Early Intervention for Symptomatic Youth at Risk for Bipolar Disorder: A Randomized Trial of Family-Focused Therapy

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Objective: Depression and brief periods of (hypo)mania are linked to an increased risk of progression to bipolar I or II disorder (BD) in children of bipolar parents. This randomized trial examined the effects of a 4-month family-focused therapy (FFT) program on the 1-year course of mood symptoms in youth at high familial risk for BD, and explored its comparative benefits among youth in families with high versus low expressed emotion (EE). **Method:** Participants were 40 youth (mean 12.3 ± 2.8 years, range 9–17) with BD not otherwise specified, major depressive disorder, or cyclothymic disorder who had a first-degree relative with BD I or II and active mood symptoms (Young Mania Rating Scale [YMRS] >11 or Child Depression Rating Scale >29). Participants were randomly allocated to FFT–High Risk version (FFT-HR; 12 sessions of psychoeducation and training in communication and problem-solving skills) or an education control (EC; 1–2 family sessions). **Results:** Youth in FFT-HR had more rapid recovery from their initial mood symptoms (hazard ratio = 2.69, $p = .047$), more weeks in remission, and a more favorable trajectory of YMRS scores over 1 year than youth in EC. The magnitude of treatment effect was greater among youth in high-EE (versus low-EE) families. **Conclusions:** FFT-HR may hasten and help sustain recovery from mood symptoms among youth at high risk for BD. Longer follow-up will be necessary to determine whether early family intervention has downstream effects that contribute to the delay or prevention of full manic episodes in vulnerable youth. Clinical trial registration information—Early Family-Focused Treatment for Youth at Risk for Bipolar Disorder; http://www.clinicaltrials.gov/; NCT00943085. J. Am. Acad. Child Adolesc. Psychiatry; 2013;52(2):121-131. **Key Words:** expressed emotion, high risk, early warning signs, psychoeducation, psychosocial intervention.

Bipolar I and II disorder (BD) affect approximately 2.5% of U.S. adolescents, with the risk for syndromal mania doubling from the early to the late teen years.[1] There is increasing agreement on clinical phenotypes of children and adolescents who are at elevated risk for progression to fully syndromal BD.[2,3] Among children of parents with BD, subthreshold "high-risk" forms of the disorder can be detected as many as 10 years before the onset of BD I or II.[3]

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Significant controversy exists regarding the diagnostic boundaries of early-onset BD; however, agreement is substantial that BD and its subthreshold antecedents have a considerable impact on general functioning and quality of life.[4] Youth who meet a stringent operational definition of BD Not Otherwise Specified (BD-NOS)—characterized by brief, recurrent subthreshold (hypo)manic and depressive periods with a clear change in functioning—have cumulative affective morbidity, impairment, suicidal ideation, and comorbidity comparable to or exceeding that of youth with BD I.[2,5] When combined with a family history of mania in first- or second-degree relatives, more than 50% of youth with BD-NOS progress to fully syndromal BD I or II over 5 years.[6]

Children or adolescents with major depressive disorder (MDD) also have elevated risk of conversion to BD I/II (15%–49%) in the 2 to 4 years after onset of their first depressive episode.[3,7] Conversion to BD I or II is highest among depressed patients with a family history of mania, early onset of symptoms, subthreshold hypomania, psychosis, or episodic mood lability.[8,9]

At present, little empirical evidence exists to guide the treatment of individuals at high risk for BD. Pharmacological studies during the phases preceding fully syndromal BD have not produced conclusive results.[10,11] Currently, high-risk youth tend to be treated with a wide variety of medications and therapies, or do not receive any treatment.[5] Delays to first treatment of BD are associated with greater depressive morbidity and less time euthymic in adulthood.[12] Without early intervention, the social, intellectual, and emotional development of youth at high risk for BD may be seriously compromised.

Well-timed psychosocial interventions in young high-risk individuals may allow a more normative acquisition of life skills, such as achieving personal autonomy, academic success, and strong peer relationships before the more debilitating bipolar syndrome begins. Furthermore, environmental-contextual factors that may increase risk for mood symptoms—such as whether parents exhibit high expressed emotion (EE) attitudes toward the child (i.e., high levels of criticism, hostility, or emotional overinvolvement)—may be most amenable to change early in the course of the disorder.[7] Few studies, however, have examined the effects of early psychosocial intervention on youth with high-risk phenotypes. One 12-month waitlist trial found that multi-family psychoeducation groups protected against conversion to bipolar spectrum disorders in a sample of school-aged children with depressive spectrum disorders.[13]

Family-focused treatment (FFT) is a manual-based psychoeducational intervention designed to reduce familial stress, conflict, and affective arousal by enhancing communication and problem-solving among patients and caregivers. In a two-site randomized controlled trial (RCT) of adolescents with BD I and II, 9 months of FFT and best-practice pharmacotherapy were associated with more rapid and complete remission from depressive episodes over 2 years than brief psychoeducation and pharmacotherapy.[14] Similar protective effects of FFT on patients' symptomatic and functional outcomes have been observed in four RCTs of adults with BD.[15] Furthermore, in two trials, adolescent or adult patients in high EE families had a greater magnitude of treatment response compared with patients in low EE families.[16,17]

This randomized trial examined whether a brief (4-month) early family intervention (FFT–High Risk protocol [FFT-HR]) was effective in stabilizing mood symptoms among youth who were at high risk for BD. In a previous open trial of FFT-HR, offspring of parents with BD I or II who were diagnosed with MDD or BD-NOS showed significant improvements in depression and hypomania scores and psychosocial functioning over 1 year.[18] We hypothesized that the 12-session FFT-HR protocol would promote more rapid symptom recovery, more time in remission, and greater improvement in depressive and hypomanic symptoms over 1 year compared with a family education control (EC). A secondary aim was to explore whether high-risk youth from high-EE parental households showed a greater magnitude of response to FFT-HR than those from low-EE households.

METHOD

Participants

Children between ages 9 years, 0 months and 17 years, 11 months who had a first-degree relative with BD I or II were recruited at the University of Colorado or the Stanford University School of Medicine between June 2008 and August 2010. Referrals originated from community practitioners, parent support groups, e-mail advertisements, and inpatient settings. After a full explanation of the procedures, children and parents read and signed University Institutional Review Board–approved assent and consent forms.

Eligibility criteria included the following: English speaking; at least one first-degree relative who met *DSM-IV-TR* criteria for BD I or II, based on the Mini-International Neuropsychiatric Interview (MINI)[19]; child met *DSM-IV-TR* criteria for a lifetime diagnosis of BD-NOS, MDD, or cyclothymic disorder, and had significant current affective symptoms (1-week Young Mania Rating Scale [YMRS] score >11 or 2-week Children's Depression Rating Scale, Revised [CDRS-R] score >29).[20,21] The diagnostic criteria for BD-NOS were the same as those used in the Course and Outcome in Bipolar Youth (COBY) study and included the following: a distinct period of abnormally elevated, expansive, or irritable mood plus two (three, if irritable only) *DSM-IV-TR* symptoms of mania that caused a change in functioning, lasted ≥ 4 hours in a day, and occurred for a total of 4 or more days across the child's lifetime.[2] If the main diagnosis was MDD, the youth must have had a full *DSM-IV* major depressive episode