Family-Focused Therapy Study Raises New Questions

> How wonderful that we have met with a paradox. Now we have some hope of making progress.
>
> —Niels Bohr

Miklowitz and colleagues' report in this issue (1) on a meticulously conducted and elegantly analyzed comparison of family-focused therapy and a brief psychoeducation intervention as adjunctive (to medication) treatments for adolescents with bipolar disorder raises as many questions as it answers. Because questions—perhaps more so than answers—propel science forward, this work is of considerable importance to the field.

For adolescents with bipolar disorder, the authors found no difference between treatment with family-focused therapy and a three-session psychoeducation intervention on the primary outcome measures of time to remission, time to recurrence, and proportion of weeks ill over a 2-year period. From a methodological standpoint, this study evidences the highest standards of clinical trial design and execution. The investigators implemented important quality-control measures, such as careful assessment procedures, interrater reliability, therapy adherence measures, oversight of treatment, and blind ratings. Power calculations were conducted to ensure that a type II error did not obscure true differences between treatments. Given the excellence of the work, there is no reason to doubt the results. And yet these findings challenge seven previous controlled trials (including two with adolescents) in which family-focused therapy was found to be superior to enhanced usual care in both the acute and maintenance phases of treatment. By contradicting earlier results, this study calls into question the prevailing wisdom that patients will be better off with family-focused therapy than with a less intensive intervention. Perhaps, this study suggests, a short course of psychoeducation will suffice.

Results from this study suggest that a less intensive intervention (three sessions of psychoeducation) may be sufficient for many adolescents with bipolar disorder, especially if delivered in conjunction with guideline-concurrent pharmacotherapy.

Better outcomes with bipolar-specific psychotherapies are a well-replicated finding in bipolar disorder research. In multiple trials, bipolar-specific psychotherapies, such as family-focused therapy, group psychoeducation, cognitive-behavioral therapy (CBT), and interpersonal and social rhythm therapy, have consistently and repeatedly shown advantages over control treatments on time to recovery from mood episodes and prevention of recurrences. The effect sizes reported for these interventions have been comparable to or larger than those reported for pharmacotherapy trials (2). For instance, in the large, multisite Systematic Treatment Enhancement Program for Bipolar Disorder study of acute depression in individuals with bipolar disorder receiving mood stabilizers, the

addition of antidepressant medications had no greater effect than placebo (3), whereas the addition of bipolar-specific therapies (including family-focused therapy) hastened recovery (4). Given the robustness of the data demonstrating their utility, bipolar-specific psychotherapies are recommended as a key component of treatment for bipolar disorder in evidence-based guidelines from the United States (5), Canada (6), and Europe (7).

In the adult bipolar literature, there have been over 35 published randomized controlled trials of bipolar-specific psychotherapies, the vast majority of which show differential effects of active and control conditions (H.A. Swartz et al., unpublished data). There are, however, four notable exceptions. Scott et al. (8) conducted a multicenter pragmatic trial (N=253) comparing 22 sessions of CBT to usual care and found no difference between the active intervention and the control condition in time to recurrence or symptom burden over 18 months. Post hoc analyses demonstrated that CBT was significantly more effective than treatment as usual in patients with fewer than 12 previous episodes, but less effective in those with more episodes. Meyer and Hautzinger (9) compared 20 sessions of CBT and 20 sessions of supportive psychotherapy (N=76) and found no differences in relapse rates between the conditions. Pellegrinelli et al. (10) compared 16-session group psychoeducation and usual control group therapy (N=55) in euthymic individuals with bipolar disorder and found no difference between groups in number of relapses or symptoms over 12 months. Finally, Parikh et al. (11) compared 20 sessions of CBT and six sessions of group psychoeducation and found no differences in symptomatic outcomes between groups over 72 weeks. The absence of differential effectiveness/efficacy in these four adult trials was explained by high levels of illness acuity (i.e., psychiatric comorbidity, large numbers of previous mood episodes, long duration of illness) (8–11), heterogeneity of symptomatic presentation (11), and high intensity of the comparator condition (9).

There have been far fewer studies of psychotherapy as treatment for bipolar disorder in children and adolescents (12), and all randomized controlled trials to date have shown differential efficacy (13–15)—until now. An initial trial of Fristad's (13) multifamily group psychoeducational psychotherapy (MF-PEP) compared six sessions of MF-PEP and a waiting list control condition in 35 children ages 8–11 with depression and bipolar spectrum disorders. At 6-month follow-up, patients assigned to MF-PEP had significantly greater knowledge about mood symptoms and family functioning than those assigned to the waiting list condition, but there were no differences on symptomatic outcomes. A follow-up study (N=165) of similar design (14) showed significant reductions in mood symptoms among patients receiving MF-PEP compared with those in the waiting list condition. The initial study by Miklowitz et al. of family-focused therapy for adolescents (15) showed more rapid recovery from mood symptoms and lower depression severity scores over 2 years among patients who received family-focused therapy compared with those who received three sessions of psychoeducation. Family-focused therapy has also been modified as a treatment for youths 9–17 years of age who are at risk for developing bipolar disorder by virtue of having a diagnosis of major depressive disorder, bipolar disorder not otherwise specified, or cyclothymic disorder or having a first-degree relative with bipolar I or II disorder. A comparison of family-focused therapy and 1–2 sessions of psychoeducation in 40 high-risk youths showed more rapid recovery from initial mood symptoms, more weeks in remission, and a more favorable trajectory of mania scores over 1-year follow-up (16).

So why, then, does this new study find comparable efficacy for 20 sessions of family-focused therapy and three sessions of psychoeducation? Unlike explanations for lack of differential efficacy in the adult studies, Miklowitz et al. attribute their findings, at least in part, to the high quality of pharmacotherapy management provided by the investigative team. They note that "it is possible that the quality of pharmacotherapy in this trial limited the degree to which the effects of psychotherapy could be observed over and above medication effects." Indeed, high rates of recovery (87% over 2 years) suggest that the overall impact of treatment was substantial. However, 58% of those who recovered experienced a recurrence, indicating that there is also room for improvement.

Thus, results from this study suggest that a less intensive intervention (three sessions of psychoeducation) may be sufficient for many adolescents with bipolar disorder, especially if delivered in conjunction with guideline-concurrent pharmacotherapy. It also suggests, however, that there may be those for whom a more intensive treatment is indicated—perhaps, as articulated by the authors, with additional strategies to help adolescents better address peer and romantic relationships. In earlier studies, family-focused therapy showed greater benefit for families with high levels of expressed emotion (16, 17), and therefore this may be a subgroup for whom family-focused therapy is indicated. A stepped-care approach to treating bipolar disorder in adolescents might permit efficient allocation of higher-intensity resources in a clinically meaningful way. Of course, evaluating these hypotheses would require further testing. Had the Miklowitz et al. study confirmed earlier research findings, there would be less impetus to further refine and optimize treatments for youths with bipolar disorder. Although this may not have been the expected outcome, publication of a trial that refutes earlier work may help us improve treatments for youths with bipolar disorder precisely because it does not allow clinicians and researchers to be complacent. In the end, the true measure of a study's success rests with its ability to stimulate new ideas and questions. By this metric, the investigators have achieved much.

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