



Unexplored Areas of Psychotherapy in Bipolar Disorder

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Abstract: Several psychological interventions—including group psychoeducation, family-focused psychoeducation, and interpersonal social-rhythm therapy—have demonstrated prophylactic efficacy as an adjunct to medication in bipolar disorders (BDs). The field of psychological interventions for BD has experienced impressive progress over the last 15 years. Certain unexplored areas, however, require further research in order to establish the full potential of psychological interventions for BD. Such research should focus, among other things, on cognitive impairment associated with BD, BD in the elderly, comorbid anxiety disorders and other comorbidities, the treatment of BD in pregnant women, and the improvement of patients' overall physical health.

Keywords: bipolar disorder, depression, elderly, psychological interventions, psychotherapy

INTRODUCTION

The number of available psychological interventions for bipolar disorders (BDs) is striking, especially in view of the fact that evidence-based interventions in this field were completely lacking only 15 years ago. Until the late 1990s, not a single well-designed randomized, controlled trial (RCT) on the efficacy of a psychological approach for BD had been published.¹ This situation was set to change. A 1999 study—the first well-designed RCT of its kind—assessed the efficacy of a simple, user-friendly, individual psychoeducational intervention.² In that trial of 69 patients, Perry and colleagues² analyzed the results of an intervention that aimed to teach patients to detect and manage early signs of relapse. Results showed significantly fewer manic relapses (27% vs. 57%), fewer days in hospital, and better functioning over 18 months in the intervention group compared to the control group. This seminal study was followed in quick succession by a series of studies demonstrating the efficacy of other psychological interventions. They included group

psychoeducation,³ cognitive-behavioral therapy (CBT),⁴ family-focused psychoeducation,^{5,6} and interpersonal social-rhythm therapy.⁷ Not all results were positive, however. In 2006, a study demonstrating unfavorable results with CBT was published⁸—a noteworthy result since many trials with negative outcomes are never published, and the publication bias leans distinctly toward positive studies.⁹

Advances in the field continued, and the longest follow-up study for any psychological intervention was published in 2009.¹⁰ Several comprehensive studies on the cost-effectiveness of such interventions followed.^{11,12} Other interesting studies looked at the relationship between the number of previous BD episodes and the response to psychoeducation.^{13,14} Some studies have shown poor efficacy of CBT in BD. An RCT published in 2011 with 50 euthymic BD patients found that the time to recurrence and number of episodes were no different in the intervention group (patients treated with CBT) than in the control group (treatment as usual).¹⁵ Similarly, a two-year follow-up study found no difference in relapse rates when comparing CBT to supportive therapy, suggesting that certain shared characteristics (e.g., information, systematic mood monitoring) might explain the effects of psychosocial treatment for BD.¹⁶

One important focus of the recent literature is on response mediation, especially in relation to the potential and combined role of staging, illness progression, and cognitive impairment in treatment response. To some extent, the results parallel what often occurs with drugs. According to several studies, cognitive-behavioral techniques, psychoeducation, and family-focused strategies might lose efficacy with each relapse, which highlights the importance of staging and cognitive impairment in this population.¹⁴ Both caregiver-oriented and patient-directed psychological interventions are advised to be administered as early as possible in the

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course of the illness since certain treatments may be more useful in patients at earlier stages of BD.^{13,14}

The targets of different psychological interventions may vary, although their boundaries are blurred, and they often address similar issues. Some authors have recently attempted to determine the efficacy of adjunctive psychological interventions for BD in terms of the number needed to treat (NNT).¹⁷ The NNT was calculated from all published RCTs that assessed the efficacy of psychological interventions in BD patients aged 18 years and over using comparator groups. The results and the characteristics of the included trials are shown in Table 1.

A novel metric, the polarity index, was used to rank interventions according to their ability to prevent manic versus depressive episodes. The index, first described in 2012²⁰ and validated in 2014 for the pharmacological treatment of BD,²¹ is the ratio between the NNT for the prevention of depression and the NNT for the prevention of mania. This information may be helpful in choosing a specific adjunctive psychotherapy in the context of individualized, long-term treatment of BD.¹⁷

METHODS

A PubMed search of all English-language articles published until June 2013 was performed, using the search terms *psycho* intervention* cross-referenced with *bipolar disorder*. The search was supplemented by a manual review of the reference lists from the identified publications; 126 articles were reviewed. We selected RCTs comparing the efficacy, tolerability, or feasibility of psychological interventions in BD patients aged 18 and over to defined groups. All articles were independently reviewed by two of the authors (Drs. Colom and Popovic), who appraised the overall methodological quality and relevance to the question at hand. Only relevant, good quality studies were included—assessments that were determined based on the authors' clinical opinions. Discrepancies were resolved by consensus. The aim of this study was to assess all the trials published to date in order to highlight unexplored areas deserving further research.

RESULTS

Adjunctive psychotherapies for BD are based on educating patients or caregivers on the identification of early warning signs and symptoms, and of relapse indicators; on the regulation of lifestyle; and on stress-management strategies. As in any evolving field, research on psychological interventions for BD ranges from those areas that have a solid evidence base (e.g., relapse prevention, adherence enhancement, identification of early warning signs) to unexplored territory that requires further investigation. The latter is described in more detail below.

Bipolar Depression

When used in combination with mood stabilizers, bipolar-specific psychotherapies were hypothesized to shorten time

to recovery in patients with BD.^{22,23} A small proof-of-concept study (n = 17 patients) on interpersonal and social rhythm therapy (IPSRT) suggested its feasibility in treating acute depression in BD II patients,²⁴ but the dearth of any evidence-based research is glaring. IPSRT, an adaptation of interpersonal psychotherapy for depression, uses a problem-solving approach to interpersonal problems by encouraging patients to regulate daily routines and circadian rhythms. In a recent pilot study assessing the feasibility and acceptability of IPSRT compared to treatment with quetiapine as a treatment for BD, no differences in outcomes were detected.²³ In addition, given the extremely small sample size of 25 and the lower observed response rates across groups than in all prior trials of quetiapine for BD II, the results are unpersuasive.

One study, STEP-BD, suggested that intensive psychosocial treatment as an adjunct to pharmacotherapy was more beneficial than brief treatment as a means of enhancing stabilization in BD.²² Given, however, that the data on the efficacy of psychological interventions for BD are inconclusive, psychotherapy for BD remains absent from treatment guidelines. Nevertheless, in view of the risks associated with antidepressants²⁵ and the limited action of other agents,²⁶ psychosocial and psychotherapeutic interventions for BD are much needed.

Cognitive Impairment

Cognitive deficits in BD are reported to be present across all mood states, with executive functioning, episodic memory, verbal memory, psychomotor speed, and sustained attention being most consistently impaired.^{27,28} Given the impact of cognitive problems on psychosocial outcomes in BD even after adequate control of symptoms, the development of psychotherapeutic interventions targeting cognitive dysfunction is imperative for improving recovery rates and quality of life. In addition to influencing functional outcome and quality of life, this cognitive dimension of the illness is also a potential predictor of response to evidence-based psychosocial interventions.²⁹ Evidence of the positive effects of integrated psychological therapy on neurocognition, social cognition, psychosocial functioning, and negative symptoms in patients with schizophrenia is encouraging.³⁰ Pooled data coming from small studies on bipolar and schizoaffective disorders are also promising.³¹ Functional remediation,³² a technique addressed at effectively improving not only cognition but also functioning in BD patients, will probably represent the next big step in psychotherapy for BD in the upcoming years.

Bipolar Disorder in the Elderly

Existing psychotherapy trials exclude individuals above 65 years of age. The cutoff is not unusual when trialing a new intervention; however, given the aging population and the predicted growth in the number of older adults, studying and understanding this population may have important implications for intervention strategies in clinical care and also for geriatric research. A pilot study on skills training for medication adherence in older adults showed improvement in

Table 1 Double-Blind, Randomized, Controlled Trials Assessing the Efficacy of Adjunctive Psychotherapies in Maintenance Treatment of Bipolar Disorder: Characteristics and Efficacy^a								
Study	Trial characteristics				Study results			
	Intervention	Control	Inclusion criteria (maintenance phase)	Trial components	NNT mania	NNT depression	Depression vs. mania	Polarity index
Perry et al. (1999) ²	Brief technique-driven interventions	Routine care	BD I or II ≥ 2 relapses, 1 in previous year Age: 18–75 years No primary substance abuse	7–12 sessions	3.9	13.1	Mania > depression	3.36
Lam et al. (2003) ⁴	CBT	Treatment as usual	BD I ≥ 2 episodes in past 2 years or 3 episodes in past 5 years Age: 18–70 years No substance use disorders; not suicidal Pharmacological treatment Current euthymia; BDI < 30 & MRS < 9	14 sessions in first 6 months + 2 booster sessions in second 6 months Performed by psychologist	9.6	3.2	Depression > mania	0.33
Miklowitz et al. (2003) ⁵	Family-focused therapy	Crisis-management & treatment as usual	BD I or II acute episode in past 3 months Age: 18–65 years No substance use disorders in previous 6 months No developmental disability or neurologic disorder Regular contact with a caregiver English-speaking	2 years, with pharmacotherapy for entire length of study Active interventions (for initial 9 months of study): Family-focused therapy: 21 sessions ^b Crisis management: 2 sessions ^c Duration: 9 months pharmacotherapy for 2 study years	13.2	5.6	Depression > mania	0.42
Colom et al. (2003) ³	Psychoeducation	Meetings without intervention	BD I or II Age: 18–65 years No substance abuse, mental retardation, organic brain damage, or deafness 6 months of euthymia (YMRS < 6; HDRS-17 < 8)	21 x 90-minute sessions + 2-year follow-up	7.5	5.5	Depression > mania	0.73
Lam et al. (2005) ¹⁸	CBT	Treatment as usual	BD I: ≥ 2 episodes in past 2 years or ≥ 3 episodes in past 5 years No substance use disorder; not actively suicidal	30 months CBT + medication vs. medication alone 12–18 individual sessions in 6 months	5.7	3.6	Depression > mania	0.63

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Table 1 Continued		Trial characteristics				Study results		
		Intervention	Control	Inclusion criteria (maintenance phase)	Trial components	NNT mania	NNT depression	Depression vs. mania
Reinares et al. (2008) ^f	Caregiver group psychoeducation	Meetings without intervention	Caregivers of BD I or II patients Age: 18–60 years On pharmacological treatment for BD Euthymia ≥ 3 months	12 weeks of intervention and 1-year follow-up	5.0	8.9	Mania > depression	1.78
Colom et al. (2009) ^{10,b}	Psychoeducation	Meetings without intervention	BD I or II Age: 18–65 years No substance abuse, mental retardation, organic brain damage, or deafness 6 months of euthymia (YMRS < 6; HDRS-17 < 8)	21 x 90-minute sessions + 5-year follow-up	7.5	3.7	Depression > mania	0.78
Lobban et al. (2010) ⁹	Enhanced relapse prevention for BD	Treatment as usual	BD I or II: ≥ 2 relapses, 1 in past 12 months or 2 in past 3 years No primary substance abuse, rapid cycling, or organic cause Euthymic ≥ 4 weeks	6 x 1-hour sessions Care coordinators (trained by a nurse)	40	40	Mania = depression	1
Meyer & Hautzinger (2012) ¹⁶	CBT	Supportive treatment	BD I or II Age: 18–65 years No current substance dependency, cognitive impairment, current psychological treatment, primary diagnosis of non-affective disorder, current affective episode, substance-induced affective disorder, or affective disorder due to a general medical condition	20 sessions of CBT or supportive therapy over 9 months Follow-up: 24 months	19	5.4	Depression > mania	0.89

BD, bipolar disorder; BDI, Beck Depression Inventory; CBT, cognitive-behavioral therapy; HDRS, Hamilton Depression Rating Scale; MRS, Bech-Rafaelsen Mania Rating Scale; RCT, randomized, controlled trial; YMRS, Young Mania Rating Scale.

^a Adapted and expanded from Popovic et al. (2013).¹⁷

^b The number of prior episodes for the family-focused therapy group was 7.9 ± 17.9.

^c The number of prior episodes for the crisis-management group was 5.7 ± 13.4.

^d This study was the five-year follow-up of the sample in Colom et al. (2003).³

medication adherence, management ability, depressive symptoms, and selected indices of health-related quality of life.³³ Notwithstanding the limitations imposed by the small sample size of 21, the absence of a comparator, and the lack of follow-up data, the promising preliminary data justify an RCT. As yet, such a study has not been undertaken, and the need for interventions designed for BD patients in later life remains unmet.

Poor Physical Health in Bipolar Patients

Patients with severe mental illnesses, including BD, have around 20% (13–30 years) lower life expectancy than the general population. High mortality rates in these patients are mostly attributable to cardiovascular and cerebrovascular causes, most likely due to poor life style and high rates of smoking, obesity, and metabolic syndrome.³⁴ Reported rates of obesity (defined as ≥ 30 body mass index) and metabolic syndrome in BD are around 70% and 22%–30%, respectively.³⁴ Given that many of the widely prescribed medications have weight-related side effects,³⁵ a psychoeducation program oriented toward physical wellness—one encouraging regular exercise³⁶ and the monitoring of metabolic abnormalities³⁷ (e.g., waist circumference measurements, glycemia monitoring, lipemia and insulin physiology)³⁸ could be beneficial in this population.

Anxiety as a Mediator

Anxiety disorders represent the most frequent comorbidity of BD.³⁹ A review examining the effect of psychosocial treatments in the BD population conducted by Provencher and colleagues⁴⁰ highlighted a surprising paucity of studies on the topic, which were all small-scale and exploratory. In view of the small number of studies and the potential interactions between treatments, the review suggested that the most promising option was sequential CBT treatment, followed by mindfulness-based CBT and relaxation training. Interpersonal therapy, family therapy, and psychoeducation alone did not seem to be valid alternatives. Furthermore, the review found that the effects may diminish in long-term treatment, and adaptations were hypothesized to be necessary in order to augment and sustain intervention benefits. However, the largely preliminary data available to date—consisting primarily of case studies, open trials, and secondary analyses—are clearly insufficient. They illustrate the need both to perform RCTs comparing different forms of psychotherapy and to develop new protocols specifically designed for bipolar patients with comorbid anxiety disorders.

Other areas that require further research include the potential role of preventive psychotherapy in pregnant women who do not take medication, behavioral interventions to reduce the burden of medical comorbidity linked to BD, and the design of specific interventions for patients with comorbid disorders (such as obsessive-compulsive disorder).

Existing BD psychotherapy trials have had flawed trial designs, which may have influenced outcomes and render

them difficult to compare. All of the following raised potential problems for reaching coherent conclusions from the available studies:

- Variations in the number of sessions
- Variations in defining placebo comparators
- Lack of trials comparing adjunctive interventions to “treatments as usual” (as the control comparators)
- Variations in patients’ medications (which were often not even specified)
- Heterogeneous study samples (with some including patients with BD I, some including both BD I and II, and some including euthymic or acute patients)
- Variations in definitions of euthymia (and of its required duration)
- Variations in exclusion criteria (e.g., number of previous episodes and presence of comorbid pathologies)
- Variations in scales and outcome measures
- Variations in treatment protocol even when the same intervention (e.g., CBT) is used¹⁷

In view of the above shortcomings of the available research, this area presents many research challenges that are as exciting as they are unexplored.

CONCLUSIONS

BD, both in research and in clinical practice, frequently shows harmonic integration between drug treatment and psychological intervention. A critical need to better define the profile of BD patients most likely to respond to specific interventions—either by genomics or by identification of (bio)markers—remains unmet. Despite recent advances in knowledge, the field of psychological therapies for treating BD continues to be a major clinical challenge. Future research should establish the potential role of psychological interventions in this population.

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