	95%	63	94%	χ^2=0.88, p=0.64
Panic Disorder in Parent	41	55%	31	42%	36	54%	χ^2=2.27, p=0.32
Depression in Parent	54	72%**	35	48%	49	73%**	χ^2=10.80, p=0.0045

Note: Socioeconomic status refers to the Hollingshead Four Factor class (ranging from 1, highest, to 5, lowest; see Methods section). Families were considered intact if the child's biological parents were living together and were not divorced or separated. Significances versus the group of children without BD or BI:

* p<0.05,

** p<0.01,

† p<0.1.

Table 3

Lifetime Diagnoses of Children with BD, BI and Neither

	Disinhibited Children (N=75)		Non-Inhibited, Non-Disinhibited Children (N=73)		Inhibited Children (N=67)		Significance (BD vs Non-BI, Non-BD) with SES, sex, and parental depression covaried
	n	*%*	*n*	*%*	*n*	*%*	*z,p, Odds Ratio[95% CI]*
Any DBD	30	40%	14	19%	16	24%	z= 1.68, p=0.094, OR=2.00[0.89–4.49]
ADHD	26	35%	14	19%	13	19%	z= 1.06, p=0.289, OR=1.62[0.67–3.93]
ODD	20	27%	8	11%	10	15%	z= 1.46, p=0.145, OR=1.98[0.79–4.96]
Conduct	3	4%	1	1%	0	0%	p=0.37, by Fisher's Exact
Any Mood Disorder	15	20%	7	10%	5	7%	z= 0.63, p=0.532, OR=1.39[0.50–3.87]
MDD	12	16%	6	8%	5	7%	z= 0.45, p=0.654, OR=1.28[0.44–3.71]
Dysthymia	3	4%	0	0%	2	3%	p=0.12, by Fisher's Exact
Bipolar	3	4%	1	1%	2	3%	p=0.37, by Fisher's Exact
Mood + DBD	11	15%	1	1%	4	6%	**z= 2.15, p=0.031, OR=8.44[1.21–58.96]**
Any Anxiety Disorder	45	60%	40	55%	37	55%	z= −0.10, p=0.923, OR=0.96[0.43–2.14]

Abbreviations: Any DBD=any disruptive behavior disorder; includes attention-deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), or conduct disorder (CD). Any Mood Disorder=includes major depressive disorder (MDD), dysthymia, or bipolar disorder (I or II). Mood+DBD=indicates the presence of both a mood and a disruptive behavior disorder in the same individual. Any Anxiety Disorder=includes panic disorder, agoraphobia, social anxiety disorder, specific phobia, obsessive-compulsive disorder, or generalized anxiety disorder.

Table 4

Current Diagnoses of Children with Behavioral Disinhibition (BD), Behavioral Inhibition (BI) and Neither

	Disinhibited Children (N=75)		**Non-Inhibited, Non-Disinhibited Children (N=73)**		**Inhibited Children (N=67)**		**Significance (BD vs Non- BI, Non-BD) with SES, sex, and parental depression covaried**
	n	*%*	*n*	*%*	*n*	*%*	*z,p, Odds Ratio[95% CI]*
Any DBD	22	29%	7	10%	11	16%	**z=2.06, p=.040 OR=2.78 [1.05–7.36]**
ADHD	11	15%	4	6%	5	8%	z=1.21, p=.22 OR=2.24 [0.61–8.23]
ODD	17	23%	4	5%	7	10%	**z=2.08, p=.037 OR=3.47 [1.08–11.20]**
Conduct	2	3%	0	0%	0	0%	p=0.50, by Fisher's Exact
Any Mood	5	7%	2	3%	3	4%	p=0.44, by Fisher's Exact
MDD	3	4%	2	3%	2	3%	p=1.0, by Fisher's Exact
Dysthymia	2	3%	0	0%	1	1%	p=0.50, by Fisher's Exact
Bipolar	0	0%	0	0%	1	1%	*NS*
Mood + DBD	5	7%	0	0%	2	3%	p=0.058, by Fisher's Exact
Any Anxiety	29	39%	15	21%	23	34%	z=1.73, p=.083 OR=2.00 [0.91–4.38]

Abbreviations: Any DBD=any disruptive behavior disorder; includes attention-deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), or conduct disorder (CD). Any Mood=any mood disorder; includes major depressive disorder (MDD), dysthymia, or bipolar disorder (I or II). Mood+DBD=indicates the presence of both a mood and a disruptive behavior disorder in the same individual. Any Anxiety=any anxiety disorder; includes panic disorder, agoraphobia, social anxiety disorder, specific phobia, obsessive-compulsive disorder, or generalized anxiety disorder.

Table 5

Rates of Disorders of Children Assessed for Behavioral Disinhibition at Ages 21 Months, 4, Years, and 6 Years

	Children with BD		Non-BI, Non-BD Children	
Lifetime Mood +DBD	*n, %*		*n, %*	
Assessed at 21 Months	1/14	7%	0/9	0%
Assessed at 4 Years	7/40	18%	0/45	0%
Assessed at 6 Years	3/21	14%	1/19	5%
Any Current DBD				
Assessed at 21 Months	7/14	50%	1/9	11%
Assessed at 4 Years	9/40	23%	3/45	7%
Assessed at 6 Years	6/21	29%	3/19	16%
Current ODD				
Assessed at 21 Months	7/14	50%	1/9	11%
Assessed at 4 Years	5/40	13%	2/45	4%
Assessed at 6 Years	5/21	24%	1/19	5%

Abbreviations: BD=behavioral disinhibition, BI=behavioral inhibition, Any DBD=any disruptive behavior disorder; includes attention-deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), or conduct disorder (CD).