Psychosocial interventions and medication adherence in bipolar disorder

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Recent research has indicated that psychosocial interventions can have a valuable role in reducing the substantial psychosocial disability associated with bipolar disorder. Randomized controlled trials of these interventions indicate that improvements are seen in symptoms, psychosocial functioning, and treatment adherence. These interventions, systematically presented in the form of standardized treatment manuals, vary in format, duration, and theoretical basis. All are meant to augment pharmacotherapy, which represents the standard of treatment in the field. Modalities that have gathered the most empirical support include cognitive-behavioral therapy, family-focused therapy, interpersonal and social rhythms therapy, and psychoeducation. The enhancement of adherence to pharmacotherapy is a common therapeutic target, due to the association of nonadherence with higher relapse rates, hospitalization, and health care costs among people with bipolar disorder. Given the complexity of nonadherence behavior, multicomponent interventions are often required. In this review, we provide an overview of the rationale, evidence base, and major psychotherapeutic approaches in bipolar disorder, focusing on the assessment and enhancement of medication adherence.

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The functional consequences of bipolar disorder are staggering. Bipolar disorder is the sixth leading cause of years lost to disability among all medical conditions, according to the World Health Organization.[1] The annual costs of treating bipolar disorder are estimated at 45 billion dollars per year. Employed people with bipolar disorder experience about 65 lost work days per year, more than double than that of people with major depression,[2] and patients report a high degree of other psychosocial impairments in large cross-national surveys.[3] Approximately 10% of people with bipolar disorder die by suicide—among the highest rates of any psychiatric disorder. To attempt to reduce the severity of this disability, psychosocial interventions have served as a complement to pharmacotherapy for many years. However, structured augmentative psychosocial interventions for bipolar disorder have only recently been empirically evaluated in large, randomized, controlled clinical trials. The theoretical and practical approaches in these interventions vary. However, the enhancement of adherence to mood-stabilizing medications is a common goal to nearly all of them, as adherence generally serves as a foundation for rehabilitation strategies, and nonadherence is a risk factor for multiple negative outcomes (eg, hospitalization).

In the following review, we describe the current approaches to psychotherapeutic interventions in bipo-

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Selected abbreviations and acronyms

CBT	*cognitive behavioral therapy*
FFT	*family focused therapy*
IPSRT	*interpersonal and social rhythms therapy*
STEP-BD	*Systematic Treatment Enhancement Program for Bipolar Disorders*

lar disorder and the evidence for their effectiveness, with a focus on methods for enhancing adherence to psychopharmacological treatment for bipolar disorder. Our review is based on a literature search through PubMed, google.scholar.com, and PsycINFO, from which we selected English-language articles published in peer-reviewed journals published after 1990 describing psychosocial interventions for bipolar disorder and medication adherence.

Emergence of psychotherapy

There are a number of hypothesized reasons as to why psychotherapy was not a widely accepted component of treatment recommendations for bipolar disorder until recent years. The disorder was thought to have a biological diathesis, given the evidence for its heritability. Therefore, it was assumed that modifying the course of the illness would be difficult through behavioral and environmental means. Another reason for the lack of study of psychotherapy for bipolar disorder was the belief that attainment of interepisode recovery was largely achievable through pharmacotherapy; that is, provided that individuals adhered to mood stabilizers, acute manic or depressive episodes could be resolved, and the return to a state at or near to premorbid functioning could be expected. According to Kraeplin,[4] this interepisode recovery was among the primary differentiating features of "manic depression" from schizophrenia, the latter diagnosis was assumed to follow a progressive deteriorating and chronic course. Lithium was heralded as a breakthrough medication, and it was held that it would produce a high probability of prophylaxis against mania, which was thought to the most important therapeutic target of the illness in comparison with bipolar depression.

However, research connecting stressful life events and other perturbations to episode onset (eg, disruptions to sleep/wake cycles) suggested that environmental factors could modify the course of the illness (eg, the "kindling" model)[5,6] and, subsequently, that there were potentially modifiable aspects of bipolar disorder. In addition, the evidence from longitudinal prospective studies suggested that interepisode recovery was far less common than previously thought, even among individuals receiving state-of-the-art pharmacotherapy.[7,8] Naturalistic prospective studies sponsored by the National Institute of Mental Health's Collaborative Depression Study[7,9] and the Stanley Foundation Research Network[10] indicated that, when symptoms were monitored on a weekly basis, most people with bipolar disorder spent most of the time experiencing some level of psychiatric symptoms and related functional impairment. Furthermore, the functional consequences of bipolar disorder were quantified and compared with other chronic mental and physical illnesses, and this research strongly indicated that the impact of bipolar disorder on employment and other psychosocial domains was severe and enduring.[8,11,12]

Longitudinal research also indicated that bipolar depression is, on average, the most typical state and the most disabling aspect of the illness, compared with mania. The pharmacologic treatment of bipolar depression is a long-standing clinical controversy, with concerns over antidepressant-associated switch to mania coupled with limited efficacy of mood stabilizers in preventing or reducing bipolar depressive episodes.[13] Psychosocial interventions have been used effectively to treat unipolar depression for many years, without concerns over side effects.

The above factors provide a strong rationale for adjunctive psychosocial treatment in bipolar disorder. Over the past two decades, there have been a number of psychotherapeutic modalities specifically developed for the treatment of bipolar disorder. These therapies include cognitive behavioral therapy (CBT), interpersonal and social rhythms therapy (IPSRT), family-focused therapy (FFT), and psychoeducation. We will describe in greater detail these specific models (we elected not to discuss marital therapy or intervention for dually diagnosed individuals).

All of these psychotherapeutic modalities are intended to augment, not replace, pharmacotherapy. Each has been manualized, and each has been evaluated in at least one randomized controlled clinical trial. However, the theoretical basis and format of the therapies differ in a number of ways. These interventions vary in intensity (ranging from 3 to 25+ sessions), whether interventions are delivered to individuals, groups, or families, and what the therapeutic targets are. As with medication, psychosocial interventions can be assessed for their ability

to reduce symptoms of mania or depression, for their ability to prolong remission from active episodes, and improve ancillary outcomes such as medication adherence and psychosocial functioning.

Perhaps the most compelling evidence in favor of psychotherapy's effectiveness in bipolar disorder has come from the recently completed National Institute of Mental Health sponsored multisite effectiveness trial on the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD).[14] Within this large multisite practical trial, 293 participants with either bipolar disorder I or II, experiencing active depressive episodes were randomized to one of three intensive psychosocial interventions (CBT, IPSRT, or FFT) or to a control condition consisting of a three-session collaborative care intervention. Over 1 year, participants in the intensive conditions had a higher probability of recovery. A total of 64% in the intensive conditions vs 52% in collaborative care intervention attained recovery from depression, along with a experiencing a briefer median time to recovery (113 days vs 146 days). Greater improvement on a standardized measure of psychosocial functioning was also seen.[15] Interestingly, in secondary analyses, there was little distinction in effectiveness between the three intensive conditions. However, we will briefly describe the theoretical model and structure of these therapies, along with how adherence is integrated into their content.

Cognitive behavioral therapy

Adapted from the core components of cognitive therapy for depression, cognitive therapy for bipolar disorder has been evaluated in a number of open and randomized controlled trials, including the STEP-BD study described above.[16-18] These therapies typically last from 20 to 25 sessions, and are delivered in individual or group format. Activities in CBT for bipolar disorder include self-monitoring of moods and cognitions, addressing dysfunctional beliefs, and implementing healthier thinking patterns. The theoretical model undergirding CBT for bipolar depression is quite similar to that employed in unipolar depression—reducing and replacing cognitive distortions coupled with behavioral activation. The prevention of hypomania and mania is accomplished through reduction in impulsive behaviors, by teaching attention to excessively goal-oriented thoughts and destabilizing behaviors (eg, working around the clock on a new project).

Addressing adherence and beliefs about bipolar disorder is accomplished through examining attitudes and beliefs about medications. For example, the decisional balance is a cognitive task that is frequently used to elucidate the benefits and drawbacks for taking medications or not taking them (in a 2X2 matrix). The aim of this task is to highlight the potential risks of not taking medications, and to identify modifiable aspects of the drawbacks of taking medications (eg, weight gain). As described by Newman and colleagues, the goal of CBT in regard to adherence is to help the individual to "make peace" with medication.[16] The largest clinical trials in CBT for bipolar disorder have occurred in the United Kingdom. In a study conducted by Lam et al, CBT was positively associated with relapse prevention in a single-site randomized controlled trial with euthymic patients.[19] However, in a large multisite "pragmatic' trial which enrolled 253 patients in noneuthymic states, Scott et al[20] found little effect of CBT compared with a treatment as usual condition, except for those patients with shorter duration of illness.

Interpersonal and social rhythms therapy

IPSRT integrates interpersonal therapy with a behavioral component focusing on enhancing routine and structure of day-to-day events.[21,22] The theory emerged from research indicating that disruptions in social rhythms, such as interpersonal conflicts, effectively destabilized bipolar illness and the timing of daily activities. The therapeutic approach is individualized, and involves education about bipolar disorder, tracking and stabilizing daily events, and the psychodynamic interpersonal therapy component that is an evidence-based treatment for unipolar depression. The social rhythm component includes monitoring of daily routines (eg, time of awakening) with a tool called the Social Rhythm Metric,[23] and targeting stability in the timing of these routines. Medication adherence in IPSRT is typically addressed through education about bipolar disorder; however, the routinization of daily life also may include taking medications at structured times of the day, which may, in turn reduce the frequency of unintentional nonadherence. In addition to the STEP-BD study, there has been one other clinical trial comparing IPSRT with an intensive clinical management intervention.[22,24] There were few immediate differences between conditions on symptoms,[22] but an advantage in relapse prevention for IPSRT was seen at 2 years post-treatment.[24]

Family focused therapy

FFT was developed out of research on the role of expressed emotion in relapse in people with schizophrenia—in particular that interpersonal conflict and hostility are important disruptors representing the "stress" in the stress-vulnerability model of bipolar disorder. The goals of FFT are to enhance communication skills among family members, and increase supportive behaviors, along with increasing problem-solving behaviors.[25] There is a sequence of three modules: (i) psychoeducation, (ii) communication training, 7 to 10 sessions, and (iii) problem-solving training, 4 to 5 sessions. Prior to its evaluation in the STEP-BD study, Miklowitz et al found that FFT in comparison with a brief clinical management intervention showed longer survival intervals in terms of duration of remission along with improvements in adherence. The impact of FFT on adherence was posited to revolve around the depiction of bipolar disorder as a biological illness that is treatable, and that family involvement and "buy-in" to this model increased the family unit's attendance to medication adherence as a desired and shared goal.

Psychoeducation

Psychoeducation has been evaluated in clinical trials in Europe and in large health care systems in the United States. The content and intensity of these interventions vary. Psychoeducation can be delivered in a group format or individually. Session length ranges from three sessions to upwards of 20 sessions.[26] The content of psychoeducational interventions is generally in the development of self-management skills in coping with the illness, through providing education about the disorder and the importance of adherence, developing skills in identifying early warning signs, and avoiding dangerous activities such as substance abuse.[27,28] Participants are taught to monitor their moods using charts, recognize early warning signs of episode onset (eg, reduced sleep, irritability), and engage in action steps in effort to stave off full-blown mania or depression.

The effectiveness of these interventions has been evaluated in several large studies in the United States and Europe. In the United States, two multisite intervention trials have incorporated the Life Goals intervention into the chronic care approach, one in a private insurance population[29] and the other in a Veteran's administration population.[30] Interestingly, the intervention appeared to have greater effectiveness in reducing manic rather than depressive symptoms in the private insurance population study.[31] In Spain, Colom et al evaluated a 21-session psychoeducational program and found improvement in terms of recurrences, time to depressive, hypomanic, and manic episodes, and in hospitalization rates.[26] A tentative conclusion from the various studies on psychoeducation is that a longer duration of treatment strengthens effects, although a longer duration of treatment is also likely associated with higher rates of attrition.

Summary of psychosocial modalities

A number of tentative conclusions can be drawn from the rapidly growing body of research. First, it appears as though augmentative psychotherapy for bipolar disorder is feasible and implementable among people in various clinical states. As the practical trial in the STEP-BD study indicated, patients need not be in euthymic states or free of comorbidities to benefit from psychosocial treatment. Second, although not all trials have been positive, there is compelling evidence that psychotherapies can be beneficial in augmenting standard pharmacotherapy in bipolar disorder in terms of symptom reduction, episode prophylaxis, and improvement of adherence and psychosocial functioning. Third, there is some evidence, rather surprisingly, that these interventions are better at delaying the onset of mania than in addressing the active symptoms of depression (the STEP-BD study targeting bipolar depression is a notable exception).

The next evolution of clinical research on psychotherapy for bipolar disorder would need to address: (i) which intervention works best for which patients; (ii) how these interventions can be made available outside of academic medical centers; and (iii) what the essential ingredients of psychotherapy for bipolar disorder are. Bipolar disorder is an enormously heterogeneous condition, and it is highly likely that therapies would need to target subgroups of people with bipolar disorder to be adequately personalized. Presently, there are few evidence-based moderators or mediators of treatment effectiveness in bipolar disorder. In their negative trial of CBT for bipolar disorder, Scott et al[20] found that individuals with fewer previous episodes appeared to derive benefit from treatment, whereas those who had more episodes did not. Although these kinds of mediators require replication over multiple studies, it will be important to understand

who will and who might not benefit from augmentation with psychotherapy. In addition to clinical variables that might moderate outcome, whether and how interventions are accepted and experienced in different ethnic groups deserves study. In psychosocial interventions for other conditions, major efforts have been undertaken to adapt psychosocial treatments to culture-based preferences and values. There are also efforts under way to modify the above intervention modalities to address subgroups of people with bipolar disorder, such as those with chronic physical illnesses.[32]

In addition, understanding how these interventions can be successfully transported to community settings is a needed next step. While approximately half of the STEP-BD sample had attended counseling or psychotherapy in the community prior to their enrolment,[33] it is doubtful that many have access to the evidence-based psychotherapies described above. It is also unlikely, due to financing and staffing limitations, that 20-session packages, as implemented in the research studies cited above, will be feasible in many settings. A few multisite studies have examined how psychosocial interventions that are considerably less intensive than the STEP-BD interventions can be incorporated into a chronic care model approach in large health care settings (ie, the Veteran's Administration and a large Health Maintenance Organization), guided by an understanding of the organizational barriers and facilitators to implementation.[34]

Finally, the active ingredients of bipolar psychotherapy are difficult to ascertain. There are few or no identified differences in effectiveness between the modalities described above and, thus far, there have been no "dismantling" studies as have been conducted in psychotherapy for depression. Among the most often mentioned candidates as an active ingredient (and therapeutic outcome) is the enhancement of medication adherence. In the next section, we will briefly review the literature on medication adherence in bipolar disorder and we will present a model to enhance it.

Focus on medication adherence

The therapeutic approaches described above are divergent in their methods to a certain extent, but each involves education about bipolar disorder and its treatment, and each has some content oriented toward enhancing medication adherence. Nonadherence is likely one of the greatest reasons why medications may not work as well in the community as they do in efficacy studies evaluating pharmacotherapy.[35] Of course, adherence, in and of itself, is not a guarantee of good outcome, but medication remains the backbone of treatment for most people with bipolar disorder.

Suboptimal adherence to medications for bipolar disorder is common. Estimates for the prevalence of nonadherence in bipolar disorder vary greatly by study population and instruments used to assess adherence. However, it is estimated that 20% to 60%, with a mean of 40%, of individuals with bipolar disorder are nonadherent to prescribed medications at any given time.[36] A longitudinal study found that, among people who initiated lithium, the median time to discontinuation was only 76 days.[37] In that same study, the probability of hospitalization was twice as high among discontinuers versus continuers. Other studies have indicated that the consequences of nonadherence in bipolar disorder include greater propensity to relapse, higher hospitalization rates, and greater health care costs.[36,38,39]

Types of nonadherence

Nonadherence is a complex phenomenon with a variety of distinctions and risk factors. There no is definition as to what the optimal level of adherence is in bipolar disorder, as there is in pharmacotherapy for the infectious diseases (eg, HIV). Furthermore, nonadherence is a not a unitary or steady state phenomenon; nonadherence can be intermittent or continuous, and it can be specific to a single medication or to multiple medications. Moreover, nonadherence may be voluntary, such as deliberately not taking medication due to perceptions about its ineffectiveness, or it can be involuntary, such as forgetting or misinterpreting instructions. Nonadherence may also involve consuming too much medication. In a study examining service utilization among San Diego County public mental health clients with schizophrenia, the group with highest health care costs were those who were "overfillers" of antipsychotic medications, rather than "underfillers."[40]

Assessing nonadherence

In addition to its definition, the mode of measurement of nonadherence is also challenging, as there is no "gold standard." The choices of measurement strategies include self-report, pill counts, blood level, or microelectronic

devices. Subjective measures of adherence, such as self-report, offer probably the most convenient measure of adherence, although numerous studies in bipolar disorder or in other chronic illnesses have shown that they are subject to underestimation of actual rates of nonadherence. Caregiver reports may be less subject to under-reporting biases, yet a substantial proportion of people with bipolar disorder do not have caregivers who are aware of the individual's daily intake of medications.

More objective measures include pharmacy records, blood levels, and direct pill counts. The degree of difference in days between successive actual and prescribed refill dates identifies individuals who have taken fewer pills than prescribed; the outcome derived from these analyses include the Cumulative Gap Ratio or the Mean Possession Ratio.[41] The disadvantage of pharmacy data is that it must be intuited that refills completed on time equate to taking the medication, and time between refills is often over the course of months. Blood levels and pill counts are more direct measures of adherence, but unless they are a part of routine clinical care, they are impractical in many clinical and research settings. Furthermore, it still is possible to "fake" either of these measures, such as by throwing pills away in the case of pill counts or in taking medication on the day of the blood test. A newer technology, Micro Electronic Monitoring Systems (MEMS), involves tiny sensors placed in pill bottles that record a time stamp upon opening the bottle. These units are costly and may be impractical in a clinical setting, particularly among people with multiple medications to track.

Generally, the best approach to measuring adherence in both clinical and research settings is the use of multiple measures to converge on an estimate of adherence. By combining information from multiple measures, it is possible to form a composite measure of adherence by averaging, or by using the adherence measure with the lowest estimate of adherence. In patients with HIV, algorithms for deriving an estimate of adherence from multiple sources have been developed.[42]

There are ancillary measures that help to identify the processes involved in nonadherence. Performance-based measures do not address medication adherence directly, however, they measure medication management ability in a controlled setting. The Medication Management Ability Assessment[43] is an example of this kind of measure; it entails a mock medication regimen that the respondent is told to arrange the medications as they would in their daily life. Errors on this test can identify individuals who are at risk for unintentional nonadherence, along with the pattern of the errors. Attitudes and beliefs about medication, as well as satisfaction with medications, are also important covariates of nonadherence; an example of self-report measures addressing these construct is the Drug Attitude Inventory[44] and the Brief Evaluation of Medications Attitudes and Beliefs.[45] Another useful assessment tool is the AIDS Clinical Trials Group's Adherence Measure,[46] which includes a set of questions about reasons for nonadherence. Gathering the individual's perspective about what causes nonadherence behaviors can be essential to formulating an intervention strategy.

Risk factors for nonadherence

There are multiple and interacting risk factors for medication nonadherence, with no single profile for high risk for nonadherence. Conceptually, these can be divided into *patient-related*, *medication-related*, and *provider-related* risk factors.[47] Most research has been focused on patient-related risk factors.[48] Among patient characteristics that appear to be risk factors for nonadherence, the strongest support appears to be for comorbid substance use, younger age, lower education level, and cognitive impairment.

Additionally, attitudinal factors, particularly the denial of the need for medications/severity of the illness appear to account for a substantial proportion of variance in adherence.[49] In the Health Beliefs Model, an individual is likely to engage in a behavior, such as adherence, if they believe their condition is severe enough to warrant treatment, if the perceived benefits of treatment outweigh the drawbacks, and if cues to action are provided to initiate and maintain the behavior. It is likely that these factors change over the course of the illness. In the early stages, acceptance of the illness is lower and avoidance coping is higher,[50] potentially accounting for the relationship found between younger age and worse adherence. In our work with older adults, we have hypothesized that cognitive impairment and increasing medication burden may heighten the importance of cues to action in maintaining adherence.[51]

Medication-related risk factors are less clear, with some studies finding that higher rates of side effects, and greater medication burden (ie, more medication and/or more frequent dosing) related to worse adherence,

whereas some have found no association or the inverse.[52,53] Interestingly, in a large cross-national European survey, fears about future side effects (eg, fear of toxicity) or dependence on medication were more related to nonadherence than were experienced side effects, which were rarely endorsed a reason for stopping medications.[54]

Provider-related predictors of adherence include the quality of the therapeutic alliance and satisfaction with care provided.[48] Factors involved in the alliance would include the degree of agreement between in terms of treatment outcomes and importance of side effects. Another important correlate of nonadherence that has received less attention is problems with accessing health care and financing. It is unclear whether and to what degree financial barriers impact treatment utilization in bipolar disorder.

The strength of these risk factors may differ depending on the kind of nonadherence that is being assessed. Intentional nonadherence involves a conscious decision not take medication, and may relate more strongly to dissatisfaction with treatment and lack of perceived need for treatment.[48] Unintentional nonadherence may relate to cognitive deficits and to lower health care literacy, and may be of particular concern given the cognitive deficits associated with bipolar disorder. Adherence is described by Park and colleagues[55-57] as including a series of cognitive processes:

1. *Working memory* in transferring data from pill-bottle labels
2. *Prospective memory and executive functioning* in organizing and planning to take medications
3. *Long-term memory* in recalling medication dosage times.

This model has been applied to adherence and interventions for medically ill older adults,[57,58] although not to late-life psychiatric disorders. Cognitive impairment has been identified as a risk factor for nonadherence in bipolar disorder.[48,59] In a study of older adults prescribed antidepressants, cognitive impairment was the greatest risk factor for unintentional nonadherence.[60] From the larger body of literature on cognitive abilities and adherence in other chronic illnesses (eg, HIV), evidence suggests that memory deficits are not the sole cognitive ability implicated in nonadherence.[61] Deficits in executive function and attention relate to worse adherence[61,62] and medication management ability.[63,64] Cognitive deficits may reduce ability to comprehend the purposes and instructions of medications, which may also contribute to problems with adherence.[57]

Interventions to enhance medication adherence in bipolar disorder

Among therapeutic modalities for bipolar disorder, some address adherence more centrally than others. In a review of the effectiveness of psychotherapy for enhancing medication adherence in bipolar disorder, 7 of 11 clinical trials reviewed showed positive effects on medication adherence,[65] with greater effect found for multicomponent interventions that focused on medication adherence versus interventions that covered a broad set of problems or those that only included education.

The goal of psychosocial interventions focusing on medication adherence enhancement is typically to alter attitudes toward bipolar illness and need for medication, thus targeting intentional adherence. An implicit assumption is that once the participant is willing to take the medication, they will be able to manage medications and maintain adherence. However, examining the broader spectrum of interventions that have been evaluated in older adults with schizophrenia[66] or other chronic illnesses,[67] multicomponent interventions include training in medication management skills, as well. The following is a description of a model to enhance adherence in bipolar disorder that we have developed, which includes three components: education, motivational interviewing, and compensatory skills training.

Education

The primary goal is to increase knowledge about the properties of medications and awareness of the patient's role in managing medication. At a minimum, educational interventions should include printed information about the basic properties of mood stabilizers, antipsychotics, and antidepressants, such as their purposes, dosages and instructions, and factors that affect medication effectiveness. Coupled with medication-related education, the causes and consequences of bipolar disorder, and particularly useful to draw parallels to other chronic medical illnesses such as diabetes. Education should also strive to highlight the personal impacts of the illness, in order to make information more salient to the individual. A useful method of increasing personal awareness of bipolar disorder symptoms is to have participants complete mood and life charts.

Motivational interviewing

The goal of motivational enhancement interventions is to increase the probability of behavior change (ie, taking medications consistently), by highlighting the advantages of adherence, developing strategies to counteract the drawbacks, and, in general, increasing participant activation in developing a treatment plan. A useful tool is the "decisional balance" activity, which solicits perceived benefits and drawbacks of taking medications, a technique commonly employed in motivational interviewing.[68] To address the primary drawback of side effects, the use of a side-effect tracking form may assist in recognizing side effects, and subsequently a personalized plan can be developed to counteract chronic side effects. For example, goal-setting with respect to behavioral strategies to counteract weight gain or fatigue can be employed.[69]

Compensatory skills training

To reduce the amount of effortful cognitive processing in daily adherence behaviors, interventions encourage consistent medication taking habits and by simplifying the act of organizing medications. Interventions in this category are primarily intended to address unintentional nonadherence. A wide variety of strategies are available to increase the ease of taking medications, including medication tracking forms and external reminders/tools (eg, pillboxes, electronic medication reminders). These external cues are best coupled with behavioral strategies that facilitate recalling medication, including pairing activities with medication taking, developing routines around medication taking, and placing cues in the environment to trigger medication-taking behavior. It is vital that these strategies be personalized, and that the emphasis is on making the process of medication taking easier and less effortful.

In our pilot study of this intervention, which was an open trial that included 21 participants over the age 50, we evaluated a 12-session group intervention delivered to 6 to 8 participants with bipolar disorder at a time. The dropout rate was 25%, with attrition mostly due to transportation problems and medical comorbidities. Small to moderate pre-post effect sizes were seen in self-reported adherence and some depressive symptoms. These preliminary results suggest that the group treatment was feasible, acceptable, and produced pre-post improvements along important dimensions, although future clinical trials with objective measures of adherence and a credible control group would be necessary to ascertain its effectiveness.

Provider-level interventions

The interventions described above are all focused on enhancing adherence by increasing knowledge, acceptance, and management skills in the patient. However, there are a number of approaches to improve adherence by changing provider behavior. These can be categorized into attempts to: (i) increase ease of administration and (ii) enhance the working alliance. Simplifying dosing strategies by consolidation can enhance adherence and providing reminders and pillboxes. The working alliance and satisfaction with treatment can be enhanced by providing client-centered care, making effort to involve the patient in planning medication strategies and outcomes, and defining patient values in weighing treatment options.[48,69]

Emerging directions

In addition to discovering the mediators and moderators of psychotherapy's effectiveness in bipolar disorder, along with broadening access to evidence-based interventions, there are a number of other modalities that are in the earliest stages of development.

Integrative interventions addressing medical comorbidities

The medical burden in bipolar disorder appears to be higher than among nonaffected individuals.[70] The convergence of bipolar disorder and chronic physical illnesses, such as cardiovascular (eg, diabetes) and infectious diseases (eg, HIV, hepatitis) arise from a number of shared risk factors, including unhealthy lifestyles, risk-taking behaviors, and medication side effects.[70] In addition to increasing the burden and complexity of adherence vis a vis higher intensity of medication management, comorbid medical conditions negatively impact quality of life and health care utilization.[71] Furthermore, access to medical services may be diminished in bipolar disorder. Research identifying shared risk factors for nonadherence and other outcomes in bipolar disorder, such as cognitive impairment (see Moore et al in this issue, p 256), will inform future interventions.

Cognitive training and functional rehabilitation

In light of the cognitive deficits that have been identified in bipolar disorder,[72] it may be that cognitive remediation, either through restorative interventions (eg, boosting attention skills) or compensatory functional training (eg, using external reminders) could be useful. These interventions have been assessed in patients with schizophrenia.[73] Interventions that directly address specific functional consequences of bipolar disorder, such as difficulty maintaining employment, have also been called for.[15]

Consumer-driven care

To allay some of the impracticalities associated with providing intensive psychosocial treatments, peer-provided services may be useful in bipolar disorder. People with bipolar disorder could be trained to deliver manualized interventions, they could provide augmentative functions, or could extend the availability of services beyond the consultation of structured professionally led groups. Given that bipolar disorder is a chronic condition, these community-based approaches are attractive in that they can be and are already are sustained in the community. Mutual support interventions exist for bipolar disorder, and are exemplified by the support groups sponsored by the Depression and Bipolar Support Alliance (www.dbsalliance.org).

Sequence or stepped-care based strategies

A number of recent practical clinical trials have evaluated sequential treatment strategies. For example, the National Institutes of Mental Health-funded Sequenced Treatment Alternatives to Relieving Depression (STAR-D) trial first administered citalopram to all participants and then randomized unrecovered subjects to a variety of different treatment arms.[74] Such sequenced approaches to care mimic real world clinical decision making, and could be applied to the study of psychotherapy for bipolar disorder. The sequence of brief psychoeducation to intensive psychotherapy in unremitted individuals could be one logical approach to allocating psychosocial treatment to people with bipolar disorder.

Conclusions

These are turbulent times in the history of the treatment of bipolar disorder. Along with the expansion in medication options for bipolar disorder, the role of psychotherapy as an augmentative treatment has grown from a place of questionable utility to approaching evidence-based care in a relatively brief period of time. There are a number of modalities of psychosocial intervention for bipolar disorder that have been evaluated in randomized clinical trials, along with some emerging directions for future psychotherapeutic approaches. There is an inadequate understanding about the essential ingredients of these psychotherapeutic approaches, and little evidence to determine which works best for which subgroups of patients. However, addressing medication nonadherence is a common factor in many of these modalities, and has long been recognized as a central clinical concern in managing bipolar disorder. Limited evidence suggests that adherence can be improved with multicomponent interventions aimed at improving patient knowledge, acceptance, and management of pharmacotherapy, along with enhancing participation in the treatment decision-making process. A structured approach to the enhancement of medication adherence should be a part of the treatment regimen for all patients with bipolar disorder. While it certainly would help if medications were more effective with fewer side effects in the treatment of bipolar disorder, the combination of pharmacotherapy and psychosocial intervention may be the most potent route to attaining recovery. Discovering how to make evidence-based psychosocial intervention available and palatable to people with bipolar disorder will be a challenge for the future. ❑

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Adherencia a las intervenciones psicosociales y a la medicación en el trastorno bipolar

La investigación reciente ha señalado que las intervenciones psicosociales pueden tener un valioso papel en la reducción de la considerable incapacidad psicosocial asociada al trastorno bipolar. Los ensayos controlados y randomizados de estas intervenciones muestran que se ha obtenido mejoría en los síntomas, en el funcionamiento psicosocial y en la adherencia al tratamiento. Estas intervenciones sistemáticamente presentadas como manuales terapéuticos estandarizados, varían en el formato, la duración y las bases teóricas. Todas están referidas a aumentar la farmacoterapia, lo que representa el estándar de tratamiento en este campo. Las modalidades que han reunido el mayor soporte empírico incluyen la terapia cognitivo conductual, la terapia focalizada en la familia, la terapia interpersonal y del ritmo social, y la psicoeducación. El aumento de la adherencia a la farmacoterapia es un objetivo terapéutico habitual, debido a la asociación entre la falta de adherencia y la mayor frecuencia de recaídas, hospitalizaciones y costos de salud entre las personas con trastorno bipolar. Dada la complejidad de la conducta de mala adherencia, a menudo se requiere de intervenciones con múltiples componentes. En esta revisión se entrega una panorámica de las principales aproximaciones psicoterapéuticas - fundamentadas y basadas en la evidencia- para el trastorno bipolar, enfocándose en la evaluación y el aumento de la adherencia a la medicación.

Observance médicamenteuse et actions psychosociales dans les troubles bipolaires

Des travaux récents ont montré que l'inadaptation psychosociale importante liée aux troubles bipolaires pouvait être améliorée par des actions spécialisées dans ce domaine. Des études randomisées contrôlées récentes de ces dernières ont apporté des preuves que des améliorations sont possibles en termes de symptômes, fonctionnement et observance thérapeutique. Ces actions, systématiquement présentées dans des manuels d'utilisation standardisés, varient dans leur forme, leur durée et leur base théorique. Toutes sont censées potentialiser la pharmacothérapie, base du traitement de la maladie. Parmi les modalités les plus validées se trouvent la thérapie cognitivo-comportementale, la thérapie familiale, la thérapie interpersonnelle et des rythmes sociaux et la psychoéducation. L'objectif thérapeutique commun est une meilleure observance médicamenteuse car sa mauvaise qualité est associée à une augmentation des taux de récidive, d'hospitalisation, des coûts de santé parmi la population bipolaire. Compte tenu de la complexité des comportements de mauvaise observance, des actions composites sont souvent nécessaires. Dans cet article, nous proposons une mise au point des principales approches psychothérapeutiques basées sur des preuves et justifiées, en nous centrant sur l'évaluation et l'amélioration de l'observance thérapeutique.

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