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Early-Onset Bipolar Disorder

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Introduction

Although 20% to 40% of adults with bipolar disorder (BP) retrospectively report onset in childhood[1,2], there was previously debate about the onset of BP during childhood and adolescence.[70] Recent research provides overwhelming evidence that early-onset BP (here defined as prior to age 18) exists, can be reliably diagnosed, and is associated with substantial functional impairment.[3-5] The prevalence of early-onset BP appears to increase during late adolescence[6-8] with a prevalence as high as 6% in the United States.[9] The timely recognition and treatment of early-onset BP is critical given the elevated risk for deleterious outcomes, including substance abuse, risky sexual behavior, and suicide.[10,11] Yet, data suggest that, on average, individuals display symptoms of the illness for 10 years before they receive proper diagnosis and treatment.[12]

Clinical Presentation

BP is characterized by extreme alterations in mood, energy, sleep, and thought that alternate between periods of depression and periods of hypomania (in BPII) and mania (BPI).[13] During these mood episodes, the individual exhibits a significant change (can be positive or negative) from his/her usual functioning that is observable by others.

One of the major challenges inherent in identifying early-onset BP is that the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria used to diagnose BP were developed for

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adults rather than youth.[14] Although work by several independent research groups shows that some youth meet the full DSM criteria for BP, others present with significant and impairing hypo/manic symptoms that do not meet full DSM-IV or DSM-V criteria for BPI or BPII.[14] These youth may be diagnosed with BP not otherwise specified (BP-NOS; DSM-IV) or other specified/unspecified BP (DSM-V).[15] Thus, when accounting for psychosocial development, research indicates that the symptoms of early-onset BP are similar to those among adults. Data indicate the main reasons youth are diagnosed with BP-NOS (rather than BPI or II) is insufficient duration and severity of hypo/manic symptoms;[14,15] yet, youth with BP-NOS have similar phenomenology of hypo/manic symptoms, comorbid disorders, and family psychiatric history.[16] Importantly, studies show that youth who meet operationalized criteria for BP-NOS exhibit similar impairment and risk for suicidal behavior as those with BPI and II, and nearly 50% exhibit illness progression such that they meet full DSM-IV criteria for BPI or II over time.[15]

Mania

A recent meta-analysis[17] identified the most common manic symptoms among youth diagnosed with BP as increased energy, irritability and mood lability, distractibility, and goal-directed activity (all approximately 75%); hypersexuality, hallucinations, and delusions were the least frequent (all approximately 25%). Grandiosity and hypersexuality were the most specific symptoms, but also relatively less common (57% and 32%, respectively).

One major source of controversy in the field has been whether (per DSM criteria) manic symptoms must be episodic in nature, or whether youth with BP may present with a more chronic course of mania.[18,19] Prospective naturalistic data from a large cohort of youth with BP followed longitudinally clearly indicate that early-onset BP is an episodic illness.[3,11,20]

Depression

Major depressive episode(s) can predate the onset of mania, such that some youth initially diagnosed with unipolar depression may then be diagnosed with BP upon exhibiting manic symptoms. Indeed, adults with BP retrospectively report significant depressive symptoms prior to age 18,[1,21] and research further indicates that over half of youth with a BP diagnosis report a prior diagnosis of major depression.[14] As such, youth presenting in clinical settings with depressive symptoms should be assessed for a history of threshold or subthreshold manic symptoms.

Diagnosis

The diagnosis of BP in youth presents multiple challenges. Primarily, to some extent, several symptoms of mania can look developmentally normative in youth. For example, silliness and difficulty modulating speech rate and tone are common in children in certain situations (e.g., at a birthday party or amusement park). In order to distinguish normative behavior in childhood from mania, it can be helpful to examine whether the mood and behavior are developmentally normative for youth his/her age, represent a clear change from the child's "normal" or baseline, and affect the child's functioning.[22]

Differential Diagnosis

Another challenge in the diagnosis of early-onset BP is that youth with BP commonly have comorbid disorders, including attention deficit hyperactivity disorder (ADHD 53%), and oppositional defiant disorder (ODD 42%)[17] — many of which share common core features. To illustrate, rates of irritability (98% BP vs. 72% ADHD), accelerated speech (97% vs. 82%), distractibility (94% vs. 96%) and increased energy (100% vs. 95%) are similar in BP and ADHD, rendering these symptoms both diagnostic of each condition and also nonspecific.[23] Thus, such symptoms should only be attributed to mania when they show a clear temporal association with the abnormally elevated, expansive, and/or irritable mood. That is, symptoms of mania must cluster together in time and show temporal episodicity rather than presenting as a smattering of symptoms that occur independently over time.[22] Studies have also identified some symptoms that are more specific to BP as compared with ADHD, including euphoria, grandiosity, decreased need for sleep, hypersexuality (in the absence of sexual abuse history), and hallucinations.[23] Psychotic symptoms, family history of BP, and medication-induced mania may be helpful information in the broader clinical assessment to help distinguish early-onset BP from other conditions.[24-28] Alternatively, chronic symptoms (e.g., irritability, impulsivity) should alert the clinician to the possibility of an alternative diagnosis unless these symptoms intensify episodically with mood and/or energy changes.

Use of some substances (both illicit and prescribed) may also induce mood changes that can mimic symptoms of mania. If manic symptoms that temporally onset with use of substances do not abate after discontinuing the substance, then a BP diagnosis should be considered. It is also important to acknowledge the overlap between symptoms of borderline personality disorder and BP when considering differential diagnosis.

Assessment

Semistructured interviews are most often considered the gold standard in clinical research studies to diagnose early-onset BP and discern episode frequency, intensity, and duration.[29] The most widely used semistructured interviews in BP research studies are the Kiddie Schedule for Affective Disorders and Schizophrenia for School Age Children — Present and Lifetime version (K-SADS PL)[30] and the Washington University KSADS (WASH-U-KSADS).[31] However, due to the time required to conduct these interviews, these are infrequently used in clinical settings.

Two clinician-administered rating scales are commonly used to assess manic symptoms in youth: the KSADS Mania Rating Scale (K-SADS-MRS)[32] and the Young Mania Rating Scale (YMRS).[33] Although some data indicate the YMRS may not be valid in youth.[34]

Youth self- and parent-report scales of manic symptoms are recommended as a means of gathering additional information helpful to the diagnostic and ongoing assessment process. The General Behavior Inventory (GBI),[35] the Child Mania Rating Scale (CMRS),[36] and the Mood Disorders Questionnaire[71] are brief, validated scales that are widely used in clinical practice. It should be noted that caregiver reports have been shown to be more effective in identifying mania than youth reports.[34] That being said, direct interview with the youth and parent(s) is recommended to enhance diagnostic accuracy.[37]

Mood timelines can be a valuable clinical tool in assessing a child's mood disorder by helping the clinician and family visualize the onset and course of mood episodes over time. These timelines can be completed retrospectively upon initial assessment, as well as prospectively to measure triggers and treatment response. Generally, timelines chart daily, weekly, and/or monthly changes in mood, along with corresponding life events and treatments. Mood timelines can be completed using standardized templates (e.g., the Life Chart Methodology),[38] a blank sheet of paper with a "timeline," and/or a plethora of free websites and mobile applications based on the clinician, patient, and family's preferences.

Evidence from adoption, twin, family, and high-risk studies indicates that BP is one of the most heritable of all psychiatric disorders.[39-41] Greater familial loading is not only associated with greater risk for developing BP but also earlier illness onset.[42,43] As such, family history should be carefully considered in the context of differential diagnosis. Additional areas to assess during a comprehensive evaluation for early-onset BP include suicidal and homicidal thoughts, neglect/abuse, and psychosocial functioning across domains, as well as medical conditions.

Course and Outcome

Longitudinal naturalistic studies of youth with BP indicate that most youth with the disorder (70% to 100%) will recover (i.e., two months without clinically significant symptoms) from their acute mood episode.[19,44] Unfortunately, the majority who recover will also recur at least once over a two- to five-year follow-up. Furthermore, studies have demonstrated that in addition to full threshold recurrences of illness, youth also display substantial subsyndromal symptoms over follow-up — rendering up to 60% of follow-up time over four years symptomatic according to one study.[44] Fluctuations in mood appear to characterize pediatric BP more so than adult BP,[45] with repeated changes in symptom polarity being a common presentation.[4,19,46]

The illness has a substantial impact on psychosocial functioning across domains both during acute mood episodes and, to a lesser extent, between mood episodes.[47] Furthermore, youth with BP are high health care utilizers: they are more than three times as likely to require inpatient psychiatric hospitalization, and more than twice as likely to visit the emergency department for overdose than adolescents with other mood disorders; they are 16 times more likely to have a medical admission for overdose than adolescents with non-mood psychiatric disorders.[48] These findings further highlight the elevated risk for suicidal behavior and completed suicide among youth with BP.[47,49,50] Psychosis [51] and substance abuse[71] also commonly occur among youth with BP.

Generally speaking, worse course and outcome among youth with BP has been associated with the following: low socioeconomic status, early age of onset, mixed episodes, psychosis, abuse, and familial psychiatric disorders.[44,51-53] A recent study used latent growth class analysis[20] to identify four trajectories of illness over a nine-year follow-up among youth with BP: 1) "predominantly euthymic" (24.0%); 2) "moderately euthymic" (34.6%); 3) "ill with improving course" (19.1%); and 4) "predominantly ill" (22.3%). These data highlight both the possibility that some youth may display long symptom-free periods into young adulthood, as well as the general tendency for individuals with early-onset illness to recur into young adulthood.

Treatment

Guidelines for the treatment of pediatric BP recognize both pharmacotherapy and psychotherapy as important components of optimal treatment.[37]

Pharmacotherapy

Studies support the use of atypical antipsychotics followed by mood-stabilizing medications (e.g., lithium, and anticonvulsants such as valproate, carbamazepine, and lamotrigine[37,54]) as the foundation for the treatment of acute manic/mixed episodes in pediatric BP. Unfortunately, few studies have been conducted to guide treatment of BP depression in youth. Lithium, valproate, and atypical antipsychotics have been demonstrated to be effective for BP depression in adults.[55] The use of adjunctive antidepressants may be considered, but may trigger mania, hypomania, mixed episodes or rapid cycling, or agitation, particularly in the absence of mood stabilizer treatment.[22,37]

Given that BP is currently conceptualized as a chronic illness, ongoing treatment should be considered, though current data to guide decision-making are limited. In adults, lithium, lamotrigine (only for depression), and atypical antipsychotics have been shown to effectively prevent new mood episodes.[56,57]

Psychotherapy

Given that BP substantially disrupts the vast developmental tasks of adolescence (encompassing social, family, academic, and identity contexts),[37] adjunctive psychotherapy for youth with BP has the potential to minimize the long-term debilitating effects of the illness.

Several different manualized psychotherapy approaches for youth with BP have been examined in the literature to date and demonstrated positive outcomes. Miklowitz and colleagues demonstrated the efficacy of an intensive psychoeducational approach, Family-Focused Therapy for Adolescents (FFT-A), on BP depression in adolescents.[58] Goldstein and colleagues demonstrated enhanced outcomes, including less suicidality, among adolescents with BP receiving an adapted version of Dialectical Behavior Therapy (DBT).[59] Hlastala and colleagues[60] modified Interpersonal and Social Rhythm Therapy (IPSRT),[61] a treatment focused on regularizing social rhythms, for adolescents with BP and documented improvement in manic and depressive severity from pre- to posttreatment.[62] For school-aged children with mood disorders, Fristad et al. demonstrated the efficacy of a multifamily psychoeducational program,[63] as well as its impact on the quality of mental health services utilized,[64] while Pavuluri, West, and colleagues developed a cognitive behavioral intervention for BP children.[65,66] These treatments, while distinct, share common components considered critical to effective psychosocial treatment of early-onset BP, including psychoeducation on causes, symptoms, course, and treatments of BP. A focus on establishing and maintaining stable circadian patterns has been shown to be an important component, as have communication skills, problem-solving skills, and safety planning.[37,67] In each of these treatment models, parents are engaged in their children's therapy and referred to treatment if they have clinically significant mood symptoms themselves.

Comorbid Conditions

Since comorbid disorders can exacerbate BP,[22] treatment of comorbid conditions is critical. Yet, data to guide decision making remains limited. Generally speaking, evidence-based medications and/or psychotherapies for comorbid conditions should be carefully considered.

Prevention / Early Intervention

Recent studies have also begun to explore the potential for early psychosocial intervention to ameliorate, delay, or even prevent the onset and/or progression of BP among youth at high risk for the disorder. Goldstein and colleagues[68] developed a modification of IPSRT for the adolescent offspring of parents with BP who themselves have not yet developed BP. An open pilot study demonstrated the feasibility and acceptability of the intervention for this group, and identified pre-post treatment improvement in sleep and circadian patterns that may contribute to increased risk for illness onset. Additionally, given the risk for youth with mood disturbance and a positive BP family history to develop BP and progress to BP-I/II over time, Miklowitz and colleagues[69] examined whether FFT-A could be a beneficial early intervention for mood-disordered adolescents (i.e., those with BP-NOS, cyclothymia, depression) with a family history of BP. Recent findings demonstrated more rapid recovery from mood symptoms, more weeks symptom-free, and lesser manic symptoms over one year among high-risk youth receiving FFT-A as compared with those receiving a single session family educational intervention.

Conclusions

BP is a severe and impairing psychiatric disorder that can be reliably diagnosed early in life. The disorder presents with clear episodes of mood and energy dysregulation, and most youth will experience recurrences into adulthood. High rates of comorbid psychiatric conditions, as well as substantial diagnostic overlap with other common psychiatric conditions in childhood, contribute to the challenge of accurate diagnosis of the disorder. Early and accurate recognition and treatment of BP in children and adolescents is critical in order to optimize outcomes for youth with BP. The combination of evidence-based pharmacological and psychosocial interventions for these youth and their families may help optimize outcomes and reduce the risk for recurrence, hospitalization, poor functioning, and suicidal behavior.

Clearly, further study of the role of early intervention for at-risk youth is warranted to determine timing and selection of those most likely to benefit, as is conduct of genetic and biological studies to better understand the causes and treatments for early-onset BP.

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