Prevalence, Clinical Correlates, and Longitudinal Course of Severe Mood Dysregulation in Children

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Background: Controversy concerning the diagnosis of pediatric bipolar disorder (BD) has focused attention on children with chronic irritability and hyperarousal. This syndrome has been called the "broad BD phenotype" or severe mood dysregulation (SMD). This study examines prevalence, concurrent Axis I diagnoses, and longitudinal outcome of SMD in an epidemiologic sample.

Methods: Data were drawn from the Great Smoky Mountains Study, a longitudinal epidemiological study. Items from the Child and Adolescent Psychiatric Assessment were used to generate SMD criteria.

Results: Among 1420 children, the lifetime prevalence of SMD in children ages 9–19 was 3.3%. Most (67.7%) SMD youth had an Axis I diagnosis, most commonly attention-deficit/hyperactivity disorder (26.9%), conduct disorder (25.9%), and/or oppositional defiant disorder (24.5%). In young adulthood (mean age 18.3 ± 2.1 years), youth who met criteria for SMD in the first wave (mean age 10.6 ± 1.4 years) were significantly more likely to be diagnosed with a depressive disorder (odds ratio 7.2, confidence interval 1.3–38.8, p = .02) than youth who never met criteria for SMD.

Conclusions: Severe mood dysregulation is relatively common in childhood and predicts risk for early adulthood depressive disorders. Research should continue to explore the course of illness in children with SMD.

To facilitate research on pediatric bipolar disorder (BD), Leibenluft et al (2003) described a clinical syndrome called severe mood dysregulation (SMD). The hallmark of SMD is extreme, impairing, and chronic irritability, accompanied by hyperarousal symptoms. Severe mood dysregulation can be seen as one specific subtype of what has been called the "broad phenotype" of pediatric BD (National Institute of Mental Health 2001), a general term used to describe children whose nosologic status vis-à-vis BD is unclear. Children in the community with symptoms of SMD often receive a BD diagnosis (Pogge et al 2001), but disagreement continues regarding their proper classification. Longitudinal data might provide important insights in this regard (Carlson 1995, 1998).

Leibenluft et al (2003) use the term "SMD," as opposed to "broad phenotype BD," to refer to these children, because it remains unclear whether SMD is a BD phenotype. In fact, the primary purpose of developing the SMD category was to facilitate comparisons of SMD youth with those who clearly meet DSM-IV criteria for BD. Unlike classic BD, which involves episodic mood changes, Leibenluft et al defined SMD as a condition characterized by an abnormal baseline mood (i.e., irritability, anger, and/or sadness, noticeable to others and present most of the time). In addition, SMD involves hyperarousal (i.e., at least three of the following: insomnia, physical restlessness, distractibility, racing thoughts or flight of ideas, pressured speech, intrusiveness) and increased reactivity to negative emotional stimuli (e.g., temper outbursts) at least three times/week. These symptoms must begin before age 12, persist for at least 1 year (i.e., without any symptom-free periods exceeding 2 months), and cause functional impairment in at least two of three domains (i.e., home, school, peers).

Clinical studies provide preliminary data comparing SMD and narrow phenotype pediatric BD. Dickstein et al (2005) found that SMD children had an earlier age of symptom onset and higher rates of attention-deficit/hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD) than children with BD. Bipolar disorder children, in contrast, had more psychiatric hospitalization and suicide attempts than those with SMD. Similarly, Bhangoo et al (2003) found that children with episodic irritability were more likely to have parents with BD and more likely to exhibit suicide attempts, psychosis, or major depressive episodes, relative to children with chronic irritability.

Thus far, studies on SMD have been based entirely in clinical samples. Although data in clinical settings suggest that the SMD presentation might be more common than BD (Pogge et al 2001), generalizable data on prevalence are more likely to emerge from epidemiological studies. Due to referral biases, children with SMD in clinical settings are likely to represent a biased subsample of children with SMD, with children in clinical samples likely to exhibit a more severe illness, higher levels of comorbidity, and a poorer prognosis than children in the community (Cohen and Cohen 1984). Moreover, clinical groups are more likely to have been treated with psychotropic medications, which might influence the prevalence, pattern, and course of their symptoms (Lewinsohn et al 1995). Prospective epidemiologic studies enable researchers to examine the relationship between early symptoms, such as chronic irritability and hyperarousal, and later diagnoses without the limitations inherent in cross-sectional, retrospective, or clinic-based studies (Cohen and Cohen 1984; Pine et al 1999). However, benefits in epidemiological studies carry complementary disadvantages. For example, because most mentally ill children in the community do not present to clinics, features of an illness identified in the community might differ from those ascertained in the clinic.

The current study applied SMD criteria to the Great Smoky Mountains Study (GSMS), a community-based sample of 9–19-year-olds. The investigation had three primary goals. First, with

Table 1. Definition of Severe Mood Dysregulation With Corresponding CAPA Items

Criterion (adapted from Leibenluft et al 2003)	CAPA Section(s) and Item(s)
Abnormal mood (anger or sadness) present at least one-half of the day most days and of sufficient severity to be noticeable by people in the child's environment (e.g., parents, teachers, peers)	Depression section: 1) touchy or easily annoyed, 2) angry or resentful, or 3) depressed mood
Markedly increased reactivity to negative emotional stimuli. For example, the child responds to frustration with temper tantrums, verbal rages, and/or aggression toward people or property. Such events occur, on average, at least three times/week for the past 4 weeks.	Oppositional/Conduct section: 1) losing temper, 2) temper tantrums; or Depression section: 1) irritability, or easily precipitated irritable mood
Hyperarousal, as defined by at least two of the following:	
Insomnia	Sleep problems section: 1) insomnia (general), 2) initial insomnia, 3) middle insomnia, or 4) terminal insomnia
Physical restlessness	Hyperactivity/ADD section: 1) difficulty remaining seated, 2) rushes or climbs on things, 3) overactivity/fidgetiness, or 4) restlessness
Distractibility	Hyperactivity/ADD section: 1) difficulty concentrating, 2) easily distracted, 3) inattention, 4) fails to pay attention, 5) difficulty following through on instruction; or Depression section: 1) inefficient thinking
Racing thoughts or flight of ideas	Hypomania and Mania section: 1) subjective flight of ideas; or Depression section: 1) subjective rushing thoughts
Pressured speech	Hyperactivity/ADD section: 1) talks excessively
Intrusiveness	Hyperactivity/ADD section: 1) often interrupts or intrudes, 2) difficulty waiting turn, or 3) blurts out answers
The symptoms are severe in at least in one setting; in addition, there are at least mild symptoms (distractibility, intrusiveness) in a second setting.	Symptoms present in at least two of three: home, school, or elsewhere

CAPA, Child and Adolescent Psychiatric Assessment.

the Child and Adolescent Psychiatric Assessment (CAPA) (Angold and Costello 1995; Angold et al 1995), we determined the prevalence of SMD. Second, we examined the co-occurrence of SMD with DSM-IV Axis I diagnoses in order to classify the symptoms of SMD children in the context of standard nosology (because SMD is not in the same nosological system as DSM-IV Axis I diagnoses, we use the term "co-occurrence" instead of "comorbidity" throughout this paper). Third, to examine longitudinal outcome, we compared the prevalence of DSM-IV diagnoses in early adulthood between subjects who had met versus those who had not met SMD criteria as children. We hypothesized that SMD would predict a high risk for an early adult depressive disorder. This prediction was based on a previous study in a different epidemiological sample that showed an association between chronic irritability in adolescence and major depressive disorder (MDD) in early adulthood (Leibenluft et al 2006). Finally, because cases seen in the clinic might be more severe than those seen in the community, we repeated our analyses of prevalence, co-occurrence, and outcome after applying additional impairment criteria in order to identify the most severely ill SMD children (SMD+).

Methods and Materials

Subjects and Procedures

The GSMS is an ongoing, 15-year longitudinal population study of psychiatric disorders. Procedures were approved by the Institutional Review Board of the Duke University Medical Center. As reviewed by Costello et al (1996), a multistep probability sampling procedure was used. First, a representative sample of three cohorts of children ages 9, 11, and 13 was identified in 11 counties in western North Carolina. Then, a screening questionnaire, derived from the "externalizing" scale

of the Child Behavior Checklist (Achenbach and Edelbrock 1981; Achenbach et al 1995) was administered to a parent. Children scoring above 20 (approximately 25% of the population) plus a 1-in-10 random sample of those scoring below the cutoff were recruited. The response rate was 96% at the screening phase and 80% at the interview phase, for a total sample of 1420 youth. Between 78% and 95% were re-interviewed at each wave annually until age 16. The final wave used in the present analyses occurred approximately 3 years later when children were ages 18.3 ± 2.1 years. Informed consent was obtained from the parent, and informed assent was obtained from the child at the time of the interview.

Measures

Items from the CAPA (Angold and Costello 1995; Angold et al 1995), a parent- and child-based interview, were used to identify SMD and non-SMD youth. We used a modified version of the SMD criteria specified in Leibenluft et al (2003). Specifically, the criteria used were: 1) chronically irritable, angry, or depressed mood; 2) markedly excessive reactivity (at least three times/week); and 3) hyperarousal (at least two of six symptoms: insomnia, distractibility, pressured speech, physical restlessness, racing thoughts/flight of ideas, and/or interpersonal intrusiveness [e.g., interrupts conversations]; see following text regarding the requirement of two of these symptoms in this study rather than three as in Leibenluft et al (2003).

Individual items from five CAPA sections (depression, hypomania/mania, hyperactivity/ attention deficit disorder [ADD], sleep disorders, and oppositional defiant/conduct disorder) were used to ascertain whether the symptoms of SMD were present in the preceding 3 months (Table 1 notes the CAPA section from which each SMD assessment item was drawn). All CAPA items had intensity ratings, and most symptoms had follow-up fre-

quency and onset questions. Intensity items were used to determine whether a feature had occurred during the preceding 3-month period. Intensity refers to the strength or force of a symptom/behavior and the extent to which it was intrusive, interfering, and generalized across a range of activities. A rating of "2" or higher indicates that the symptom was present at a threshold level of intensity. Frequency items reflect the number of occurrences during the last 3 months.

For the present analysis, chronic irritable, angry, or depressed mood was coded as present if a child was prone to feelings of anger, bad temper, or resentment at least 45 times in the past 3 months (i.e., approximately 3–4 times/week). Similarly, excessive reactivity was quantified as a child having discrete episodes of temper manifested by shouting or name-calling or discrete episodes of excessive frustration or upset, manifested by shouting, crying, or stamping, at least 45 times in the past 3 months. Of the hyperarousal items, only one CAPA insomnia item included a frequency assessment (general insomnia). For all other items (racing thoughts, distractibility, physical restlessness, intrusiveness, and talks excessively), only intensity ratings were available (Table 1). For these items, a symptom was rated as present if it occurred in at least two settings and was uncontrollable at least some of the time during the rating period.

Unlike in Leibenluft et al (2003), here two (instead of three) hyperarousal symptoms were judged as satisfactory to meet SMD criteria because, in the CAPA, the pressured speech item was only asked in the context of episodic mood changes. Because, by definition, children with SMD do not have episodic mood changes, questions on pressured speech, as ascertained by the CAPA, were not relevant to SMD classification. However, an item in the hyperactivity/ADD section did assess the degree to which a child talked excessively. Because children with SMD had not been asked specifically about the presence of pressured speech, in the analysis reported here the threshold for hyperarousal was lowered so that only two positive items were required to meet criteria. In addition, the "talks excessively" item from the hyperactivity/ADD section was included if present. Thus, there were six hyperarousal items, and two were required to be present for the child to meet the hyperarousal symptom of the SMD criteria.

The SMD symptoms, as rated in this study, had to begin before 12 years of age and occur in at least two domains, consistent with Leibenluft et al (2003). The CAPA age-of-onset questions were used to ascertain the former, and questions inquiring whether symptoms occur at home, school, and/or elsewhere were used to determine the latter. Due to the nature of the CAPA items, the third domain "elsewhere" used in the present analysis differed from the "peers" domain used in Leibenluft et al's criteria. Other domains were identical to Leibenluft et al's SMD criteria. As in clinical research studies of SMD, a symptom was considered present if it was endorsed either by the parent or child.

To identify the most severely impaired SMD children (SMD+), criteria were generated with items from the "Incapacity Section" of the CAPA. This group might more closely resemble severely ill children seen in the clinic. Symptoms causing functional impairment from numerous domains were included. Items were drawn from the following incapacity sections of the CAPA: parental relationships, sibling relationships, homework, school life (i.e., school non-attendance, school performance, school suspension/expulsion, and/or teacher relationships), peer relationships, self-care, chores, spare time activities, and/or employment. These items were categorized into three domains: home, school, and

elsewhere. To meet "severe impairment criteria," SMD+ youth had to demonstrate functional incapacity in at least two domains.

As per the exclusionary criteria for SMD outlined in Leibenluft et al (2003), children with substance abuse or dependence (n = 1), a history of mania or hypomania, or with any of the individual symptoms specific to mania/hypomania (episodic elevated/expansive mood, grandiosity/inflated self-esteem, decreased need for sleep, or increased goal directed activity) (n = 18) were excluded from the SMD group.

As described previously (Angold and Costello 1996), DSM-IV Axis I diagnoses were generated by computer algorithms. Because marked irritability in children might represent a symptom of bipolar-spectrum illness, we ascertained whether subjects met criteria for BD–not otherwise specified (NOS), in addition to hypomania or mania. For BD-NOS, we applied a less stringent version of the definition described by Birmaher et al (2006), which requires elated mood plus two associated DSM-IV symptoms or irritable mood plus three DSM-IV associated symptoms, present for a minimum of 4 hours within a 24-hour period. Although Birmaher et al also specifies that episodes include a total of 4 cumulative lifetime days, that information was not available for the present analysis. Thus, modified criteria were used in the present analyses, and a subject was labeled BD-NOS if they had symptoms for at least 4 hours in at least 1 day.

Data Analysis

To answer our first question regarding the lifetime prevalence of SMD, we calculated weighted percentages. Weights inversely proportional to the probability of selection were included in the data analyses to obtain population prevalence estimates. Second, within the SMD group, weighted percentages were computed to determine the point prevalence of Axis I diagnoses at the time youth met criteria for SMD.

Weighted logistic regressions were used to answer our third question (i.e., the association between SMD status in the first wave and Axis I diagnoses in the last wave of data). We employed wave-1 data in this analysis in order to include those youth with the earliest onset of SMD and to identify a homogenous group of children. In addition, this approach allowed us to generate the longest diagnostic prediction from the first to last wave of data. Children who met criteria for SMD after wave-1 were excluded from this analysis. Analyses modeled the association between last wave diagnosis and wave-1 SMD status. To control for the possibility that the diagnosis being predicted in the last wave (e.g., last wave ADHD) might also be present in the first wave, we entered as a covariate whether the Axis I diagnosis was present in wave-1 (e.g., wave-1 ADHD). Gender was also included as a covariate. When SMD was a significant predictor of a specific diagnosis in the last wave, secondary exploratory analyses were performed in which additional diagnostic covariates were entered into the model.

The three analyses (i.e., prevalence, Axis I diagnoses in SMD group, and association between SMD and later diagnoses) were first completed with the complete SMD sample (n = 96). These analyses were then repeated including only the most impaired SMD+ youth (n = 62).

Results

Question 1: Prevalence of SMD

In the sample of 1420 youth, 96 met criteria for SMD at one or more waves, indicating a weighted lifetime prevalence of 3.3% in children ages 9–19 years old. Of the entire SMD sample (n = 96),

Table 2. Demographic Characteristics of Youth With Severe Mood Dysregulation (SMD) and Youth Without SMD (non-SMD) (weighted)

	SMD youth (n = 96)	Non-SMD youth (n = 1324)	p Value
Gender			
Male	77.6%	50.1%	.001
Female	22.4%	49.9%	
Race			
Caucasian	93.3%	89.3%	ns
African American	2.8%	7.0%	
American Indian	3.9%	3.7%	
Mean Age	11.7 ± 2.1	13.9 ± 2.9	.001
	(9.0–16.9)	(8.8–20.6)	

most children were Caucasian (93.3%) and male (77.6%), with a mean age of 11.7 ± 2.1 when first meeting SMD criteria (Table 2). Approximately one-half (n = 54, weighted 49.1%) with SMD met criteria in the first wave (mean age 10.6 ± 1.4 years). Most SMD youth (82.5%) met SMD criteria in only one wave; 13.2% met criteria in two waves, 2.9% met criteria in three waves, and 1.4% met criteria in four waves. When the sample was limited to those who met SMD criteria in two consecutive waves, the weighted prevalence decreased to .4%. Of the SMD youth (n = 96), the majority (n = 62) also met additional severe impairment criteria (SMD+). The weighted prevalence of this most severe subset of SMD+ youth was 1.8%. The demographics of SMD+ children resembled the larger SMD group; the majority of SMD+ youth were Caucasian (91.7%) and male (66.3%), with a mean age of 11.9 ± 2.2 years.

## Question 2: DSM-IV Diagnoses of SMD Youth

Weighted percentages were computed to ascertain co-occurrence of SMD with DSM-IV diagnoses with data from the first assessment during which subjects met SMD criteria. Among youth with SMD, 67.7% met criteria for a concurrent DSM-IV diagnosis.

The most common diagnoses were ADHD (26.9%), conduct disorder (CD) (25.9%), and ODD (24.5%) (Figure 1). Many SMD children also received diagnoses of anxiety (14.7%) and depressive (13.4%) disorders. Because the definition of SMD (Leibenluft et al 2003) excludes children meeting DSM-IV criteria for BD, no SMD children met criteria for BD (I, II, or NOS). In addition, by definition, no SMD children met criteria for substance abuse or dependence. This pattern of results was similar for SMD+ youth (Figure 1).

Question 3: Axis I Diagnosis in Early Adulthood

With logistic regression, weighted odds ratios (ORs) were calculated to document associations between SMD at wave-1 (mean age 10.6 ± 1.4 years) and DSM-IV diagnoses in the last wave (mean age 18.3 ± 2.1 years) (Table 3). Axis I diagnosis at the last wave was regressed on SMD status at wave-1, gender, and whether the Axis I diagnosis being predicted was also present at wave-1. Children with SMD at wave-1 were significantly more likely than non-SMD youth to meet criteria for a depressive disorder at the last wave (OR 7.2, confidence interval [CI] 1.3–38.8, p = .02). In contrast, a depressive disorder at wave-1 (the covariate) did not predict a depressive disorder at the last wave (OR .6, CI .03–14.3, p = .77).

However, youth with SMD at wave-1 were not significantly more likely than non-SMD youth to be diagnosed with ADHD,
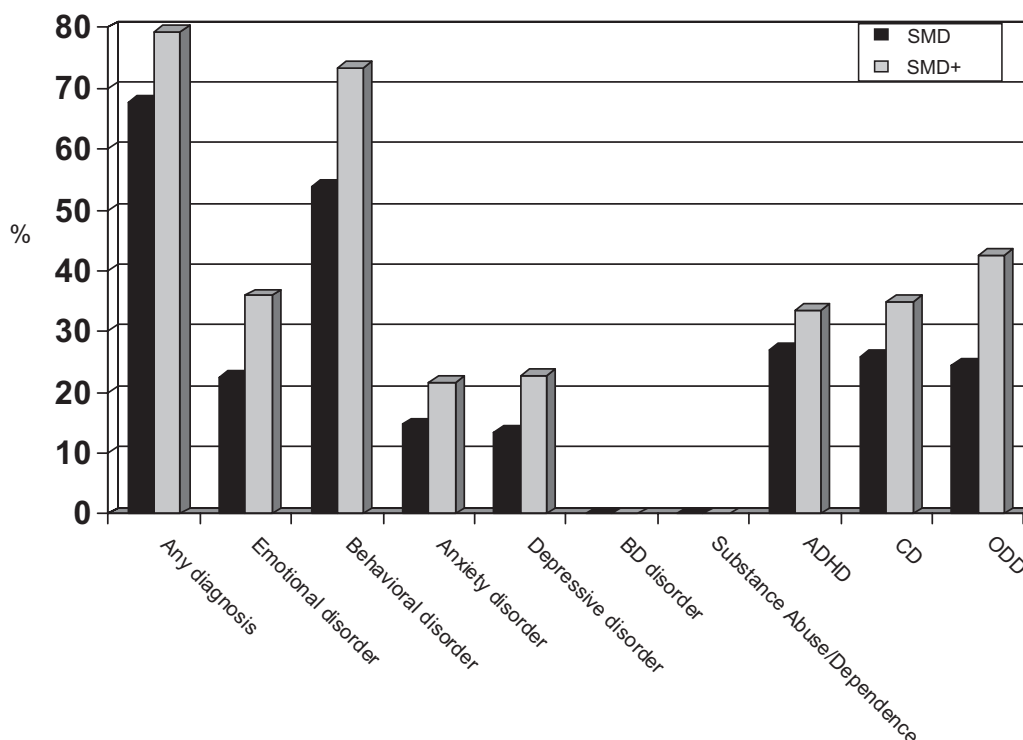
Figure 1. The percent of youth with severe mood dysregulation (SMD) and SMD+ (i.e., a subset of the most severely impaired SMD sample) meeting criteria for each DSM-IV Axis I diagnosis. For youth who met SMD criteria at more than one wave, DSM-IV diagnoses are presented for the first wave at which the child met SMD criteria. Weighted values were used to compute percentages. dx, diagnosis; BD, bipolar disorder; ADHD, attention-deficit/hyperactivity disorder; CD, conduct disorder; ODD, oppositional defiant disorder.

Table 3. Comparison of Axis I Diagnoses in the Last Wave Youth With Severe Mood Dysregulation (SMD) and Youth Without SMD (non-SMD) in Wave-1

Diagnosis	% SMD	% Non-SMD	OR	CI	p Value
Any Diagnosis	38.9	24.5	1.91	.79–4.57	.15
Any Emotional Disorder	9.8	6.1	1.73	.42–7.21	.45
Any Behavioral Disorder	33.1	19.6	1.78	.69–4.59	.24
Any Anxiety Disorder	4.0	4.5	.78	.09–6.59	.82
Any Depressive Disorder[a]	7.8	2.2	7.21	1.34–38.85	.02
Substance Abuse/Dependence	7.8	8.8	.73	.15–3.44	.69
ADHD	21.9	.7	.99	.06–16.94	.99
CD	3.8	1.0	.92	.08–9.97	.95
ODD	2.1	.6	3.94	.20–79.09	.37

The table presents the weighted percentage, odds ratio (OR), 95% confidence interval (CI), and p value, comparing DSM-IV Axis I diagnoses in the last wave in youth who met SMD criteria at wave-1 with those who did not meet SMD criteria at wave-1, while covarying the diagnosis or diagnoses being predicted at wave-1. ADHD, attention-deficit/hyperactivity disorder; CD, conduct disorder; ODD, oppositional defiant disorder.

[a]Major depressive disorder, dysthymia, or depression not otherwise specified.

CD, ODD, substance abuse/dependence, or an anxiety disorder at the last wave. Odds ratios were not computed to compare SMD and non-SMD youth on the prevalence of an eating disorder or BD (BD-I, II, or NOS) in the last wave because of the low prevalence of these diagnoses in both groups.

Follow-up analyses further explored the relationship between wave-1 SMD and final-wave depressive disorders. These included multiple covariates beyond a depressive disorder at wave-1 (i.e., ODD, CD, and ADHD). The association between early SMD and later depressive disorders remained significant, regardless of covariates, none of which individually predicted the prevalence of a depressive disorder in the last wave. These data suggest that SMD exhibits stronger associations with future depressive disorders than do DSM-IV diagnoses occurring concurrently with SMD.

Weighted logistic regressions were also used to examine outcome in the SMD+ group. Also, SMD+ at wave-1 predicted a high risk for a depressive disorder in the final wave (OR 12.0, CI 1.1–133.0, p = .04), while covarying a depressive disorder at wave-1. Early SMD+ did not significantly predict any other diagnoses in the last wave.

Discussion

A syndrome of severe, chronic irritability and hyperarousal (severe mood dysregulation, or SMD) has been recognized as a common problem in clinical settings. However, it remains unclear how to categorize children with this presentation. Specifically, the prevalence, clinical characteristics, and relationship to later psychiatric disorders have not received systematic study. Whereas most research on pediatric bipolar phenotypes relies on clinical samples, it is vital to extend this work to epidemiological settings to overcome referral biases (Cohen and Cohen 1984). Clinical groups provide a biased perspective on most forms of psychopathology. Children with BD or SMD seen in clinics might have higher levels of comorbidity and medication exposure as well as a poorer prognosis than those with BD or SMD ascertained in the community (Lewinsohn et al 1995). Thus, it is essential to study highly irritable children ascertained from a large community-based sample. Employing data from the GSMS, we determined prevalence of SMD in the community, examined its associations with DSM-IV diagnoses, and considered associated risks for early adult disorders. We were particularly interested in the relationship between early SMD and later mood disorders.

We found a lifetime SMD prevalence of 3.3%, which is higher than most estimates of childhood depression (Costello et al 1996, 2002) or BD (Carlson and Kashani 1988; Johnson et al 2000;

Lewinsohn et al 1995; Wittchen et al 1998). Although the prevalence of the most severely impaired SMD+ group of 1.8% was somewhat lower than that of the entire SMD group, this lower prevalence is consistent with other rates of childhood mood disorders. For example, in prior epidemiological work in pre-adolescents, most studies show a prevalence of approximately 2% for childhood depression (see Costello et al 1996 for review) and .1%–1.5% for BD (Carlson and Kashani 1988; Costello et al 1996; Johnson et al 2000; Lewinsohn et al 1995; Wittchen et al 1998). If, in fact, SMD is as common as childhood depressive disorders and BD, then it is crucial for future studies to focus on the pathophysiology of this group.

To examine associations with DSM-IV diagnoses, we computed the point prevalence of Axis I diagnoses occurring concurrent with the first manifestation of SMD. Not surprisingly, SMD youth met criteria for many DSM-IV disorders. However, rates in the present sample (see Figure 1) are lower than in clinical samples of SMD (Dickstein et al 2005), where 93.8% of SMD youth met criteria for ADHD, 84.4% met criteria for ODD, and 46.9% met criteria for an anxiety disorder. This discrepancy suggests that the children identified in the present study might be less ill than those in clinical samples. However, it is important to note that the demographic characteristics of the Dickstein et al (2005) clinical SMD sample (i.e., 78.1% male, mean age = 11.04 years) are similar to those of the SMD group described here (see Table 2).

Controversies regarding pediatric BD largely center on the boundary between BD on the one hand and disruptive behavior disorders on the other (Biederman 1998; Spencer et al 2001). Consistent with this, the most common DSM-IV diagnoses of SMD children were ADHD, CD, and ODD. In addition, over 20% of SMD youth met criteria for an emotional disorder (i.e., an anxiety and/or depressive disorder). Although numerous studies have demonstrated a high rate of anxiety disorders in BD youth (Harpold et al 2005; Johnson et al 2000; Lewinsohn et al 1995; Masi et al 2001), only one study (Dickstein et al 2005) examined rates of anxiety disorders in SMD. Both clinicians and researchers should recognize the extent to which chronically irritable children have significant mood and anxiety symptoms, in addition to their more obvious externalizing disorders. Given that SMD youth do not fit neatly into any one DSM-IV diagnostic category, it is not surprising that this group has been at the center of a diagnostic debate (Leibenluft et al 2003).

Compared with non-SMD children, those with SMD at wave-1 (mean age 10.6 ± 1.4 years) were more likely to meet criteria for a depressive disorder (i.e., MDD, dysthymia, or depression NOS)

during the last wave (mean age 18.3 ± 2.1 years). Severe mood dysregulation predicted high risk for future depressive disorders, independent of any concurrent DSM-IV diagnoses, including depressive disorders, ADHD, ODD, and/or CD. Perhaps surprisingly, SMD in wave-1 predicted later depressive disorder, whereas a depressive disorder at wave-1 did not. The same association with later depressive disorder was also demonstrated in the SMD+ group. This relationship between irritability and later depressive disorders is consistent with the developmental modifications in DSM-IV for MDD, where irritability qualifies as a criterion only in children and adolescents. In addition, the data presented here are consistent with our findings from the Children in the Community study (Leibenluft et al 2006), where we found an association between chronic irritability in early adolescence and MDD in early adulthood.

With regard to bipolar spectrum illness, only one child with SMD later met criteria for BD-II, and none met criteria for BD-I or BD-NOS. In interpreting these data, it is important to note that the criteria used to diagnose BD in the CAPA conform precisely to DSM-IV in all respects and that the prevalence of BD in the GSMS population is quite low. In addition, there was low longitudinal stability of BD. Of the six non-SMD subjects who developed BD, none met BD criteria in the last wave. We also used a less rigorous version of the criteria described by Birmaher et al (2006) to generate a BD-NOS diagnosis; again, there was no association between SMD and BD.

The lack of a relationship between SMD and BD must be interpreted with caution. Due to the low prevalence of BD in this sample, statistical power is limited in analyses of relationships between SMD and BD. In addition, it is possible that some former SMD children with a depressive disorder at the last wave were actually experiencing the onset of BD in the form of a depressive episode and that these children ultimately will develop hypomanic or manic episodes. In fact, by the last wave of data (mean age 18.3 ± 2.1 years), many subjects had still not passed through average age-of-onset of either BD or MDD (Goodwin and Jamison 1990), so it is possible if not likely that some individuals will meet criteria for these illnesses later in life. Moreover, because the CAPA assesses symptoms in the preceding 3 months, it is possible that some youth had experienced hypomanic or manic or depressive episodes before the interview period, but because they were euthymic in the 3 months preceding the interview, they were not identified as having had a hypomanic or manic episode. This would, again, increase the false negative rate of BD and subsequently decrease our ability to detect a potential relationship between SMD and BD. Future researchers should continue to follow SMD youth longitudinally, track depressive symptoms, and develop a more comprehensive understanding of the relationship between SMD and depressive disorders.

Several additional limitations must be considered when interpreting our findings. Most importantly, this was a post hoc analysis of an existing dataset. This is potentially problematic for several reasons. First, the CAPA, the diagnostic interview used in the study, was not designed specifically to assess SMD. It was therefore necessary to modify the SMD criteria in Leibenluft et al (2003) for use in the present analyses. In addition, the majority of hyperarousal symptoms were based on the ADHD section of the CAPA. Although many of these SMD hyperarousal symptoms were assessed accurately with items from the ADHD section of the CAPA, the construct of "pressured speech" was not assessed in the CAPA unless the child had an episodic mood change. Because of this, we modified the SMD criteria to require two instead of three hyperarousal symptoms and substituted an item

assessing the degree to which a child "talks excessively" for the pressured speech item.

Because it was necessary to modify the SMD criteria, it is possible that the SMD youth identified in this study might differ from those seen in clinical settings. Specifically, the children with SMD described here might have less impairment and less severe symptoms than children with SMD seen in the clinic. We attempted to address this limitation by creating the SMD+ subset of most severely ill children within the SMD group. Similar to the entire SMD group (n = 96), the SMD+ subset of children (n = 62) were significantly more likely to develop a depressive disorder in the last wave compared with non-SMD youth, suggesting that SMD and SMD+ resemble each other. Nevertheless, even the SMD+ youth in the current study might differ from those seen in the clinic, because most youth with psychopathology identified in epidemiological studies do not necessarily present to psychiatric clinics, and those who do present to clinics are likely to be at the most impaired end of the clinical spectrum.

Finally, the majority of the youth in the present epidemiological study were Caucasian. It is unclear how the prevalence of SMD would change in a more diverse population study. It is important to note, however, that the study over sampled for American Indian youth. Costello et al (1997) demonstrated no significant differences in the 3-month prevalence of psychiatric disorders in American Indian and Caucasian youth. Nonetheless, researchers are encouraged to include a diverse and ethnically heterogeneous sample in both clinical and future epidemiological studies of SMD.

The present study suggests that chronic irritability and hyperarousal, or SMD, has a relatively high lifetime prevalence of 3.3% in rural and urban youth. When additional severe impairment is required for SMD+, the prevalence decreases to 1.8%. Researchers and clinicians have had difficulty classifying children with SMD, and these youth typically meet criteria for multiple DSM-IV Axis I diagnoses. Whereas behavioral disorders are especially common, anxiety and depressive disorders are also found in a significant number of SMD youth. In young adulthood, youth with SMD in childhood are more likely than comparison subjects to meet criteria for a depressive disorder, suggesting SMD might be an early developmental presentation of depression. Future research should follow individuals with an early SMD symptom pattern longitudinally further into adulthood and should compare clinical, neural, familial, and neuropsychological features of narrow phenotype BD versus SMD children. Finally, treatment trials in SMD youth are particularly important, because one cannot assume that medications shown to be effective in adults or youth with clear DSM-IV BD will be effective in children with SMD.

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