

## Bipolar disorder – from a biological to an integrative approach. The role of cognitive-behavioral therapy in the treatment of bipolar disorder

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**Summary:** Bipolar disorder (BD) used to be considered as a pure biological condition, with episodic course and good remissions. Nowadays long-term consequences and psychosocial disturbances persisting beyond manic or depressive episodes have been recognized. Priority, acute phase treatment was the main target of therapeutic strategies. Currently the maintenance treatment and prevention including periods of remission but beginning already in the acute phase became the most important aims of BD treatment. The consequence of such an approach is the inclusion of psychotherapy and social interventions in combination with pharmacotherapy. Psychotherapy enables achieving social recovery, relapse prevention as well as improvement of compliance which determines largely the efficacy of treatment. Cognitive – behavioral therapy presents especially encouraging results in this field.

**Key words:** bipolar disorder, psychotherapy, cognitive-behavioral therapy, compliance, comorbidity

### Introduction

Since Kraepelin's concept of manic-depressive illness as a psychotic illness with "endogenous" etiology, traditional approach to bipolar disorder (BD) has been largely biological. Indeed, there is compelling evidence for its biological etiology e.g. heritability rate for BD is only comparable to autism and attention-deficit/hyperactivity disorder (ADHD) [1]. Unfortunately, as a consequence of the biological approach, a bipolar patient has been classified as a bad candidate for psychotherapy either due to poor insight, strong or excessive dependence on clinician or due to symptoms specific to acute manic phase like poor concentration, distractibility, labile mood etc. While research in neurobiology is central to understanding of BD, psychosocial research appears to be equally vital. Given the emerging realization that mind and brain are not different entities belonging to different realms of experience and growing acceptance for the vulnerability-stress model, the distinction between the biological and psychosocial aspects of illness – which is the heritage of the reductionistic Cartesian dualism - begins to break down. Both – medication and psychotherapy are acting through the same final common pathway – the brain. This view is supported by recent work in obsessive-

compulsive disorder (OCD), where behaviour therapy was shown to produce similar changes in PET neuroimaging as did medication treatment, leading Baer to suggest that behaviour therapy may be a form of “endogenous serotonin therapy” [2].

### **Rationale for combined treatment of BD**

According to clinical data concerning a variety of problems related to bipolar disorder there are five main reasons for combined treatment: 1. Influence of life events and regular rhythm of life routine, 2. Unsatisfactory results of pharmacotherapy, 3. Comorbidity, 4. Non-compliance, 5. Complexity of BD.

#### **Influence of life events and regular rhythm of life routine**

It has been proven, that influence of life events and regularity of everyday life routine play an important role in the period prior to the onset of a bipolar episode. Disruption of sleep and routine can lead to deregulation of circadian rhythms and the motivational system, resulting in prodromal symptoms. Disrupted social rhythm significantly increases risk of manic episode [3]. Factors like unstable working schedule, disruptions of circadian rhythms or long distance travel – especially those connected with jet lag – hold mania inducing potential [4]. The exact nature of life events and social disruptions may determine the specific prodromal symptoms that occur – events involving goal attainment are associated with the development of manic symptoms [5], whereas negative life events, low social support and low self-esteem predict the development of depressive symptoms [6]. Since life events and regular life rhythm are surely not biological in nature, there is a clear indication for combining pharmacotherapy with psychosocial interventions.

### **Unsatisfactory results of pharmacotherapy**

Studies in the 1960's and 1970's suggested that lithium was an effective form of prophylaxis in BD treatment. However, reviews of more recent randomised controlled double-blind trials of mood stabilisers have suggested that these medications are not as effective at preventing relapse as initially reported [7]. There are still relatively high rates of relapse. 40% of bipolar patients relapse in one year [8], and only one third of bipolar patients achieve full symptomatic remission. Lifetime relapse rates for bipolar I and II are respectively as high as 72.9% and 60% [9]. Furthermore, a significant proportion of patients with BD do not seem to benefit from mood stabilising medication with lithium either because of inadequate response or poor compliance due to side effects. Although further research trials are required to assess efficacy of other medications as carbamazepine and valproate, their efficacy appears to be similar to that of lithium [7]. It is worth noting that combined medication i.e. lithium plus other mood stabiliser such as carbamazepine or valproate appears superior to monotherapy in achieving prophylaxis [10, 11, 12]. Nonetheless there are still relatively high rates of relapse on combined medication. For example, Denicoff et al [11] reported that combined lithium and carbamazepine had some success in only 50% of patients with rapid-cycling BD. Despite advances in the pharmacologic treatment of bipolar disorder,

it is clear that additional strategies are needed to provide patients with longer-term mood stability.

### **Comorbidity**

Bipolar disorder is a highly comorbid condition. In the National Comorbidity Survey, all identified bipolar I individuals suffered from at least one, and often up to three or more, comorbid disorders [12]. The most common comorbid disorders include the full range of anxiety disorders, substance use disorders, and personality disorders. The estimates of comorbidity in BP vary among studies due to use of various criteria and diagnostic tools as well as populations studied (general, out-and/or inpatient). Reported lifetime prevalence of alcohol and drug abuse/dependence in BP subjects range from 21 to 69% [13, 14, 15, 16, 17, 18]. The estimates of lifetime anxiety comorbidity are similarly high and range from 24 to 61% [19, 20, 21]. The most common comorbid anxiety disorders in majority of studies are panic disorder with or without agoraphobia and OCD. The reported prevalence for social phobia, generalized anxiety disorder and post traumatic stress disorder are also elevated in many studies. Moreover for categorically defined personality disorders the prevalence range can exceed 60% [22].

Comorbidity has been associated with suicidality, higher relapse rate, younger age at onset of affective symptoms, more depressive episodes, more mixed features, more severe episodes, poorer compliance, rapid-cycling, more hospitalizations, resistance to pharmacotherapy and lower Global Assessment of Functioning Scale (GAF) scores across studies [23, 24].

Psychotherapy proved its effectiveness in majority of the mentioned disorders, thus regarding the fact that the presence of comorbid conditions appears to be the rule rather than the exception in people with BD, there is a clear indication for combined psychosocial treatment.

### **Noncompliance**

Nonadherence to treatment has been identified as a frequent cause of recurrence or relapse of bipolar disorder [25, 26]. Recent reports show, that one in three persons with bipolar disorder fail to take at least 30% of their medication [27]. Even among those receiving outpatient treatment, as many as 75% have been found to experience disruptions in consistent medication maintenance within a 1-year period [28]. General prevalence of nonadherence with mood stabilizers ranges from about 18% to 52% [29]. These issues are particularly important to address, because poor medication adherence is one of the most robust predictors of hospitalization as well as suicide [30, 31].

High rates of nonadherence are common to many medical treatments. However some issues may be specific to bipolar disorder. One of the most important problems occurring in the course of treatment of the manic episode is a patient's inclination to refuse medication due to a feeling of being deprived of happiness and power. In this case symptomatic improvement results in the lack of motivation for treatment. Simultaneously impaired motivation for treatment characterizes depressed patients.

However in a depressive episode, it is one of the core symptoms of disease. Since other factors – like side-effects – commonly contribute to treatment rejection in BD, promotion of treatment adherence must be integrated into medication management of bipolar illness if optimum outcomes are to be achieved [32].

ComplexityBD is a biological disorder with non-biological, long-lasting consequences. It grossly interferes with many areas of life. Its common negative consequences are: 1. Global impairment of life quality, 2. stigmatization in work and family, 3. social isolation, 4. guilt and decreased self esteem resulting in hopelessness, 5. demoralization and dramatically increased suicidality. Since medication influences those areas only indirectly and non-specifically, again psychotherapy is strongly recommended.

Life quality of bipolar patients is significantly worse than among monopolar subjects. Most mental health consumers report stigma from family members, employers and even within their religious organization [33]. Hence, isolation and self esteem consequences of this disorder are very important [1].

One third of individuals remain unemployed a full year after hospitalization for mania [34]. BD is projected to become the sixth leading medical cause of disability-adjusted life years worldwide by the year 2020 [35]. Regarding high relapse rates and the difficulties in maintaining unemployment and social relationships, it is not surprising that hopelessness and demoralization are common in this population. Suicide rates reaching 0.4% per year in men and women diagnosed with bipolar disorder are over 20–30 times higher than in the general population [8, 9, 36].

Treating BD with medication alone appears to be only a partial solution. Even an unquestionable upgrade of drug treatments does not ensure good social outcomes, coping with subsyndromal symptoms and sufficient maintenance management. Effective, long-term approach requires pharmacological and non-pharmacological treatments combined with therapeutic alliance that facilitates a proactive, preventive approach to the illness [37].

### **Non-pharmacological strategies in the treatment of bipolar disorder**

Various psychotherapeutic approaches have been conducted with bipolar patients. They are primarily psychoeducational and cognitive-behavioral although research has been done with family therapy, marital therapy, cognitive-behavioral therapy, interpersonal and social rhythm therapy, behavioral family management therapy and interpersonal therapy, either in individual and group mode [38, 32, 39]. Researches on effectiveness of psychotherapy in BD are still in their infancy, however, a range of them appears to benefit people with bipolar disorder. Among the mentioned approaches cognitive-behavioral therapy (CBT) deserves attention for a few pragmatic reasons: it shares the characteristics of a clinically effective short-term psychological intervention [40] and it impacts on symptoms, social functioning and risk of relapse [41]. CBT is also one of best researched approaches so far. Other interventions (excluding psychoeducation) do not appear to be supported by sufficient evidence [42]. Furthermore, therapies based on teaching patients new coping skills, like cognitive

therapy, may be particularly appropriate for bipolar disorder according to recent evidence that particular coping skills and behavioral responses are important in the course of bipolar illness [7].

### **Cognitive-behavioral therapy of BD**

CBT is based on an assumption that thinking, mood and behavior influence each other reciprocally. Therefore the therapist teaches patients to develop awareness of their thoughts, moods and behaviors in order to alter those thoughts and behaviors that are dysfunctional. Combination of thoughts monitoring and behavioral change is complementary to the psychosocial research on prodromes and routine in patients with BD, indicating that CBT may be a useful approach in such cases [7]. CBT for bipolar disorder has been conceptualized as an adjunct to medication rather than as a replacement for it. Furthermore, it has been designed as a relapse prevention treatment, not as an acute treatment, thus attempts to modify CBT for BD have concentrated on working with relatively euthymic patients outside of major depression or manic episode [7].

The main goals of cognitive-behavioral therapy in patients with bipolar disorder are: 1. To facilitate acceptance of the disorder and the need for treatment; 2. to help the individual to recognize and manage psychosocial stressors and interpersonal problems; 3. to improve medication adherence; 4. to teach coping strategies for depression and hypomania; 5. to teach early recognition and monitoring of relapse symptoms and specific to them coping techniques; 6. to improve self management through homework assignment and 7. to identify, monitor and modify negative automatic thoughts and underlying maladaptive assumptions and beliefs; 8. to develop structured daily schedules [43, 44, 45].

The number of reports on the efficacy of adding either individual or group CBT to medication in BD is still not numerous yet continuously growing. Over the past twenty five years small group studies and case reports were published. Many researchers [46, 43, 47, 48, 49, 50] have reported that combined cognitive-behavioral and pharmacological treatment produced significantly reduced relapse in comparison to routine mood stabilizing treatment. In 1984 Cochran reported that patients receiving group cognitive therapy had significantly fewer hospitalizations and were more adherent to lithium therapy than standard clinical care group. The patients were randomized, however, the principal limitation of the study was small sample size ( $n=28$ ). [36]. In the study by Fava et al CBT proved it's effectiveness in reducing of residual symptomatology and enhancing lithium prophylaxis in a group of bipolar I patients (a 2- to 9-year follow-up;  $n=15$ ) [39]. Scott et al [50] in a 42-patient randomized pilot study examined the effect of 20 sessions of cognitive therapy (CT). At 6-month follow-up, subjects allocated to the cognitive therapy group showed statistically significantly greater improvements in symptoms and functioning as measured on the Beck Depression Inventory, the Internal State Scale, and the Global Assessment of Functioning than those in control group. 70% of subjects from the therapy group viewed CT as highly acceptable. Though encouraging, these studies had small sample sizes, such

that any conclusion from them needs to be tentative [7]. Perry et al in a single blind randomized controlled trial with a larger sample (n=68) of bipolar remitted patients proved, that patients who learned to identify early symptoms of relapse and seek prompt treatment from health services had significantly fewer manic relapses and days in hospital than control subjects. Moreover they presented significantly higher levels of social functioning and better work performance. However, this trial was of more psychoeducational than cognitive-behavioral nature and had no significant impact on depression, therefore researchers suggested that more formal cognitive therapy may be important in producing significant changes in this area. [51]. Lam et al [52] have reported that combining of routine mood stabilizing medication with cognitive therapy significantly reduces relapse rates in bipolar patients in comparison to mood stabilizers alone. More recently, a full-scale randomized controlled trial of cognitive therapy for bipolar disorder has been completed [52]. 103 patients with bipolar I disorder were randomized either to treatment-as-usual group or to combined therapy (medication + CBT) group. At 12 months the combined therapy group comparing to treatment-as-usual group had significantly fewer bipolar episodes reflected by cumulative relapse rates (44% vs. 75%); fewer days in bipolar episodes (27 vs. 88); fewer hospitalizations and were more adherent to treatment [52]. That trial was continued and in the follow-up phase of the study [53] the cognitive therapy group had a significantly better outcome characterized by longer time to relapse, however the effect of relapse prevention appeared mainly in the first year. The cognitive therapy group also spent fewer days in bipolar episodes. Multivariate analyses of variance showed that those patients exhibited significantly better mood ratings, social functioning, coping with bipolar prodromes, and dysfunctional goal attainment cognition [53].

### Conclusion

Combination of psychotherapy and pharmacotherapy appears successful in allowing bipolar patients to achieve better symptomatic and functional recovery as their therapeutic goals are complementary. A growing body of evidence documents the value of structured psychotherapeutic interventions for the co-management of BD in the context of ongoing medication treatment. Preliminary results regarding effectiveness of cognitive-behavioral therapy in the treatment of bipolar disorder are encouraging and indicate that CBT has particular characteristics that may benefit bipolar patients. It's collaborative, stepwise approach may be helpful in increasing compliance, improving quality of life and functioning, early symptoms recognition, decreasing depressive symptomatology, number of hospitalizations and risk of relapse. To improve medication compliance and to help patients to identify prodromes of relapse it should be considered early in the course of illness. Still more precise, larger-scale and rigorous randomized clinical trials are needed to confirm the short-term and long-term efficacy of CBT in bipolar disorder. Understanding of cognitive processes specific for BD is necessary in order to allow us to refine and develop techniques and interventions unique for this disorder.

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