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Early-Onset Bipolar Spectrum Disorders: Diagnostic Issues

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Abstract

Since the mid 1990s, early-onset bipolar spectrum disorders (BPSDs) have received increased attention in both the popular press and scholarly press. Rates of diagnosis of BPSD in children and adolescents have increased in inpatient, outpatient, and primary care settings. BPSDs remain difficult to diagnose, particularly in youth. The current diagnostic system makes few modifications to accommodate children and adolescents. Researchers in this area have developed specific BPSD definitions that affect the generalizability of their findings to all youth with BPSD. Despite knowledge gains from the research, BPSDs are still difficult to diagnose because clinicians must: (1) consider the impact of the child's developmental level on symptom presentation (e.g., normative behavior prevalence, environmental limitations on youth behavior, pubertal status, irritability, symptom duration); (2) weigh associated impairment and course of illness (e.g., neurocognitive functioning, failing to meet full DSM criteria, future impairment); and (3) make decisions about appropriate assessment (differentiating BPSD from medical illnesses, medications, drug use, or other psychiatric diagnoses that might better account for symptoms; comorbid disorders; informant characteristics and assessment measures to use). Research findings

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concerning these challenges and relevant recommendations are offered. Areas for further research to guide clinicians' assessment of children with early-onset BPSD are highlighted.

Keywords

Bipolar disorder; Children; Adolescents; Diagnosis; Phenomenology

Introduction

Does a 7-year-old child who demonstrates significant "rages," has clear evidence of ADHD and a family history positive for depression on the maternal side and bipolar disorder on the paternal side represent a safe candidate for stimulant treatment of his ADHD? What if he also has episodic day-long periods of being excessively giggly, needing little sleep, and appearing more active and talkative than usual? Does this represent a natural variant of childhood or is this a child who is showing early signs of a pediatric bipolar spectrum disorder (BPSD) and who will be at risk for future substance use, legal problems, incarceration, and suicide attempts?

Diagnosis of pediatric BPSDs—Bipolar Disorder-I (BP-I), Bipolar Disorder-II (BP-II), Cyclothymic Disorder (CYC), and Bipolar Disorder Not Otherwise Specified (BP-NOS)—is challenging because there are many important facets to consider (Carlson and Meyer 2006; Findling et al. 2002). In the past 20 years, research interest on early-onset BPSD has grown exponentially (Lofthouse and Fristad 2004). Heightened public interest due to stories and books in the popular press has increased the number of parents specifically asking clinicians whether BPSD is the cause of their children's problematic behavior (Carlson and Youngstrom 2003). Amplified public interest is one of many probable contributing factors to the increase in rate of diagnosis in the past two decades (Blader and Carlson 2007; Harpaz-Rotem and Rosenheck 2004; Moreno et al. 2007). Parents and insurance companies want definitive diagnoses and treatment strategies, but many relevant questions have not been answered by available data from longitudinal, prospective, or cross-sectional studies. We have information about some of the difficult diagnostic questions about early-onset BPSD: appropriate diagnostic criteria, developmental differences in symptom presentation, associated cognitive deficits, impairment in youth not meeting strict criteria, continuity of symptoms, differential diagnoses to rule out, common comorbidities to look for, heritability, informant choice, and reliable measures to screen for or identify BPSD. However, the many unanswered questions about BPSD suggest key areas for future exploration.

For clarity, we will use the term "children" to refer to persons age 12 and younger, "adolescents" for those ages from 13 to 18, and "youth" when referring to a sample with a mixed age group, recognizing there are individual differences in the age of onset for puberty.

Increased Attention to Pediatric BPSD

Diagnosis and course of early-onset BPSD has gained the attention of many mental health researchers and clinicians. Prior to 1980, only 26 journal articles and book chapters about childhood BPSD could be found in MEDLINE and PsycINFO (Lofthouse and Fristad 2004). This increased to 36 in the 1980s, and nearly doubled to 66 in the 1990s. In the first 2 years of this decade alone, 46 more articles were published, indicating an exponential rise in professional attention to the topic (Lofthouse and Fristad 2004). A recent review found 227 publications related to pediatric bipolar disorder (PBD) between 2000 and 2005 (Moreno et al. 2007).

This trend is mirrored by the increased public interest in early-onset BPSD (Egan 2008). A Google search in 2005 yielded 483,000 results for "childhood bipolar disorder" and 248,000 results for "childhood mania" (Leffler and Fristad 2006). In 2009, these numbers increased to 3.25 and 2.93 million, respectively. The Papolos and Papolos book for parents, The Bipolar Child: The Definitive and Reassuring Guide to Childhood's Most Misunderstood Disorder (1999) raised awareness of possible signs and symptoms of early-onset BPSD and triggered intense public interest in the diagnosis of BPSD in youth. It is now in its third revision (Papolos and Papolos 2007). As a result, parents of many children with "manic"-like symptoms began seeking psychiatric care for their children (Carlson and Young-strom 2003). As parents of children with dysregulated mood started asking clinicians if their children had BPSD, and clinicians were exposed to mounting evidence that the diagnosis occurs in youth, the rate of children diagnosed with BPSD rose (Blader and Carlson 2007; Egan 2008; Moreno et al. 2007).

Increasing Rates of Pediatric BPSD Diagnosis

Critics have argued that early-onset BPSDs have become a "fad diagnosis" without science to validate the prevalence, symptom presentation, course, and prognosis (e.g., Hammen and Rudolph 2003), but there are reasonable explanations for an increase in diagnosis of early-onset BPSD. The recognition that children can experience depressive, obsessive compulsive, and panic disorders also led to increases in their diagnosis (Pavuluri et al. 2005). Although overdiagnosis may occur, accurate recognition of a disorder once thought to be very rare in children is responsible for the increase as well (National Institute of Mental Health 2007, para. 4).

The concern about overdiagnosis is partly fueled by disparities in the rates of BPSD in epidemiological studies within community and clinic-referred samples (Table 1). Increased incidence of childhood BPSD and earlier onset of mood disorders have been noted in each generation born after World War II (Chengappa et al. 2003; Gershon et al. 1987; Lasch et al. 1990; Rice et al. 1987). Similarly, in a nationally representative sample of 9,282 participants, prevalence of BP-I or BP-II was significantly higher in younger cohorts: 1.0% in those over age 60, to 3.5% in 45–59 year olds, 4.5% in 30–44 year olds, and 5.9% in 18–29 year olds (Kessler et al. 2005). Increases in recognition of BPSD in adults and youth and high mortality associated with BPSD due to suicide and manic risk-taking behavior probably account for most of the generational differences in BPSD diagnosis (Chengappa et al. 2003). Kessler and colleagues' estimates are higher than those found in a different analysis of the same National Comorbidity Survey, where lifetime prevalence of BP-I was 1.0% and BP-II was 1.1% for adults, with a rate of ~4% for lifetime prevalence of BPSDs combined (Merikangas et al. 2007).

Epidemiological studies of youth have also found disparate rates of manic symptoms. In a community sample of 150 teenagers, Carlson and Kashani (1988) found 7% experienced at least four manic symptoms for a week and 13% experienced at least four manic symptoms for two or more days. A larger community sample found 1% of teens meeting criteria for a bipolar disorder and an additional 5.7% endorsing distinct periods of abnormal mood (Lewinsohn et al. 1995). In contrast, a large epidemiological sample of children, The Great Smoky Mountain Study, found no participants meeting criteria for mania and 0.1% meeting criteria for hypomania (Costello et al. 1996). The Great Smoky Mountain sample was younger than the other two and participants were only being asked about the previous 3 months, whereas the teen studies were examining lifetime prevalence. These methodological differences and the use of different instruments could account for the contrasting rates of bipolar symptoms. Clinic-referred samples have had more consistent rates of diagnosis of BPSD (see Table 1). Prevalence rates of 16 to 20% of a manic episode, thus BP-I, were found in children referred to psychiatric clinics.

The upward trend in diagnosis of BPSD in youth has been found in studies of records from inpatient psychiatric hospitals, outpatient mental health settings, and primary care (Table 2; Harpaz-Rotem et al. 2005; Harpaz-Rotem and Rosenheck 2004; Hunt et al. 2005; Moreno et al. 2007). Using a large database that compiles information from private health insurance companies across the United States to compare mental health diagnoses in patients less than 18 years of age in 1995 and 2000, researchers noted this trend among inpatient and outpatient samples (Harpaz-Rotem et al. 2005). When inpatient psychiatric admission diagnoses were examined, the proportion of child and adolescent inpatients diagnosed with BPSD increased significantly from 11% in 1995 to 18% in 2000 (Harpaz-Rotem et al. 2005). These findings are consistent with an independently collected sample of 391 consecutively admitted adolescent psychiatric inpatients, of whom 20% received a BPSD consensus diagnosis (Hunt et al. 2005).

The trend in inpatient diagnoses is mirrored by outpatient diagnoses and diagnoses of children and adolescents who visit their primary care physicians. Over a 5-year span from 1995 to 2000, private insurance company claims for outpatient services showed a significant increase in BPSD diagnoses; from 0.9% of cases in 1995 to 1.5% of cases in 2000 (Harpaz-Rotem et al. 2005; Harpaz-Rotem and Rosenheck 2004). A significant increase was noted in all age groups and both genders, except in 0–6-year-old females (Harpaz-Rotem et al. 2005; Harpaz-Rotem and Rosenheck 2004). In a national survey, Moreno et al. (2007) found a 40-fold increase in outpatient office-based physician visits for youth due to a primary diagnosis of bipolar disorder; however, this reflects a change in the base rate from 0.0025% in 1994, which many might argue was unreasonably low, to 1% by 2003. In summary, the disparity of rates of BPSD in epidemiological samples and the significant increase in reported BPSD diagnoses suggest that clinicians may benefit from clarification of diagnostic issues in pediatric BPSD.

Higher rates of diagnosis of BPSD in youth could be the result of improved recognition, better insurance coverage for major mental illnesses, decreased stigma, misdiagnosis, and/or other reasons. Clinicians may now detect BPSD in youth they would have previously regarded as having conduct problems or impaired parent–child relationships (Blader and Carlson 2007). When fewer limitations were placed on clinicians about number of appointments or eligibility for coverage of inpatient stays, clinicians may have conservatively assigned a less severe diagnosis. However, when more severe diagnoses are required to obtain better insurance coverage, clinicians may apply a more liberal diagnosis to get services that meet their client's needs. This is not to say that clinicians are fabricating bipolar diagnoses, rather, when diagnosis is ambiguous, the field is pressured to assign a more severe diagnosis for insurance to cover necessary services. In the past, when there was no associated consequence for level of care, clinicians may have forgone the more stigmatizing, severe diagnosis until they were more certain of, or at least willing to contemplate, its veracity. Increased diagnosis may also be a consequence of the wider utilization of the medical model of the BPSD diagnosis in the Diagnostic and Statistical Manual of Mental Disorders—4th ed.—Text Revision (DSM-IV-TR; American Psychiatric Association 2000).

Defining the Diagnoses

Differential diagnosis of mental illness requires clinical acumen; in youth it presents the added challenge of incorporating developmental considerations into decision making. As is the case with most clinical research with youth, findings should be interpreted with an eye to how diagnostic classifications were made. What we know about pediatric BPSD has developed through case studies and opinion papers from treating clinicians and several lines

of cross-sectional and longitudinal research. In each case, a specific definition was used to identify BPSD cases (Leibenluft and Rich 2008).

DSM-IV-TR Definitions

DSM-IV-TR makes few modifications to bipolar diagnoses for children and adolescents. For a Major Depressive Episode and Dysthymia, the primary mood can be irritable rather than sad for children and adolescents (American Psychiatric Association 2000). The minimum duration for CYC can be 1 year in children and adolescents, but is 2 years for adults (American Psychiatric Association 2000). Additional modifications of diagnostic requirements for children and adolescents in the next edition of DSM will be informed by a decade of research findings.

Research Definitions

Two longitudinal studies have provided a great deal of information about the clinical presentation and course of early-onset BPSD. The Phenomenology and Course of Pediatric Bipolar Disorders project, a longitudinal NIMH-funded research project exploring the characteristics and stability of a prepubertal and early adolescent bipolar disorder phenotype (PEA-BP), has provided copious information about the functioning of youth with bipolar disorder in comparison to those with ADHD and matched community control (CC) participants (Geller et al. 1998b). Geller and her colleagues at Washington University School of Medicine followed the first large cohort of youth with diagnosable bipolar disorder. The multi-site Course and Outcome of Bipolar Youth (COBY) study expanded on Geller's research by including a larger sample and widening the diagnostic range of youth to BPSD (BP-I, BP-II, and a carefully defined BP-NOS; Axelson et al. 2006; Birmaher et al. 2006). Demographic, recruitment, and diagnostic characteristics of these samples are summarized in Table 3. Interpreting the findings from these studies requires an understanding of the diagnostic requirements researchers used.

PEA-BP Diagnosis and Inclusion Criteria

Geller and colleagues recruited three groups of participants, those with bipolar (with or without ADHD), ADHD without mood disorder, and CC. For the most part, the inclusion criteria for the BP sample were consistent with DSM-IV diagnosis. Some noteworthy departures from DSM included: (a) irritability as the principal mood state, (b) duration of symptoms, (c) symptoms were tracked separately without distinguishing syndromal episodes, and without attempt to differentiate overlapping symptoms among disorders (allowing for "double counting" of symptoms), and (d) the definition of episodes was modified. They chose to limit their BP sample to participants with elevated mood or grandiosity (Geller et al. 1998b). Children with principally irritable mood, rather than elevated mood, were not included in the cohort even if they satisfied the DSM criterion of having at least four associated symptoms. In DSM-IV-TR, the required duration of a manic episode is ≥7 days; however, Geller and colleagues required a period of ≥14 days or ≥4 h/day for ≥180 days/year (Geller et al. 1998b). In DSM-IV-TR, the required duration of a hypomanic episode is ≥4 days; however, Geller and colleagues required a hypomanic duration of ≥2 months or ≥4 h/day for ≥180 days/year (Geller et al. 1998b). The conservative criteria for duration of 14 days and 2 months, respectively, were "to increase the likelihood of caseness" (Geller et al. 1998b, p. 84). The criteria of ≥4 h/day for ≥180 days/year were added to include participants with ultra-rapid and ultradian cycling (Geller et al. 1998b). This was the first longitudinal study of prepubertal and early adolescent mania; thus, a somewhat conservative approach to identifying cases was appropriate. On the other hand, this sample has unique qualities which may not be generalizable to all pediatric BPSD, including ways to distinguish BPSD from ADHD (discussed below).

As ADHD is commonly comorbid with BPSD in youth, this was not used as an exclusion criterion for the PEA-BP group (Geller et al. 1998b). In this sample, comorbidity with ADHD was high. Males (98.3%) were more likely to have an ADHD diagnosis than females (69.4%; Geller et al. 2000a). Comparison groups with ADHD and CC participants were matched to the PEA-BP group by gender, age, socioeconomic status, and ethnicity. CC participants had to have a Children's Global Assessment Scale (C-GAS) score of at least 70, and have no current or past ADHD, bipolar disorder, or other major mood disorders; ADHD cases could not have any comorbid mood disorder, but other comorbidities were allowed (Geller et al. 1998b).

COBY Diagnosis and Inclusion Criteria

The COBY study was designed to include a wider range of children with bipolar symptoms. COBY's BP-I and BP-II groups included children with primarily elevated mood and irritable mood, consistent with the DSM. Because the criteria for BP-NOS in the DSM-IV-TR (American Psychiatric Association 2000) are vague, these researchers created the following more specific set of minimum criteria for diagnosis (Axelson et al. 2006):

1. clinically significant bipolar symptoms that did not meet DSM criteria for BP-I or BP-II;
2. elated mood plus two or more associated symptoms from DSM-IV-TR or irritable mood plus three or more associated symptoms;
3. a change in functioning; and
4. minimum duration of 4 hours within a 24-hour period and at least four cumulative lifetime days meeting criteria.

CYC was not excluded from the BP-NOS category. This is a departure from DSM-IV-TR criteria, but a reasonable decision given the absence of validity data about the diagnosis of CYC in youth.

Of the 153 participants diagnosed with BP-NOS, 3% were one symptom short of reaching DSM-IV-TR criteria for BP-I or BP-II, and 12% failed to meet BP-II criteria because they had not had a full major depressive episode. The remaining 85% had an adequate number of symptoms with documented impairment to be diagnosed with BP-I or BP-II, but did not have the duration of symptoms for BP-I or BP-II. This is consistent with previous findings that children with BPSD often vacillate rapidly from depressive to manic symptoms or to euthymic mood, experiencing intense and impairing symptoms but not meeting duration criteria for mania or hypomania (Geller et al. 2000b). The COBY cohort includes those children who are difficult to diagnose because they do not have clear, extended episodes of depressed or manic behavior, but an episodic "mixed" presentation with impairment in functioning due to mood.

Broad, Intermediate, and Narrow Phenotypes

Given the controversy in the field, some researchers suggest a different perspective on diagnosis of BPSD using different phenotypes. The suggested narrow phenotype uses DSM-IV-TR criteria except abnormal mood has to be elevated/expansive or grandiose (Leibenluft et al. 2003b). Two intermediate phenotypes are recommended: one with episodes of shorter duration (1–3 days) and one with clearly episodic irritability (Leibenluft et al. 2003b). Both intermediate phenotypes would require meeting the other diagnostic criteria in DSM-IV-TR, and the episodic irritable mood presentation of the intermediate phenotype would technically meet DSM-IV-TR criteria for BP-I. The broad phenotype, sometimes called "severe mood and behavioral dysregulation" (SMD), includes children and adolescents with a wider range of mood and behavior problems including abnormal mood, hyperarousal, and markedly

increased reactivity to negative emotional stimuli present for at least 12 months without symptom-free periods of 2 months duration or clearly demarcated episodes (Leibenluft et al. 2003b). The broad phenotype would exclude children and adolescents who meet criteria for the other phenotypes, have substance use, have symptoms due to a drug or medical condition, or meet specific other diagnoses (e.g., schizoaffective illness) (Leibenluft et al. 2003b). The rates of transition from SMD to adult bipolar illness are not currently known, but one study suggests children with SMD do not convert to BP-I or BP-II more often than the general population, but present higher rates of behavior problems and depression (Brotman et al. 2006). The utility of this classification system has been questioned by some researchers (Staton et al. 2008).

Symptom Presentation

Which Symptoms are Prevalent in Pediatric BPSD?

Notable similarities existed between commonly reported symptoms in PEA-BP participants and those described in adult BPSD (Goodwin and Jamison 1990), including elated mood (89.0%), grandiosity (85.7%), racing thoughts/flight of ideas (70.3%), psychosis (59.3%), and irritability concurrent with elated mood (97.8%; Craney and Geller 2003). A few important differences emerged as well. Compared with adults, the PEA-BP sample had higher rates of cycling (86.8%), mixed mania (55.0%), comorbid ADHD (86.8%), and longer episode duration (Craney and Geller 2003). PEA-BP participants resembled a treatment-resistant, severely ill phenotype noted in adults (Geller et al. 2002a). Although irritable mood was most common in the PEA-BP sample (96.7%), it occurred frequently in the ADHD group as well (71.7%; Geller et al. 1998b).

A meta-analysis including seven studies examined prevalence of symptoms in youth (ages 5–18) with bipolar disorder (Kowatch et al. 2005). Taking into account the sample size and quality of the study, they calculated weighted averages of participants endorsing specific symptoms. For most symptoms there was significant heterogeneity across studies, thus the weighted averages (indicated in parentheses) should be interpreted with some caution. In decreasing order of prevalence, participants endorsed increased energy (89%), distractibility (84%), pressured speech (82%), irritability (81%), grandiosity (78%), racing thoughts (74%), decreased need for sleep (72%), euphoria/elation (70%), poor judgment (69%), flight of ideas (56%), and hypersexuality (38%) (Kowatch et al. 2005). The cardinal symptoms of euphoric mood and irritability were the most heterogeneous across studies. Four of the studies found rates of euphoric mood between 86 and 90%. The other three found 14, 33, and 60%, but these differences could not be explained by quantifiable methodological characteristics. For irritability, some of the heterogeneity was accounted for by subject age and informant, where studies with younger children and parent-report found more irritability (Kowatch et al. 2005). The variability across studies, lack of agreement in the research literature, and overlap between the most common symptoms and other disorders underscore why diagnosing pediatric BPSD presents such a challenge.

How Do Manic Symptoms Look Different in Children?

Clinicians working with children must interpret the information they gather from parents, teachers, and children in light of the child's developmental stage. For example, a child who jumps from one activity to another, has difficulty staying in his seat for meals, has difficulty waiting for others to take their turns during games, and struggles to follow multi-step instructions might be a typically developing child if aged 3. However, if these behaviors are seen in a 10-year-old, a diagnosis of ADHD would be more justifiable. One developmental consideration is whether the child can easily distinguish between reality and fantasy and whether he is describing a real or imagined ability. Playing "super hero" and pretending to

fly around the house running with a pillowcase cape flapping behind him could be part of a normal child's fantasy play. The same situation could reflect grandiosity if the child actually believes he can fly, attempts to do so, or engages in this behavior during class at school. Another important consideration when distinguishing pathological from non-pathological behaviors is whether the behavior is appropriate to the context in which it was displayed (Geller et al. 2002c). Children are typically more behaviorally inhibited at school than they are at home with family or friends because of the task demands and social parameters of the school setting.

When adults become manic, they may spend a lot of money, have sexual indiscretions, or stay awake half of the night working or doing a creative project; however, society and parents place limits on children that prevent them from engaging in these behaviors (see Geller et al. 2002c for additional examples). An adolescent *does not* have a credit card to use for a shopping frenzy. A child *cannot* go out to a club and have sexual liaisons with strangers. An adolescent *can* pack up his baseball gear in anticipation of going to spring training for a national league baseball team because he believes he plays better than anyone currently in professional baseball. A child *can* send a note professing her love for her 3rd grade teacher and telling him that she wants to have his babies. These behaviors, in an adult, are odd but do not represent the same level of pathology as they do when expressed by youth. Several publications provide excellent descriptors of course of illness in children (e.g., Axelson et al. 2006; Carlson 2009; Geller et al. 2002c) and adolescents (e.g., Axelson et al. 2006; DelBello et al. 2007). Additional examples of typical and atypical behavior related to specific symptoms in children are provided in Table 4.

Again, viewing youth behavior through the lens of what is developmentally appropriate, taking into consideration the means available to express internal states, is essential to accurate diagnosis (Consoli et al. 2007). To improve diagnostic clarity across age groups, an expert consensus group recommended using FIND (Frequency, Intensity, Number, and Duration) guidelines to determine if a behavior is a symptom (Kowatch et al. 2005). These guidelines suggest that a diagnosis is warranted if symptoms occur most days in a week (Frequency); are severe enough to cause extreme disturbance in one domain (i.e., home, school, peers) or moderate disturbance in two domains (Intensity); occur three to four times per day (Number); and occur four or more hours a day total, not necessarily contiguous (Duration; Kowatch et al. 2005). Elevated mood can be difficult to diagnose, as well, because demarcating "too happy" for the situation or for "too long" can be a difficult judgment, especially in young children who have not developed the ability to temper their excited moods. Also, parents may view periods of elated mood as a relief from angry and irritable behavior, so they may not describe elated mood as part of the presenting problem unless specifically asked (Youngstrom et al. 2008a).

Does Pubertal Status Make a Difference in Symptom Presentation?

Given questions about the continuity of BPSD across the lifespan, comparison of prepubertal to adolescent manifestations of bipolar symptoms is important. The PEA-BP cohort demonstrated the minimal impact of pubertal status on symptom manifestation—in 36 comparisons made, the only significant difference reported was that prepubertal participants were more likely than postpubertal participants to have comorbid ADHD (98.1 vs. 69.4%, respectively; Geller et al. 2000a). Although hypersexuality was more common in postpubertal participants (60.0%) than in prepubertal participants (30.2%), after correcting for Type I error this finding was not significant (Geller et al. 2000a). Clinically, it is meaningful to note that only one participant reported a history of possible sexual abuse, yet the prevalence of hypersexuality was high in children and doubled in adolescence (Geller et al. 2000).

Using present and lifetime report of parents of adolescents with BPSD, ADHD, or normal controls, Rucklidge (2008) found no strong prodromal indicators specifically for BPSD. Rucklidge (2008) had parents complete the Child Bipolar Questionnaire (CBQ), an 84-item symptom checklist about their children's behavior, in each of three developmental periods: preschool (ages 0–5 years); latency (ages 6–11 years); and adolescence (ages 12–16 years). A preliminary study suggests the CBQ is a reliable, specific, and sensitive measure of bipolar disorder, although further study is needed in samples with fewer cases of BPSD and more diagnostic diversity (Papolos et al. 2006). No differences among the normal, ADHD, and BPSD groups were noted when the participants were preschoolers. Several features differentiated the normal group from the two psychiatric groups during latency: elevated or irritable mood more than 1 h/day; depressed mood more than 1 h/day; racing thoughts; mood swings; and grandiosity (Rucklidge 2008). Only depressed mood for more than 6 h/day differentiated the BPSD from the ADHD group (Rucklidge 2008). In adolescence, many symptoms separated the normal controls from the BPSD and ADHD groups, but only elevated or irritable mood more than 6 h/day and more than 2 days in a row differentiated the ADHD and BPSD groups (Rucklidge 2008). These differences were in the expected direction, with BPSD participants scoring significantly higher on elevated or irritable mood.

The COBY study examined the relation between pubertal status and symptom presentation in children with BPSD, adolescents with childhood-onset BPSD, and adolescents with adolescent-onset BPSD (Birmaher et al. 2009b). Analyses were adjusted for sex, socioeconomic status, and duration of illness. The adolescent groups had more 'typical' and more severe manic symptoms and more melancholic, atypical and severe depressive symptoms (Birmaher et al. 2009b). While depressed, children had more irritability than adolescents. Childhood-onset BPSD was associated with more ADHD and adolescent-onset was associated with panic, conduct, and substance use disorders (Birmaher et al. 2009b).

If only Irritable Mood is Present, Can It Be BPSD?

One controversy in the field has been whether irritable mood should be included as the abnormal mood for children and adolescents. As described above, one of the major longitudinal studies of BPSD did not include participants with principally irritable mood (Geller et al. 1998b). In a meta-analysis of pediatric BPSD, two of the seven studies reported approximately 20% of their sample had irritable mood; the other five reported much higher rates, 77–98% of participants with irritable mood (Kowatch et al. 2005). Irritability is a symptom or correlate of many childhood disorders: disruptive behavior disorders, depression, adjustment disorders, and attention-deficit disorders (Leibenluft et al. 2003a). At intake, in the COBY sample, 10% had irritability without elation, 15% had elation without irritability, and the rest had both elation and irritability (Hunt et al. in press). The character of the irritability differs somewhat between these disorders (Mick et al. 2005). Using the Schedule for Affective Disorders and Schizophrenia for School-Age Children (KSADS) Epidemiologic Version, Mick et al. (2005) compared endorsements of irritability items associated with depression, mania, and oppositional defiant disorder (ODD) sections in children with ADHD with and without mood disorders. Most of the participants endorsed ODD-type irritability (76%), many endorsed depression-type irritability (38%), and some endorsed "super-angry/grouchy/cranky" irritability associated with mania (18%; Mick et al. 2005). Significantly higher percentages of participants with mood disorders endorsed more of all types of irritability than their non-mood disordered peers (Mick et al. 2005). Furthermore, participants with bipolar disorders endorsed significantly more manic irritability (77%) than those with unipolar depression (16%) and no mood disorder (8%; Mick et al.2005). These results suggest that few of the participants with ADHD who do not have bipolar disorder endorsed the extreme irritability noted as "super-angry/grouchy/cranky" and most of those with bipolar disorder do endorse manic irritability. The predictive

value of the manic-irritability item (46%) was similar to the predictive value of the elated/expansive mood item (33%, Mick et al. 2005). Clinicians should emphasize the "extreme, explosive nature" of manic irritability when asking youth and parents about bipolar disorder. Another study examined whether youth diagnosed with bipolar disorder endorsing only irritable mood or irritable and euphoric moods differed in demographic, bipolar symptom (e.g., number of cycles, age of onset, duration of illness), treatment history, and functioning (Wozniak et al. 2005). They found no differences between these groups (Wozniak et al. 2005). This research specifically addressing irritability as a cardinal symptom supported its inclusion, as suggested in the DSM (Mick et al. 2005; Wozniak et al. 2005).

Is Short Episode Duration Unique to Children?

Episode duration is one perceived difference in symptom presentation between children and adults. Researchers have noted that many children experience much shorter periods of manic symptoms lasting from a few hours to a few days, which do not fit into DSM-IV-TR diagnosis requiring periods of at least 4 days for hypomania or 1 week (unless severe enough to warrant hospitalization) for manic or mixed episodes (Geller et al. 2007). Until recently, differences in the symptom duration of child and adult bipolar disorder were thought to provide evidence that they were not the same disorder. Recently outlined spectrum models of adult bipolar disorder, however, are more consistent with the symptom presentations noted in youth (Phelps et al. 2008). Similarly, shorter duration of index mood episodes is consistent with the emerging understanding of the phenomenology of bipolar disorder in adults, who often experience manic periods of less than 1-week duration or hypomanic periods of less than 4 days early in the disorder (Angst et al. 2003; Kramlinger and Post 1996; Suppes et al. 2001). In addition, similarities in impairment of adults with rapid cycling bipolar disorder and children and adolescents with BPSD have lent credibility to the diagnosis in youth (Perlis et al. 2004). Researchers have found more similarities between child and adult bipolar disorder than previously believed (Jerrell and Shugart 2004).

The DSM-IV offers a rapid cycling specifier, defined as at least four mood episodes per year, lasting at least 1 week each, which characterizes approximately 15–54% of adults diagnosed with BPSD (Tillman and Geller 2003). For adults, rapid cycling is correlated with earlier onset of BPSD, more functional impairment, and more time spent in the depressive portion of the cycle (Perlis et al. 2004; Schneck et al. 2004; Suppes et al. 2001). Some researchers have noted that the rate of cycling is related to pharmacological response (Bauer et al. 2008; Goodwin and Jamison 2007; Masi et al. 2006). Schneck et al. (2004) found that participants with rapid cycling, 20% of their sample of adults with BPSD, reported an average of 8 to 9 times as many episodes per year as those without rapid cycling. Rapid cyclers had a striking range of episodes per year, with some adult individuals showing polarity changes (switching from depressed to manic or euthymic or vice versa) every few weeks and others showing polarity changes multiple times per day (Schneck et al. 2004).

Approximately 10–20% of adults and many youth with BPSD experience multiple mood switches per day, which some researchers have called "cycles" (Tillman and Geller 2003), but could be referred to as polarity changes (Schneck et al. 2004) or mood instability (Youngstrom et al. 2008a). Adults with mood instability are likely to be diagnosed with a mixed episode; however, mood instability in children and adolescents has led some clinicians to question the validity of the diagnosis in youth. The finding that many adults also experience this instability of manic and depressive symptoms lends credibility to the diagnosis in youth who do not experience week-long episodes of mania (Bauer et al. 2008; Angst et al. 2003). Further credibility comes from a large cohort of adults with bipolar disorder, where approximately 20% reported their first episode had been mixed (Kogan et al. 2004). This is similar to other recent findings (Perlis et al. 2004), and also is consistent with historical data, where the most common presenting mood episode in adolescents and adults

with bipolar disorder was a mixed episode (Kraepelin 1987). In summary, research on adult BPSD shows more consistency with youth than previously thought, especially in regard to rate of mood shifts. Similarly, adults with mixed episodes or rapid cycling tend to have more impairment than adults with fewer cycles (Phelps et al. 2008).

Impairment

What Areas of Cognitive Functioning Tend to Be Impaired in BPSD?

Pediatric BPSDs are associated with deficits in the following cognitive domains: executive function, working memory, attention, verbal memory, response flexibility, reversal learning, set shifting, processing speed, and visuospatial memory (Green et al. 2007; Kyte et al. 2006; Pavuluri et al. 2009). A recent quantitative and qualitative analysis of existing neurocognitive studies found a large effect size for verbal memory; medium effect size for attention, working memory, executive function, visual memory, and visual-perceptual skills; and small effect sizes for intelligence quotient, reading achievement, and motor speed (Frazier et al. 2007). These authors warn that whether these deficits are unique to pediatric BPSD or present in any psychopathology, the impact of comorbid diagnoses and mood state cannot be determined from the existing data (Frazier et al. 2007). Many of these neurocognitive deficits remain during euthymic states (Pavuluri et al. 2006b) and impact academic achievement (Pavuluri et al. 2006a). In a recent study of 26 youths with pediatric bipolar disorder (PBD) and 17 healthy controls (HC), cognitive deficits were noted in executive function, attention, verbal memory, visual memory, visuospatial perception, and working memory (Pavuluri et al. 2009). Deficits in executive function and verbal memory were compounded by a significantly slower rate of maturation in the PBD group than the HC group over a 3-year period (Pavuluri et al. 2009). Significant deficits of PBD participants to HC participants remained in all six domains at 3-year follow-up, despite the PBD group receiving ongoing, evidence-based pharmacological management (Pavuluri et al. 2009). Neurocognitive deficits are predictive of reading and writing difficulties, which occur in 40–45% of youth with BPSD (Pavuluri et al. 2006a; Wozniak et al. 1995).

Is BP-NOS Less Impairing than BP-I and BP-II?

The COBY researchers had hypothesized participants with BP-NOS would be less impaired than their BP-I and BP-II counterparts. However, they found the three groups did not differ in age of onset, number of years they had experienced manic or depressive symptoms, severity of their worst week of manic and depressive symptoms, comorbidities (except anxiety disorders, which were higher in participants with BP-II than BP-NOS or BP-I), suicidal ideation, and family history of mental illness (see Table 5; Axelson et al. 2006). Participants with BP-NOS were significantly less likely than those with BP-II to have a suicide attempt in their family (Axelson et al. 2006). Participants with BP-NOS were significantly less impaired than participants with BP-I, but similar to those with BP-II in terms of functional impairment, suicide attempts, psychiatric hospitalization, and psychopharmacological treatment (Axelson et al. 2006). The investigators concluded that youth with BP-NOS were more similar to children with BP-I and BP-II than hypothesized.

At 2-year follow-up, 263 participants (60% of the original sample) were available, with over half diagnosed with BP-I, 8% with BP-II, and 35% with BP-NOS (see Table 5; Birmaher et al. 2006). Again, there was more consistency between groups than expected; comorbid diagnoses, demographics, and family history did not vary between groups (Birmaher et al. 2006). Although, participants with BP-NOS were less likely than those with BP-I to have had a lifetime diagnosis of psychosis, the three groups did not differ significantly in their reported weekly psychotic symptoms. The presence of psychotic symptoms upgrades the diagnosis to BP-I automatically, according to the DSM-IV-TR, this practice was not

followed in COBY when psychosis was limited to depressed periods so that course of illness in BPSD could be more explicitly tracked. Although rates of recovery did not differ, median time to recovery, rate of recurrence, and median time to recurrence did distinguish the three groups (see Table 5; Birmaher et al. 2006). Participants with BP-NOS took approximately three times as long to recover from their index episode (Birmaher et al. 2006). Of note, the COBY BP-NOS definition did not exclude cases that would meet DSM criteria for CYC, which would also have a longer episode duration characterized by pervasive, low- or moderate-grade mood disturbance. Participants with BP-NOS were less likely to experience a recurrence than those with BP-II (Birmaher et al. 2006). When weekly symptom status was compared, the three groups did not differ in the percentage of time spent asymptomatic, but participants with BP-NOS were significantly more likely to have subsyndromal symptom status and changed symptom status (e.g., asymptomatic to manic, depressed to manic, depressed to subsyndromal) more often than the other two groups. In fact, approximately 30% of the participants with BP-NOS converted to BP-I or BP-II by the end of 2 years. Taken together, these findings suggest that BP-NOS has unique characteristics of longer time to recovery and recurrence, frequently shifting symptom status, and more time spent with subsyndromal symptoms but not asymptomatic, when compared with BP-I and BP-II.

The COBY study provides substantial evidence that BP-NOS has much in common with BP-I and BP-II, including the degree of functional impairment associated with the worst lifetime presentation. However, there are unique patterns of symptomology in BP-NOS that emerge only when children are examined longitudinally. Additional research with children with BP-NOS will be helpful in understanding the development of bipolar disorders. For clinicians, it is important to keep in mind children with significant mood symptoms of shorter duration than DSM-IV-TR guidelines experience impairment similar to their peers with BP-I and BP-II. It is likely that using psychotherapy techniques proven helpful to children with BP-I and BP-II and their families would be similarly useful for children with significant mood symptoms who do not meet diagnostic criteria.

Does a Diagnosis of Childhood Bipolar Disorder Predict Bipolar Disorder and/or Impairment in Adulthood?

As many as 60% of adults with bipolar disorder report that many of their symptoms began when they were children or adolescents (Chengappa et al. 2003; Hirschfeld et al. 2003; Leverich et al. 2007; Perlis et al. 2005). One study suggests that youth exhibiting conduct problems are much more likely to develop BP-II in young adulthood (Endrass et al. 2007). However, only three prospective studies have examined whether manic symptoms noted in youth continue into young adulthood (Geller et al. 2008; Birmaher et al. 2006; Lewinsohn et al. 2000). Lewinsohn et al. (2000) followed the sample of high school students with manic symptoms into young adulthood; 53% of those diagnosed in high school with bipolar disorder either failed to recover or experienced a recurrence by age 24. BPSDs were associated with marked impairment at home, at school, and with peers, and with problems generally persisting into young adulthood (Lewinsohn et al. 2000).

One study found manic symptoms showed little continuity over a 2-year span with only 1 of the 25 diagnosed with mania at baseline continuing to meet criteria and 3 of the 99 diagnosed with only ADHD at baseline developed manic symptoms (Hazell et al. 2003). Baseline mania was predictive of lower functioning 2 years later (Hazell et al. 2003). Diagnoses were made based on youth self-report on computerized, structured interviews, and parent-report was not collected (Hazell et al. 2003). Lack of insight and poor agreement among parents, children, and clinicians ratings may explain this finding. Longitudinal follow-up of the PEA-BP sample demonstrates ongoing impairment from BPD, including low rates of recovery, and among those who do recover, high rates of relapse (see Table 6

for a summary of recovery and recurrence rates from 6-month to 8-year follow-up; Geller et al. 2004, 2007). Of note, rates of "recovery" are artificially high, as participants who met full criteria for major depressive disorder (MDD) but not mania were considered "recovered" because they no longer met full criteria and severity for mania/hypomania (Geller et al. 2000b). By the 8-year follow-up 44% of those 18 years or older had already experienced manic episodes in young adulthood.

Taken together, these studies suggest children with mood problems grow into adolescents and adults with mood problems and associated impairment. Clear signs of continuity into adulthood of a bipolar diagnosis occur in approximately half of those diagnosed with PBD; longer follow-up, taking treatment histories into account, will help to shed light on what happens to the other half. More importantly, children with bipolar disorder experience impairment in adolescence and young adulthood at home, at school, with peers, and presumably in the workforce. Because there is little to no risk associated with learning about mood disorders and building mood management and interpersonal skills in children and these skills are likely to be helpful to adolescents and adults struggling with mood problems, incorporation of these topics into psychosocial treatment when mood is a concern appears warranted.

Assessment

What Medical and Medication History Should Be Collected?

Medical conditions, such as hyperthyroidism, head injury, multiple sclerosis, systemic lupus erythematosus, temporal lobe epilepsy, and hormonal imbalances, can mimic mood disorders (Kowatch et al. 2005). These possible explanations for bipolar symptoms should be ruled out before a BPSD diagnosis is given. In addition, abuse of stimulants such as amphetamines and cocaine can simulate mania. In fact, for adults, diagnostic changes to and from BPSD were significantly more common among substance abusers than non-abusers, suggesting that substance abuse can often lead to diagnostic confusion or trigger a mood diathesis (Chen et al. 1998). In a recent study conducted at a community-based substance treatment program, 12 of 21 patients with a previous BPSD diagnosis met criteria for substance-induced mood disorder rather than BPSD when interviewed by a psychiatrist using the Structured Clinical Interview for Diagnosis (Stewart and El-Mallakh 2007).

History of medication use and its relation to behavior problems is a critical aspect of the comprehensive medical history. Stimulant medications (e.g., DelBello et al. 2001) and antidepressants (e.g., Faedda et al. 2004) are suspected of inducing mania in predisposed individuals, although recent data suggest this may not be the case (Pagano et al. 2008; see Joseph et al. in press for a critical review of the SSRI antidepressant literature). History of stimulant treatment was associated with earlier age of onset of bipolar disorder (DelBello et al. 2001) and a more severe course of hospitalization, operationalized as length of hospitalization, number of seclusion and restraint orders, and number of medications administered on an as needed basis (Soutollo et al. 2002). Stimulant rebound, the daily increase in irritability noted as stimulant medication wears off, can mimic pediatric BPSD (Sarampote et al. 2002). Although stimulant rebound has not been linked to the child receiving a comorbid diagnosis of BPSD (Carlson and Kelly 1998; Galanter et al. 2003), no studies have followed children over time to determine if the stimulant rebound side effect correlates with a future diagnosis of BPSD.

History of antidepressant treatment has not been linked with age of onset of BPSD symptoms (Geller et al. 1994), but antidepressant-induced hypomania accurately predicts future development of BPSD (Strober and Carlson 1982). A retrospective case review of 82 children with BPSD found antidepressant-induced mania in 58% of the children exposed to

an antidepressant and stimulant-induced mania in 18% of the children exposed to a stimulant (Faedda et al. 2004). In a sample of 52 youth with BPSD and a parent with BPSD, 50% experienced antidepressant-induced mania and an additional 14% experienced a negative reaction to antidepressants, usually extreme irritability without associated manic symptoms (Baumer et al. 2006). Participants who had experienced antidepressant-induced mania were more likely to have BP-I and more comorbidities at the time of the study (Baumer et al. 2006). Furthermore, 25% of participants exposed to antidepressants reported onset of suicidal ideation in the first 3 months after starting the medication (Baumer et al. 2006). Careful medical and drug use histories are critical to determining whether a BPSD is present or highly likely to develop.

How are BPSD Different from ADHD and Other Behavior Disorders?

There is substantial overlap between symptoms and associated features of BPSD and ADHD including hyperactivity, accelerated speech, and distractibility, making differential diagnosis a challenge (Biederman et al. 1998a; Carlson 2009). Additionally, ADHD, disruptive behavior disorders, and BPSD are highly comorbid (Geller et al. 2002b; Kowatch et al. 2005). Rates of comorbidity vary between studies with 11–88% of youth with BPSD having ADHD, 6–88% having ODD, and 6–9% having conduct disorder (Chang et al. 2000; Kowatch et al. 2005). It is critical, when determining whether a disorder is comorbid or if observed symptoms are indicative of mood problems, to note whether symptoms are only present during a mood episode or omnipresent but exacerbated during mood episodes (Leibenluft and Rich 2008).

When comparing the first 60 participants in the PEA-BP and ADHD groups, every manic symptom except high energy and distractibility was significantly more common in PEA-BP participants (Geller et al. 1998b). PEA-BP participants were significantly more impaired (as measured by C-GAS scores) than the ADHD group (Geller et al. 1998b). The PEA-BP group had higher problem behavior subscale scores according to parents (Child Behavior Checklist, CBCL) and teachers (Teacher Report Form) (Geller et al. 1998a). Psychosocial functioning at school, at home, and with peers was more impaired in the whole PEA-BP group ($n = 93$) compared to the CC group and frequently, to the ADHD group (Table 7; ***Geller et al. 2000).

Careful assessment of symptoms, especially the pattern of symptom onset and remission, is needed to differentiate BPSD from other psychiatric disorders. One study found that elated mood, episodic grandiosity or unstable selfesteem, decreased need for sleep, racing thoughts/flight of ideas, and hypersexuality appear much more often in children with BPSD than in those with ADHD (Geller et al. 2002c). In this sample, however, participants with BP had to have elated mood or grandiosity as cardinal symptoms (Geller et al. 2002c). The cyclic nature of BPSD symptoms as opposed to the chronic and consistently present symptoms of ADHD can also aid in differential diagnosis (McClellan et al. 2007). Pediatric BP can be diagnosed in children with a single episode that lasts more than 12 months, a chronic presentation (Biederman et al. 2005). Although controversial, the explosive nature of the irritability can be used to differentiate youth with ADHD from those with BPSD (Mick et al. 2005). The presence of associated symptoms (e.g., decreased need for sleep, racing thoughts, grandiosity, and engagement in risky behaviors) sets apart youth with BPSD (Mick et al. 2005). A longitudinal framework for assessment is needed to determine whether BPSD, ADHD, or both are causing the child's difficulties (McClellan et al. 2007). Similarly, determining whether disruptive behaviors cycle with mood or are omnipresent can help differentiate BPSD and disruptive behavior disorders, as they can appear similar in a cross-sectional snapshot. Cross-sectional assessment is insufficient to determine the extent to which disruptive behaviors and mood symptoms overlap (Duffy et al. 2007). Diagnostic accuracy requires careful attention to symptoms across time and situations (Chen et al.

1998). A “streaming video” approach that allows clinicians to determine which symptoms co-occur cyclically and which ones are omnipresent is essential to differentiating the conditions.

What Do I Need to Ask About Family History?

Clinicians routinely ask about mental health history during diagnostic assessments, this is particularly important when BPSD is suspected. Offspring of parents with bipolar disorder (OBPs) are at elevated risk for mood disorders specifically, and psychopathology in general (e.g., Birmaher et al. 2009a; Henin et al. 2005; Lapalme et al. 1997; Radke-Yarrow and Zahn-Waxler 1990). OBPs are at elevated risk for BPSD (10–33% have a diagnosable BPSD) and other disorders (50–78% have a psychological disorder; Chang et al. 2000). Children with BPSD often have other family members with mood disorders. In addition to asking about specific diagnoses, clinicians should consider asking about specific symptoms. The Family History Screen (Weissman et al. 2000) includes questions about whether a relative has had periods of elevated mood, decreased need for sleep, or excessive involvement in risky activities (e.g., buying sprees, sexual indiscretions, foolish business investments) where people worried about them or it caused functional impairment. Clinical experience has found some families deny mood diagnoses and endorse many specific symptoms causing functional impairment. Other families report many members with bipolar diagnoses, but do not endorse any of the specific symptoms. The increased attention to BPSD in the popular press may account for some of these discrepancies, but lack of knowledge about specific behavior by family members or confusion about family members’ diagnoses may be responsible also.

Who Should Be Asked About Symptoms?

Different standards for what constitutes normal and abnormal behavior, as well as different task demands across settings, might account for some inconsistencies in parent, teacher, and child reports (Kahana et al. 2003; Tillman et al. 2004). There is significant disagreement among parent-, teacher-, and child-reported symptomology with kappa coefficients being in the poor to fair range (Tillman et al. 2004). Arguably the convergence of reports from several informants greatly increases the certainty of a bipolar diagnosis (Youngstrom et al. 2006). Neither children nor individuals experiencing a mood episode tend to be reliable reporters of mood symptoms due to limited insight (Youngstrom et al. 2004). Thus, information about children’s symptoms is collected from parents and teachers in addition to the children themselves.

BPSD is a highly heritable disorder (e.g., Faraone et al. 2003; Hodgins et al. 2002). Heritability can aid in diagnosis, as a positive family history of BPSD or mood disorders lends support for a child’s BPSD diagnosis. However, as in anxiety disorders and ADHD, when parent informants have the disorder, their active symptoms may distort the perception of their child’s symptoms (Diaz-Caneja and Johnson 2004; Youngstrom et al. 2006). Due to their own negative mental set, parents with a history of depression or anxiety are more likely to see problems in a child’s behavior and respond more negatively to commonplace misbehaviors or rate behavior problems as more severe (Chilcoat and Breslau 1997; Youngstrom et al. 1999; Youngstrom et al. 2000). This bias has been debated in the literature and some findings indicate the opposite, that is depressed mothers are more accurate reporters of their children’s feelings and behavior (Biederman et al. 1998b; Conrad and Hammen 1989; Ingersoll and Eist 1998; Richters 1992; Youngstrom et al. 2004a, b). There is some evidence that parents with a history of mood disorder may be more familiar with the symptoms and better attuned to the presentation, increasing their sensitivity. Overall, the validity coefficients for parent-report of mood symptoms (whether indexed as correlation or area under the curve from Receiver Operating Characteristic analyses) are

substantially larger than those for youth self-report or teacher-report about mood symptoms (Geller et al. 1998a; Youngstrom et al. 2004b); this holds true even when the parent is currently experiencing mood states that partially compromise the accuracy of their report (Youngstrom et al. 1999). Ideally, parents should be asked about their child's mood symptoms when they are not actively manic or depressed. The intense emotions that the parent may be experiencing as a part of their own mood state are likely to intensify any parent–child conflicts leading the parent to report worse functioning for the child (Bozikas et al. 2006). Reports from other caregivers and teachers can be used to corroborate parents' reports.

Which Assessment Instruments Are Helpful in Identifying BPSD?

Clinician-Rated Instruments—Unstructured clinical interviews are at the risk of missing BPSD diagnoses because clinicians do not always remember to ask about the symptoms. Semi-structured interviews, like the K-SADS, have proven effective in diagnosing BPSD, but their length is often prohibitive in clinical settings (Frazier et al. 2007). Clinician-rated measures of mood symptoms provide a succinct way to examine bipolar symptoms. The Young Mania Rating Scale (YMRS; Young et al. 1978), K-SADS Mania Rating Scale (KMRS; Axelson et al. 2003), and Children's Depression Rating Scale-Revised (CDRS-R; Pozanski et al. 1984) have shown promising psychometric properties (Frazier et al. 2007). Frazier et al. (2007) investigated the diagnostic efficiency of these three measures in a sample of 1,000+ youth (ages 4–17) with BPSD. They found that the YMRS and KMRS contributed significant unique variance to the prediction of bipolar disorder, but the CDRS-R did not (Frazier et al. 2007). The unique contributions to variance could occur because the YMRS includes items not relevant to DSM-IV diagnosis of mania and neglects some DSM-IV symptoms, whereas the KMRS is more focused on DSM-IV symptoms. The YMRS and KMRS had similar diagnostic efficiency across the age groups, indicating that they are equally useful in youth ages 4–17 (Frazier et al. 2007). The authors recommend using both instruments as they contributed unique variance to diagnostic efficiency, and use of the KMRS as a better indicator of symptom severity if only one measure is used (Frazier et al. 2007). One limitation of this study is that the clinician completing the YMRS and KMRS had completed the entire K-SADS with the participants. The utility of the YMRS and KMRS following a traditional clinical interview and in settings with lower rates of BPSD requires further study.

Parent-Rated Instruments—The diagnostic efficiency of six questionnaires was calculated for a sample of 318 youths aged 5–10 and 324 youths aged 11–17 (Youngstrom et al. 2004). Of the six measures, three were completed by parents, two by older youth, and one by teachers. The Externalizing Behaviors scale of the 1991 versions of the Achenbach scales, which are general measures of problem behaviors completed by parents (CBCL), youth (Youth Self-Report), and teachers (Teacher Report Form), were three of the measures. The Adolescent General Behavior Inventory (A-GBI; Depue et al. 1989) and Parent General Behavior Inventory (P-GBI, Youngstrom et al. 2001) are 73-item questionnaires specifically targeting depressive, hypomanic, manic, and mixed mood symptoms. The final measure was an 11-item adaptation of the YMRS into a parent-completed questionnaire (P-YMRS; Gracious et al. 2002). In the younger sample, the CBCL, P-GBI, and P-YMRS performed equally well (Cohen's $d = 1.3–1.4$) and significantly outperformed TRF (Cohen's $d = 0.2$) (Youngstrom et al. 2004b). Yet, the effect size noted in parent-ratings is less than half of that of clinician-rated YMRS (Cohen's $d = 3.3$) (Youngstrom et al. 2004b). In the older sample, parent-report outper-formed youth- and teacher-report. Effect sizes for parent-reports were similar to those found in the younger group (Cohen's $d = 1.1–1.4$) but the P-GBI performed significantly better than the CBCL in the older group (Youngstrom et al. 2004b). The A-GBI and YSR had effect sizes similar to TRF (Cohen's $d = 0.7$) in the older sample (Youngstrom

et al. 2004b). Teachers were significantly better at identifying bipolar disorders in 11–17 year olds than in 5–10 year olds (Youngstrom et al. 2004b).

Further information can be gathered from the likelihood ratios of the odds of bipolar diagnosis given low, moderately low, neutral, moderately high, high, and very high scores. Rather than providing sensitivity and specificity for a specific score, Youngstrom et al. (2004b) give odds ratios for having a bipolar diagnosis given scores on the measures. For instance, for the younger group, a CBCL externalizing score of 58 to 67 corresponded to a likelihood of 0.47, whereas a score of 78 to 81 corresponded to a likelihood of 3.15 (Youngstrom et al. 2004b). On the P-YMRS, a moderately low score (7–13) is associated with a likelihood of 0.48 and a high score (30–34) is associated with a likelihood of 6.94. The mood-specific measures (i.e., P-YMRS, P-GBI, A-GBI) tended to have higher odds ratios than the more general Achenbach scales (Youngstrom et al. 2004b). A short form of the P-GBI with only ten items discriminated bipolar disorder from unipolar depression and attention-deficit hyperactivity disorder in an academic outpatient medical center clinic (Youngstrom et al. 2008b).

A recent study of the CBCL profile in children with bipolar disorder, major depression/anxiety disorders (MDD/ANX), disruptive behavior disorders (DBD), and healthy control (HC) participants showed poor sensitivity and specificity of the CBCL using a two standard deviation cutoff (Diler et al. 2009). The CBCL-Pediatric Bipolar Disorder phenotype (CBCL-PBD) was the sum of the Anxiety/Depression, Attention Problems, and Aggressive Behaviors scales (Diler et al. 2009). Significantly more children with BPSD (58.6%) scored more than two standard deviations above average, but 41.4% of them did not. Substantial numbers of children in the other groups also scored above this cutoff: 22.8% of MDD/ANX, 37.0% of DBD, and 10.9% of HC participants (Diler et al. 2009). In this sample, the Externalizing Problems score was elevated in the DBD and BPSD groups (Diler et al. 2009). The authors argue CBCL scores can be used as one indicator of whether a child should be assessed further for severe pathology including BPSD, but should not be used independently to make a BPSD diagnosis (Diler et al. 2009).

Treatment

Although a thorough review of the treatment literature is beyond the scope of this article, one of the reasons for striving for diagnostic clarity is using the diagnosis to select appropriate treatment strategies. The majority of youth with pediatric BPSD will benefit from pharmacotherapy, to that end relevant practice parameters and medication algorithms have been developed (Kowatch et al. 2005; McClellan et al. 2007; Pavuluri et al. 2004b). Although medications decrease core symptoms of BPSD, psychotherapy is needed to teach compensatory skills necessary to address psychosocial impairment and help parents advocate on behalf of their children (McClellan et al. 2007). Researchers have data supporting the use of family-based psychoeducational psychotherapy (PEP) for adolescents, Family-Focused Treatment (Miklowitz et al. 2006) and children, Child- and Family-Focused Cognitive Behavioral Therapy (Pavuluri et al. 2004a) and PEP (Fristad 2006; Fristad et al. 2002; Fristad et al. in press). The programs differ in their emphasis on individual therapy, group therapy, and family therapy (Leibenluft and Rich 2008). These programs incorporate education about bipolar disorders for parents and youth (e.g., symptoms, course, treatment options, associated problems in functioning at home, at school, and with peers), skill building (e.g., coping, relapse prevention, communication, problem-solving), and consultation about advocacy in schools, with treatment providers, and with insurance carriers (Fristad et al. in press; McClellan et al. 2007; Miklowitz et al. 2006; Pavuluri et al. 2004a; Young and Fristad 2007). These psychoeducational approaches provide a foundation that further family or individual psychotherapy can build on to address emerging concerns.

Family treatment goals may include improved communication about mood states, expectations, and frustrations; helping families with mood disorders in households where multiple family members have mood disorders not get caught up in one another's mood swings; and fostering independence and insight in youth with pediatric BPSD.

Other promising approaches include Interpersonal Social Rhythm Therapy (IPSRT; Frank et al. 1994) and Dialectical Behavior Therapy (DBT; Goldstein et al. 2007). The theoretical framework underlying IPSRT includes research suggesting people with BPSD have vulnerability in the circadian system and are prone to neurotransmitter dysregulation (Hlastala and Frank 2006). Clients learn to reduce the number, severity, and negative impact of interpersonally based stressors by addressing interpersonal issues (Hlastala and Frank 2006). They also learn the importance of the interplay of biological forces and interpersonal situations triggering a mood episode (Hlastala and Frank 2006). Clients are encouraged to plan for social transitions and maintain circadian routine. Similarly, DBT with adolescents showed promise in a 1 year open pilot with ten adolescents (Goldstein et al. 2007). DBT with adolescents combined family skills training (e.g., mindfulness, distress tolerance, emotion regulation, interpersonal effectiveness), individual therapy (problem solving about target behaviors prioritized with the DBT hierarchy of treatment targets), telephone-based skills coaching, and keeping diary cards (Goldstein et al. 2007). Adolescents showed improvement in emotion regulation, depressive symptoms, suicidality, and non-suicidal self-injurious behavior (Goldstein et al. 2007). Clinical trial data are not yet available for IPSRT and DBT with adolescents.

Areas for Future Research

Many questions remain in the field of pediatric BPSD regarding diagnosis and treatment. Diagnosis, particularly in very young children, needs further study. Some research suggests preschool children can have BPSD (Luby and Belden 2006), but most of these children more closely resemble SMD than DSM definitions of BPSD (Leibenluft and Rich 2008). Determining whether a preschooler's joyful behavior is euphoric, indicative of mania, or just youthful exuberance is particularly difficult. Additional research on how BPSDs are being diagnosed in children could help researchers understand the ambiguities that remain for most clinicians. Further exploration of assessment methods and dissemination of the existing methods to more clinicians outside of academic medical and mental health centers is warranted.

Differential diagnosis may be aided by research into neurocognitive correlates and genotypes associated with BPSD. As technology in neuroimaging advances, our understanding of the biological underpinning and correlates of BPSD will expand if we continue examining youth. Many studies have used offspring of bipolar parents as a target population to examine risk factors in the development of BPSD. Understanding the connection between risk factors for BPSD and its development will be important if we are to insure early intervention, which should improve the course of illness. Neurobiological and genetic research holds promise as approaches to early identification of BPSD or those at highest risk for BPSD.

Another possible means of early identification of BPSD comes from a growing body of scientific evidence that a large number of children suffer from elevated symptoms of mania (ESM; Wozniak et al. 1995; Carlson and Youngstrom 2003) with accompanying impairment at home, at school, or with peers (Findling et al. 2005; Nottelmann et al. 2001). Lewinsohn et al. (1995) found 5.7% of their community sample reported having distinct periods of abnormally and persistently elevated, expansive or irritable mood, but did not meet DSM criteria for a bipolar disorder. A large proportion of parents of children on a psychiatric

inpatient unit endorse ESM (67% of sixty 5–12 year olds), although many of the children did not have a bipolar diagnosis (Carlson and Kelly 1998). Regardless of their diagnoses at the time of assessment, children with ESM suffered from high degrees of psychopathology and from pronounced psychosocial dysfunction (Birmaher et al. 2006; Carlson et al. 1998). Inpatient children with ESM had poorer self-control and longer hospitalizations than those without manic symptoms (Carlson and Youngstrom 2003). In a sample of offspring of bipolar parents, participants with ESM did not differ significantly from participants with BP on parent-rated internalizing and externalizing symptoms (Findling et al. 2005). Recruiting a clinic-referred sample of children with ESM would be a different approach to identifying and following a sample of children at high risk for the development of bipolar disorder, one that would extend the knowledge from existing high risk offspring of bipolar parent studies.

Current treatment models for pediatric BPSD are not widely disseminated. Although pediatric BPSD is not a common illness, understanding the principles behind evidence-based treatment for it would be beneficial for clinicians who work with children and families. Additional controlled clinical trials may be necessary to prove efficacy before such effectiveness research can be undertaken.

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Appendix

Appendix:

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Table 1

Rates of PBD in epidemiological and clinic-referred samples

Publication	*N*	Ages & criteria	Prevalence	Description
Epidemiological studies				
Carlson and Kashani (1988)	150	14–16 year olds in a community sample	Lifetime	13% (*n* = 20) endorsed ≥4 manic symptoms, ≥2 days duration; 11 of these 20 reported ≥7 days duration
Lewinsohn et al. (1995)	1,709	14–18 year olds in high schools of the Pacific Northwest	Lifetime	Lifetime 1% (*n* = 18) met criteria for a bipolar disorder;
				An additional 5.7% (*n* = 97) reported a distinct period of abnormally and persistently elevated, expansive or irritable mood but did not meet DSM criteria for a bipolar disorder
Costello et al. 1996	1,015	9–13 year olds in the rural Great Smoky Mountains region	3 months	0 met criteria for mania, 0.1% met criteria for hypomania
Kessler et al. 2009	347	13–17 year olds in the National Comorbidity Survey Replication-Adolescent (NCS-A)	Lifetime	2.3% bipolar I or II; 4.3% other bipolar spectrum based on CIDI; prevalence of all bipolar spectrum was 6.2% based on KSADS and 6.6% based on CIDI
Clinic-referred samples				
Wozniak et al. 1995	262	<12-year-old children consecutively referred to a pediatric psychopharmacology clinic	Lifetime	16% had experienced at least 1 episode of mania meeting DSM-III-R criteria
Hazell et al. 2003	151	9–13-year-old boys with ADHD recruited from psychiatry clinics or media	Lifetime	20% had experienced at least 1 episode of mania meeting DSM-III-R criteria

Notes: CIDI, World Health Organization Composite International Diagnostic Interview, Version 3.0; KSADS, Schedule for Affective Disorders and Schizophrenia for School-Age Children

Table 2

Diagnostic trends in inpatient, outpatient, and primary care settings according to national databases compared over time

Publication: source of database	Description	Time 1 1996	Time 2 2004
Blader and Carlson (2007): Nationally representative sample of hospital discharges	% of discharges with a primary psychiatric diagnosis		
	Children	7.5	9.7
	Adolescents	13.6	18.9
	Adults	6.5	≈6.5
	% of primary psychiatric diagnosis discharges with a bipolar diagnosis		
	Children	10.0	34.1
	Adolescents	10.2	25.9
	Adults	9.9	14.9
	Population-based rates of discharges with a primary psychiatric diagnosis per 100,000 people		
	Children	139	214
	Adolescents	498	789
	Adults	1050	1085
	Population-based rates of primary psychiatric diagnosis discharges with a bipolar diagnosis per 100,000 people		
	Children	14	73
	Adolescents	51	204
	Adults	104	162
		1995	2000
Harpaz-Rotem et al. (2005) and Harpaz-Rotem and Rosenheck (2004): Private health insurance company claims	% of inpatients with a bipolar diagnosis	11.0	18.0[a]
	% of outpatients with a bipolar diagnosis	0.9	1.5[a]
	Outpatient males		
	0–6 years	0.2	0.6[a]
	7–12 years	0.4	1.0[a]
	13–17 years	1.4	1.9[a]
	Outpatient females		
	0–6 years	0.2	0.6
	7–12 years	0.4	1.0[a]
	13–17 years	1.8	2.6[a]
		1994–1995	2002–2003
Moreno et al. (2007): Representative sample of office-based physicians	% of mental health-related visits with a primary bipolar diagnosis	0.4	6.7
	Population-based rates of office-based visits with a primary bipolar	25	1003

Publication: source of database	Description	Time 1 1996	Time 2 2004
	diagnosis per 100,000 youth		

[a] $p < .001$

Table 3

Participant characteristics in longitudinal studies of early-onset bipolar disorder

	PEA-BP ***N*** **= 93**	**COBY** ***N*** **= 438**
Age range	7 to 16	7 to 17–11
Mean age (SD)	10.9 (2.6)	13.0 (3.1)
% Male	61	53
% White	89	82
Referral source		
Pediatric and/or psychiatric outpatient clinics (%)	100	65
Inpatient units (%)		16
Advertisements (%)		11
Physician referrals (%)		8
Diagnosis		
BP-I (%)	89	58
BP-II (%)	11[a]	7
BP-NOS (%)	0	35
Mean age of onset (SD)	7.3 (3.5)	9.3 (3.9)
Mean duration of disorder (SD) (years)	3.6 (2.5)	3.3 (2.5)
Comorbidity with		
ADHD (%)	86.0[b]	59.8
ODD (%)	77.9[b]	39.5
CD (%)	12.8[b]	12.8
Any anxiety disorder (%)	17.4[b]	39.0
Psychosis (%)	60.2	27.6
Functional Impairment at Intake, C-GAS mean (SD)	43.3 (7.6)	54.6 (12.1)
Suicidal ideation (%)	24.7[c]	76.2
Suicide attempt (%)		30.7

PEA-BP Prepubertal and early adolescent bipolar phenotype

COBY Course and outcome of bipolar youth

[a] In longitudinal follow-up eight of the ten participants with hypomania, developed mania, thus only two participants retained a diagnosis of BP-II throughout the study

[b] Comorbidity data and illness onset for the PEA-BP sample is reported for the 86 participants who continued their involvement in the study for 4 years, as reported in Geller et al. (2004)

[c] Suicidality in the PEA-BP sample comes from their answers to a specific question on the WASH-U-KSADS with a rating scale from no ideation to ideation to suicide attempt. This item was rated present if the youth had a plan or intent or daily morbid ideation (Geller et al. 2000a). Rates of suicide attempts were not reported

Table 4

Examples of developmentally typical and atypical behaviors

Symptom	Typical	Atypical
Elated mood	A 7-year-old who is highly energetic and happy at her aunt's birthday party when she sees her cousins	A 7-year-old who dances around her classroom, singing about how wonderful the world is
Irritability	A 9-year-old who slams his bedroom door when told he needs to turn off the computer and go to bed not stay away chatting online with friends	A 9-year-old who knocks all of the figurines off of the bookshelf and stomps on them because his mother asked him to help clear the dinner table
Grandiosity	A 10-year-old boasts that he can swim faster than the other kids at the pool	A 10-year-old insists he will be the first pick in next year's NBA draft and looks at places to live in several likely cities
Flight of ideas	A 13-year-old who returns to school after winter break and excitedly talks about the gifts she received, jumping from a new cell phone to a cute skirt, to perfume from the guy she has a crush on to the texts she has gotten on her phone	A 13-year-old confuses his friends during his energetic and haphazard description of what he wants to do over summer vacation, how he has to study for his algebra test next week, and a phone call he got the previous night
Decreased need for sleep	A 8-year-old who cannot sleep the night before the first day of school and bounds out of bed at 6 am to get ready, but nearly falls asleep at dinner that night	A 8-year-old stays up until 1 am and wakes up his mother at 6 am to go for a walk with him and the family dog before school several days in a row
Increase in goal-directed behavior	An 11-year-old zooms around his house gathering up his clothing and football equipment the night before his first game	An 11-year-old gathers his football equipment, organizes and shines his toy car collection, and starts several school homework assignments without finishing any of these projects
Distractibility	A 13-year-old has difficulty keeping her mind on her work the day her family is going to pick up their new kitten	A 13-year-old who is usually quiet and respectful, interrupts the teacher ten times during her explanation of a poem and taps his pen until a classmate snaps at him
Hypersexuality	A 9-year-old girl titters with her friends when her handsome substitute teacher walks by	A 9-year-old girl turns in a provocative love note for her teacher with her homework
	A 16-year-old girl gossips online with friends about which boy in their class has the best body	A 16-year-old girl sets up dates with three different guys in one weekend and plans to have sex with all of them
Involvement in risky behaviors	A 12-year-old plays hooky with friends to see the new adventure movie opening at the theater	A 12-year-old packs his belongings into a backpack and is caught walking to the bus stop planning to go across the stated to spend the weekend with his aunt, whom he has never met face-to-face

Table 5

Course and outcome of bipolar youth (COBY) findings

Baseline	**BP-I** ***n*** **= 255**	**BP-II** ***n*** **= 30**	**BP-NOS** ***n*** **= 153**
Age of onset of BPSD	9.5 (4.0)	11.2 (3.4)	8.7 (3.5)
Duration of BPSD (years)	3.4 (2.7)	3.4 (2.0)	3.2 (2.2)
Most severe week of symptoms in the month prior to intake			
KSADS MRS score	23.8 (13.1)	23.6 (10.7)	21.4 (10.3)
KSADS depression score	14.6 (10.8)	18.9 (11.0)	14.2 (8.8)
Functional impairment *			
At intake	52.9 (12.2)[a]	59.3 (13.0)[b]	56.6 (11.1)[b]
Most severe lifetime	34.5 (10.2)[a]	40.3 (9.0)[b]	41.8 (9.6)[b]
Lifetime history of comorbid disorders (%)			
Any anxiety disorder	37.3[a]	60.0[b]	37.9[a]
ADHD	59.8	43.3	62.1
Conduct disorder	12.8	13.3	11.8
ODD	39.5	40.8	40.5
Substance use disorder	9.1	9.8	8.5
PDD	2.1	2.0	2.0
Lifetime phenomenological features (%)			
Psychosis	34.5[a]	20.0[ab]	17.6[b]
Suicidal ideation	76.8	93.3	71.9
Suicide attempt	35.0[a]	43.3[ab]	20.9[ab]
Psychiatric hospitalization	66.1[a]	53.3[b]	28.8[b]
Psychopharmacological treatment	96.5[a]	93.3[ab]	87.6[b]
Family history of suicide attempt in first degree relative (%)	25.5[ab]	31.0[a]	17.9[b]
Two-year follow-up	BP-I *n* = 152	BP-II *n* = 19	BP-NOS *n* = 92
Lifetime psychosis (%)	41.4[a]	21.1[ab]	21.7[b]
Rate of recovery (%)	68	79	66
Median time to recovery (weeks)	52.0[a]	42.1[a]	140.2[b]
Rate of recurrence (%)	58[ab]	87[a]	46[b]
Median time to recurrence (weeks)	45.0[a]	19.0[a]	69.0[b]
Weekly symptom status (%)			
Psychotic symptoms	3.2 (11.8)	2.3 (7.1)	3.2 (14.3)
Asymptomatic	41.1 (34.3)	51.8 (24.9)	34.9 (31.0)
Syndromal	27.2 (29.5)[a]	20.9 (19.1)[ab]	14.7 (19.3)[b]
Subsyndromal	31.7 (25.6)[a]	27.2 (20.5)[a]	50.4 (29.5)[b]

Notes: Values provided are mean (SD) unless otherwise indicated. Values with different superscripts are significantly different at $p < .05$

* Functional impairment was measured with C-GAS scores

Table 6

Longitudinal follow-up of the prepubertal and early adolescent bipolar phenotype (PEA-BP) sample

	6 months	12 months	18 months	24 months	36 months	48 months	96 months
% who recovered[a]	14.0	36.0	55.8	65.1	77.9	87.2	87.8
% who relapsed after recovery[b]	16.7	29.0	39.6	55.4	53.7	64.0	73.3
Mean time to relapse after recovery in weeks (SD)	–	–	–	28.6 (13.2)	–	40.4 (33.4)	99.0 (81.0)
Variables associated with recovery	None	None	–	Living in an intact biological family	–	None	None
Variables associated with relapse	None	None	–	Low maternal warmth	–	Low maternal warmth	Low maternal warmth

[a]Recovery was defined as eight consecutive weeks without meeting DSM-IV criteria for mania or hypomania (Geller et al. 2008)

[b]Relapse after recovery was defined as two consecutive weeks of meeting DSM-IV criteria for mania or hypomania with clinically significant impairment as evidenced by C-GAS score ≤ 60 (Geller et al. 2008)

Table 7

Characteristics and social relationships of prepubertal and early adolescent bipolar phenotype (PEA-BP), attention-deficit/hyperactivity disorder (ADHD), and community control (CC) groups

Characteristic	% PEA-BP (*n* = 93)	% ADHD (*n* = 81)	% CC (*n* = 94)
Living in an intact biological family School	54.8[a]	61.7[a]	89.4[b]
School behavior problems	78.5[a]	29.6[b]	4.3[c]
Low grades	44.1[a]	21.0[a]	1.1[b]
Peers and siblings			
Few/no friends	55.9[a]	24.7[b]	6.4[b]
Frequent teasing	52.7[a]	35.8[a]	9.6[b]
Poor social skills	63.4[a]	29.6[b]	5.3[c]
Poor sibling relations	40.7[a]	22.5[ab]	6.8[b]
Mother–child relations			
Frequent activities	76.3[a]	93.7[ab]	98.9[b]
Usually confides	47.3[a]	61.2[a]	83.0[b]
Corporal punishment ≥1× per month	30.1[a]	25.0[ab]	4.3[b]
Mutual warmth	45.2[a]	75.0[b]	94.7[c]
Father–child relations			
Usually confides	23.2[a]	38.8[ab]	52.7[b]
Frequent hostility	47.6[a]	23.8[b]	2.2[c]
Mutual warmth	29.2[a]	45.0[a]	81.7[b]
Overall frequent tension	40.2[a]	17.5[b]	2.1[b]
Marital relations			
Frequent irritability	32.9[a]	32.9[a]	7.7[b]
Frequent complaining	45.1[a]	37.0[ab]	12.1[b]
Problem solving	65.9[a]	67.1[a]	92.3[b]
Agree on child-rearing	53.6[a]	64.4[a]	89.0[b]
Infrequent overall tension	35.4[a]	49.3[ab]	77.5[b]

Notes: This table summarizes the significant results provided in Geller et al. (2000). Values with different superscripts indicate statistically significant differences (at $p < .001$) per logistic regression analyses