Treatment Moderators of Child- and Family-Focused Cognitive-Behavioral Therapy for Pediatric Bipolar Disorder

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Objective: Prior work has demonstrated the efficacy of child- and family-focused cognitive-behavioral therapy (CFF-CBT) versus enhanced treatment as usual (TAU; unstructured psychotherapy) for pediatric bipolar disorder (PBD). The current study builds on primary findings by examining baseline child, parent, and family characteristics as moderators of symptom response trajectories.

Method: A total of 69 youth aged 7 to 13 years (mean = 9.19 years, SD = 1.61 years) with *DSM-IV-TR* bipolar I, II, or not otherwise specified (NOS) were randomly assigned, with family members, to CFF-CBT or TAU. Both treatments consisted of 12 weekly sessions and 6 monthly booster sessions. Participants were assessed at baseline, 4, 8, and 12 weeks, and 6-month follow-up on mania and depression symptoms and overall psychiatric severity. Parents and youth also provided self-report data on baseline characteristics.

Results: CFF-CBT demonstrated greater efficacy for youth depressive symptoms relative to TAU for parents with higher baseline depressive symptoms and lower income, and marginally for families with higher cohesion. In addition, youth with lower baseline depression and youth with higher self-esteem showed a poorer response to TAU versus CFF-CBT on mania symptom outcomes. Age, sex, baseline mania symptoms, comorbidity, and suicidality did not moderate treatment response.

Conclusion: Results indicate that CFF-CBT was relatively immune to the presence of treatment moderators. Findings suggest the need for specialized treatment to address symptoms of PBD in the context of parental symptomatology and financial stress.

Key Words: pediatric bipolar disorder, cognitive-behavioral therapy, family-focused intervention, treatment moderators, randomized clinical trial

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Pediatric bipolar disorder (PBD) is a chronic and debilitating illness characterized by periods of episodic mood disturbance and pronounced impairments in social, academic, and family functioning.[1,2] Given the significant psychosocial dysfunction and poor long-term prognosis associated with PBD, psychotherapy is considered an essential component of the treatment approach.[3] Although research is limited, randomized controlled trials have established the efficacy of family-focused individual and group treatments for youth with bipolar disorder (BD).[4-6] Yet, beyond simply examining efficacy, the identification of patient and family characteristics that may influence or moderate treatment outcomes is critical for improving interventions for this vulnerable population. Indeed, the examination of treatment moderators has been prioritized by the National Institute of Mental Health (NIMH) to advance knowledge about optimal personalized treatment—that is, what works, for whom, and under what conditions.[7] Personalized treatment approaches are particularly relevant in PBD; the complexity of PBD symptoms and variable response to even the best evidence-based treatments suggests the presence of pretreatment factors that may influence outcomes.

The child treatment literature points to several demographic, child, and parent characteristics related to differential response to psychotherapy for anxiety, depressive, behavior, and eating disorders, including child symptom severity and comorbidity,[8-11] and parent marital adjustment and psychopathology.[8,9] Numerous studies of youth depression highlight symptom severity,[12-14] psychosocial impairment,[14-16] comorbid disorders,[15,16] parental depression,[12] and greater family difficulty (e.g., conflict, low cohesion)[13,16] as predictors of poor psychosocial treatment prognosis overall. Specific to PBD, findings suggest that the effects of evidence-based treatments may in fact be enhanced among youth and families with greater baseline impairment. Families characterized as high in expressed emotion (EE; i.e., overinvolvement and criticism) showed greater symptom improvement in response to family-focused treatment for adolescents (FFT-A) as compared to a brief educational control, whereas families with low EE responded equally to the treatment conditions.[17] Similarly, the effects of a group psychoeducational intervention for children with bipolar or depression spectrum disorders (Multi-Family Psychoeducational Psychotherapy, MF-PEP) versus waitlist control

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participants were greatest among youth with severe baseline functional impairment as compared to youth with mild impairment.[18] Thus, the effects of specialized treatment for PBD may be optimized among the higher-risk youth and families that these treatments are designed to target.

In this study, we build on findings supporting the efficacy of child- and family-focused cognitive-behavioral therapy (CFF-CBT) for PBD[6] by exploring the factors associated with achieving optimal treatment effects. CFF-CBT is an adjunctive treatment that was developed to address the unique needs of the preadolescent PBD population and their families. CFF-CBT comprises 3 innovative aspects in the treatment of PBD: it is designed to be developmentally specific to symptoms of PBD experienced by school-aged children (e.g., rapid cycling, comorbid disorders, mixed mood states) and related psychosocial impairment (e.g., low self-esteem, interpersonal difficulties); it involves intensive individual work with parents to address their own therapeutic needs and impact on parenting (e.g., parental well-being, family stress)[19,20]; and it integrates psychoeducation and cognitive-behavioral therapy with complementary techniques from mindfulness-based and positive psychology interventions to target the range of needs of families affected by PBD. Grounded in the evidence on affective circuitry and psychosocial impairment associated with PBD, the core components of CFF-CBT aim to improve child affect dysregulation and self-esteem, parent well-being, and family coping with BD.

A recent trial examined CFF-CBT as compared to a dose-matched, enhanced TAU control, and findings demonstrated the efficacy of CFF-CBT in terms of symptom and global functioning outcomes.[6] The present study extends primary findings to examine whether baseline child, parent, and family variables moderated response to CFF-CBT versus TAU. We investigated moderators within the key categories identified by expert consensus, including demographics, illness severity and comorbidity, parental psychopathology, and psychosocial variables.[21] Within these categories, we focused on the treatment predictors/moderators that have emerged in the extant literature that most closely corresponded to the theoretical model and key treatment foci of CFF-CBT: indicators of child severity (symptoms, comorbid anxiety or disruptive behavior disorders, suicidality) and psychosocial functioning (self-esteem), parent well-being (operationalized as depressive symptomatology), and family functioning (operationalized as family cohesion). The current study expands prior research exploring moderators of an empirically supported group intervention for children with bipolar and depressive disorders[18] and family-focused treatment for adolescent BD[17] by examining moderators of symptom trajectories in response to an individual family treatment for preadolescent youth with PBD. A better understanding of how baseline characteristics in the heterogeneous PBD population relate to symptom outcomes will improve treatment decision making and approaches to enhancing treatment response.

Guided by prior PBD research, we expected that youth with greater illness severity, lower self-esteem, higher parental depression, and lower family functioning at baseline would show greater reduction in symptom trajectories in response to CFF-CBT relative to TAU, given the explicit focus on these treatment targets in CFF-CBT. In addition, analyses examined potential demographic moderators (age, sex, and family income); these analyses were considered exploratory, given mixed findings in past clinical trials for PBD and depression.[12,15,16,18]

METHOD

Participants

Participants were children (n = 69) diagnosed with a bipolar spectrum disorder recruited from a specialty mood disorders clinic in an academic medical center in a large midwestern urban area from 2010 to 2014 (for details and consolidated standards of reporting trials [CONSORT] diagram, see West *et al.*[6]). Children meeting *DSM-IV-TR* criteria for bipolar spectrum disorders (BP-I, BP-II, and BP not otherwise specified [NOS]) aged 7 to 13 years were eligible to participate. BP-NOS was defined using *DSM-IV-TR* criteria as the presence of depression and mania symptoms that met symptom severity threshold but not minimal duration criteria, or the presence of recurrent hypomanic episodes without intercurrent depressive symptoms. Inclusion criteria included the following: patients stabilized on medication (defined as Young Mania Rating Scale [YMRS][22] score of $\leq$20 and Children's Depression Rating Scale–Revised [CDRS-R][23] score of <80, indicating no severe symptoms requiring immediate, more intensive care), parental consent, and youth assent. These criteria were intended to exclude children who required acute stabilization in more intensive treatment before being able to participate in psychotherapy, but still to include children who were actively symptomatic. Exclusion criteria included: youth IQ <70 (KBIT-2),[24] active psychosis, active substance abuse, neurological/medical problems that complicate symptoms (Washington University in St. Louis Kiddle Schedule for Affective Disorders and Schizophrenia [WASH-U-KSADS])[25]; active suicidality requiring hospitalization (Columbia Suicide Severity Rating Scale [C-SSRS])[26]; and primary caregiver severe depression or mania.

Procedures

Diagnosis and Randomization. All study procedures were approved by the Institutional Review Board at the University of Illinois at Chicago. Eligibility was assessed by trained raters (licensed clinical psychologists and doctoral students). After the informed consent procedure and screening, parents were interviewed using the WASH-U-KSADS,[25] with portions of the Kiddie-SADS–Present and Lifetime Version (K-SADS-PL)[25,27] used to define mood episodes with corroborating information from child report. Diagnostic interviews were reviewed during study meetings for final determination. Youth meeting diagnostic criteria for a bipolar spectrum disorder completed the baseline assessment and were randomized to study condition using Research Randomizer software.[28] Outcome assessments were conducted by a blinded rater at 4, 6, 12 (post-treatment), and 39 weeks (6-month follow-up).

Psychosocial Intervention. Participants randomized to CFF-CBT (n = 34) were assigned a study therapist in the Pediatric Mood Disorders Clinic (PMDC) and received twelve 60- to 90-minute weekly sessions in the core treatment phase and up to 6 monthly follow-up sessions in the maintenance phase over the course of 9 months. Study therapists were clinical psychology pre- and post-doctoral trainees (n = 23) who received a 3-hour initial training session on CFF-CBT and weekly expert supervision. Sessions alternated among parent, child, and family, and included 7 components that comprise the treatment acronym "RAINBOW": **R**outine