Group Therapy for Patients With Bipolar Disorder and Substance Dependence: Results of a Pilot Study

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Background: The authors' goal was to pilot test a newly developed manual-based group psychotherapy, called Integrated Group Therapy (IGT), for patients with bipolar disorder and substance dependence.

Method: In this open trial, patients with DSM-IV bipolar disorder and substance dependence (N = 45) were recruited in sequential blocks to receive either group therapy (N = 21) or 6 monthly assessments, but no experimental treatment (N = 24).

Results: When compared with patients who did not receive group therapy, patients who received IGT had significantly better outcomes on the Addiction Severity Index drug composite score ($p < .03$), percentage of months abstinent ($p < .01$), and likelihood of achieving 2 ($p < .002$) or 3 ($p < .004$) consecutive abstinent months.

Conclusion: IGT is a promising treatment for patients with bipolar disorder and substance dependence, who have traditionally had poor outcomes. It is unclear, however, how much of the improvement among the group therapy patients is attributable to the specific content of the treatment. A study comparing this treatment with another active psychotherapy treatment is warranted.

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Bipolar disorder is associated with the highest risk among all Axis I psychiatric disorders for having a coexisting substance use disorder.[1] Although patients with bipolar disorder and substance use disorder have a particularly poor prognosis,[2–5] few studies of treatment for this dually diagnosed patient population have been conducted. We know of only 3 small open pharmacotherapy trials,[6–8] with a total sample size of 24 patients. Moreover, despite growing research interest in psychotherapeutic approaches to patients with bipolar disorder[9,10] or substance use disorder,[11,12] studies of psychotherapy for these populations have generally either excluded patients with both disorders or have not focused specifically on them. Indeed, we are aware of no previous trials of behavioral treatment specifically for patients with coexisting bipolar disorder and substance use disorder.

The major purpose of this study, conducted under the auspices of the National Institute on Drug Abuse (NIDA) Behavioral Therapies Development Program, was to develop and pilot test a manual-based group psychotherapy for patients with bipolar disorder and substance dependence. The treatment, called Integrated Group Therapy (IGT), was designed to integrate therapeutic approaches that are relevant to each disorder. We conducted a 6-month pilot study in which we compared substance use and mood outcomes of patients receiving IGT with outcomes of a cohort of patients with the same diagnostic characteristics who received no experimental treatment, but had monthly assessments (the non-IGT comparison group).

METHOD

Description of the Treatment

The treatment, which has been described in detail elsewhere,[13] consisted of 12 or 20 (depending on the version; see below) weekly hour-long therapy groups, each of which focused on a topic that was relevant to both disorders; groups ordinarily consisted of 5 to 8 patients. Sample topics included (1) denial, ambivalence, and acceptance; (2) self-help groups; and (3) identifying and fighting triggers. The treatment employed a cognitive-

behavioral relapse-prevention model,[14,15] which was designed to integrate the treatment of the 2 disorders by focusing on similarities between the recovery and relapse processes in bipolar disorder and substance use disorder. For example, we adapted a concept commonly discussed in substance abuse treatment, the "abstinence violation effect,"[14] to the treatment of bipolar disorder as follows. Many substance abusers feel hopeless and are tempted to quit trying to attain abstinence after a "slip" or "lapse"; patients with bipolar disorder may similarly feel like stopping their medications altogether after experiencing a mood episode despite complying fully with their pharmacotherapy regimen. The group therapy thus reviews strategies for dealing with a temporary setback in either disorder, emphasizing the types of thought patterns and behaviors that can either ameliorate or exacerbate such a situation in each disorder.

Each session began with a "check-in," during which patients reported on their past week's experience regarding (1) drug and alcohol use, (2) mood, (3) medication adherence, (4) encountering high-risk situations, and (5) use of coping skills. After a review of the previous week's session, the therapist focused on the session topic, using a mixture of didactic presentation and group discussion. The manual provided the therapist with guidelines for conducting each session, and patients received a handout each week summarizing the major themes of the session. Videotapes of the sessions were reviewed by the senior author for the purpose of therapist supervision.

Subjects could participate in concurrent psychosocial treatment without restriction; this was tracked monthly (see below). Patients had to agree to permit us to contact their prescribing psychiatrist, both for data collection and emergency purposes.

Development of the Treatment

The development of the treatment and the associated manual involved an iterative process. IGT was conducted 3 times: once by the senior author (R.D.W.), once by one of the coauthors (S.F.G.), and once by a Ph.D.-level psychologist. The manual was modified as the result of feedback from therapists, patients, and investigators, all of whom evaluated each session's strengths and weaknesses, and through review of the manual by 2 outside expert consultants. An investigator then conducted structured, open-ended interviews with all patients after they completed IGT to elicit their opinions about the treatment and suggestions for future groups. As a result of this process, the treatment was extended to 20 sessions in its third iteration to allow for reinforcement of major principles.

Subject Recruitment

Subjects were recruited in sequential blocks either for IGT or for monthly assessments only (non-IGT); although there was no actual random assignment, subjects could not choose one condition or the other. The first non-IGT cohort was recruited while the initial version of the manual was being developed. Once the manual had been written, the first IGT cohort was recruited. After the first IGT group was completed and while the manual was being revised and a new therapist trained, more non-IGT subjects were recruited. When the revised manual was completed, the second IGT group cohort was recruited; this process was repeated for the third non-IGT and IGT groups.

Subjects for the trial were recruited while inpatients at McLean Hospital (Belmont, Mass.), although the treatment (and the 6-month naturalistic assessment period for the comparison cohort) did not begin until after discharge. During recruitment periods, a research technician reviewed the substance use histories in the medical records of all McLean Hospital inpatients over 18 years old with an admission diagnosis of bipolar disorder. Inclusion criteria included (1) current diagnoses of bipolar disorder and substance dependence based on the Structured Clinical Interview for DSM-IV,[16] administered by a trained interviewer; (2) substance use within the 30 days prior to admission; (3) taking a mood stabilizer and giving consent for us to communicate with their pharmacotherapist; and (4) ability to give informed consent. Patients were excluded if they (1) had a medical condition that would prevent regular group attendance, (2) had an organic mental disorder or mental retardation, or (3) were planning to live in a residential treatment setting in which substance use was monitored and restricted (e.g., a therapeutic community).

Among the 86 screened patients who met the basic eligibility criteria of current bipolar disorder, current substance dependence, and substance use within the past 30 days, 45 patients entered the study: 21 in the IGT cohort, 24 in the non-IGT cohort. The reasons for nonentry were living too far away (N = 16, 18.6%), inability to return for regular visits (N = 11, 12.8%), not wanting to participate in research (N = 11, 12.8%), and seeing no need for treatment (N = 3, 3.5%). No statistically significant differences were found between the IGT and non-IGT cohorts in the reasons for not participating. After complete description of the study to the subjects, informed written consent was obtained.

Assessment and Follow-up Procedures

IGT subjects were assessed at baseline, each month during treatment, and monthly for 3 months after treatment completion. The non-IGT cohort participated in 6 monthly evaluations, which were identical to those that the IGT subjects received. All subjects were paid for completing each assessment.

As part of the monthly assessments, substance use data were obtained using the Fifth Edition of the Addiction Severity Index (ASI),[17] a widely employed and empirically validated multidimensional assessment of substance-related problems. The Timeline followback[18] assessment

method, a standardized interview that uses a calendar and documents actual calendar days of use, was used to supplement the drug and alcohol section of the ASI in quantitating the number of days of drug and alcohol use. Urine toxicology screens and breath alcohol assessments were also performed at each assessment. We have previously reported the high degree of validity of our self-report data with this population.[19] In the few instances in which urine screens indicated substance use not reported by the patient, a discussion was held with the patient and the self-report data reobtained. Mood symptoms were assessed with the Young Mania Rating Scale (YMRS)[20] and the Hamilton Rating Scale for Depression (HAM-D).[21] Medication compliance was assessed with an interview, described in detail elsewhere,[22] that we adapted from Jamison et al.[23]; subjects were asked to rate (on a 5-point scale ranging from "not at all" to "100% of the time") how often they had taken their medication as prescribed in the previous month. Participation in nonstudy treatments was tracked monthly with the Treatment Services Review[24] and the Treatment Summary, which we developed to monitor treatments likely to be attended by this patient population.

Statistical Analysis

The primary outcome domains were substance use and mood. Substance use was measured each month as follows: (1) ASI drug composite score, (2) days of drug use in the previous 30 days, (3) ASI alcohol composite score, (4) days of alcohol use in the previous 30 days, and (5) number of months abstinent from both drugs and alcohol. Mood was measured each month with total scores on the YMRS and the HAM-D. For these outcome measures, chosen a priori, 1-tailed statistical tests (described below) were employed (with $p < .05$ used as the standard for significance), since we hypothesized better outcomes among the IGT cohort than among patients not receiving IGT.

The basic analytic approach for the IGT versus non-IGT comparisons of substance use and mood was analysis of change from baseline. With one exception (number of abstinent months), change scores were calculated for each primary outcome measure at each monthly assessment by subtracting baseline values from monthly values. Since not all subjects had both drug and alcohol use problems, alcohol-dependent subjects with scores of 0 for the ASI drug composite score throughout the study (N = 11) were excluded from analyses of drug use. Similarly, drug-dependent subjects scoring 0 on the ASI alcohol composite throughout the study (N = 3) were excluded from analyses of alcohol use.

The principal analytic method for comparing the IGT and non-IGT groups was generalized estimating equation-based regression modeling,[25] with the monthly data forming the panel data set. This method is tolerant of missing data, so that subjects with missing observations were not dropped from the analysis and imputation of values for missing data was not necessary. Because of distribution skewness, the continuous change scores of number of days of drug and alcohol use and ASI drug and alcohol composite scores were logarithmically transformed to achieve more tractable distribution shapes and within-group variance comparability. The modeling was done in a hierarchical manner, with IGT versus non-IGT group effects estimated first and other explanatory factors, including time (month of assessment), then added in a stepwise manner to determine if the IGT versus non-IGT main effects were sustained after adjustment for other factors. Our primary outcome analysis focused on changes from baseline to 6-month assessment, since it was our intention that IGT be able to produce effects that lasted beyond the end of active treatment. Moreover, Carroll et al.[26] have reported emergent effects after the end of a 12-week relapse-prevention treatment in a sample of cocaine-dependent patients, suggesting that the full efficacy of such treatment may not be seen until after the active treatment ends. For the binary outcome measure of abstinence or not for a particular month, generalized estimating equation-based probit analysis[27] was used to carry out the IGT versus non-IGT group comparisons.

RESULTS

Subjects

The study sample, which included 21 IGT subjects and 24 non-IGT subjects, was 51.1% male (N = 23), 86.7% white (N = 39), and 13.3% African American (N = 6); the mean ± SD age was 36.2 ± 8.7 years. Twenty percent (N = 9) were married or cohabiting, 42.2% (N = 19) had never married, and 37.8% (N = 17) were divorced or separated. The sample was 68.9% unemployed (N = 31); 71.1% (N = 32) had begun college, and 31.1% (N = 14) had graduated. The IGT cohort was significantly older than the non-IGT cohort, with a mean age of 39.9 ± 9.7 versus 33.0 ± 6.4 years ($t = 2.77$, $df = 33.9$, $p < .01$). Otherwise, no significant sociodemographic differences were found between the 2 groups.

Thirty-three patients (73.3%) were diagnosed with bipolar I disorder, 8 (17.8%) had bipolar II disorder, and 4 (8.9%) had bipolar disorder not otherwise specified. Thirty-one patients (68.9%) were diagnosed as both drug and alcohol dependent, 7 (15.6%) had drug dependence alone, and 7 (15.6%) had alcohol dependence alone. The most common primary substances of abuse (i.e., the drugs causing the most difficulty according to patient self-report) were cocaine (N = 13, 28.9%), cannabis (N = 13, 28.9%), and sedative-hypnotic drugs (N = 9, 20.0%).

During the month prior to study entry, patients reported a mean ± SD of 8.8 ± 10.9 days of drug use and 9.9 ± 10.4 days of alcohol use. The mean ± SD drug composite score on the ASI was 0.13 ± 0.13, the mean HAM-D score was 17.7 ± 11.1, and the mean YMRS score was 5.7 ± 5.1. No

significant differences were found between the IGT and the non-IGT cohorts on these baseline symptom measures. There was, however, a significant difference on the ASI baseline alcohol composite score: IGT patients had a significantly higher score, indicating more severe alcohol problems (0.39 ± 0.25 vs. 0.21 ± 0.23; t = –2.59, df = 43, p < .02).

Assessment Completion

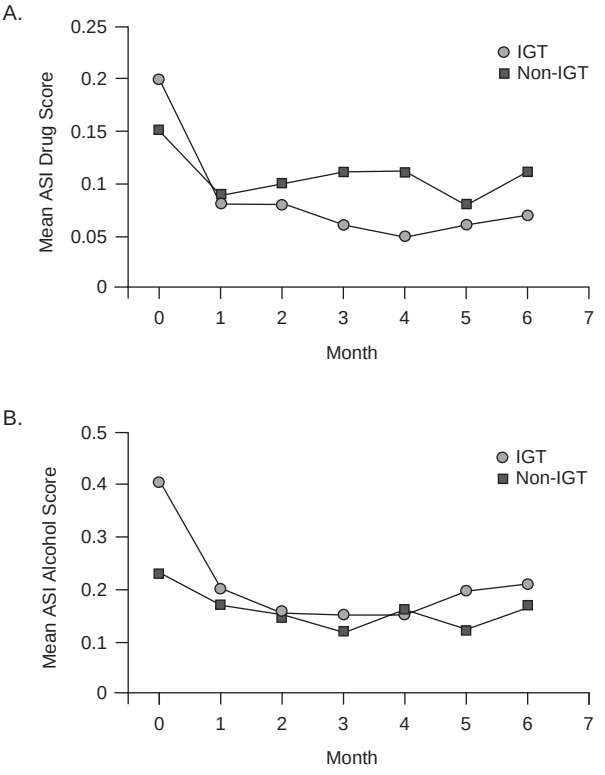
The rate of assessment completion was quite high: 215 (77.3%) of 278 scheduled assessments were fully completed, and 40 (14.4%) were partially completed. We were unable to obtain only 23 assessments (8.3%).

Outcomes

Substance use. Generalized estimating equation-based regression modeling was carried out with the following substance use outcome measures: (1) ASI drug composite score, (2) ASI alcohol composite score, (3) days of drug use, and (4) days of alcohol use. All of these measures favored the IGT group in comparison with the non-IGT group. Two comparisons were statistically significant: change in ASI drug composite score (p < .03) (Figure 1A) and change in ASI alcohol composite score (p < .02) (Figure 1B). As shown in Figures 1A and 1B, improvement in scores compared with baseline values was greater for the IGT cohort than for the non-IGT cohort. Standard deviations ranged between 0.07 and 0.13 over the repeated measures for the ASI drug composite scores and between 0.14 and 0.25 for the ASI alcohol composite scores. Variances did not differ between the IGT and the non-IGT cohorts. For the other 2 measures, change in days of drug use (p = .06) and change in days of alcohol use (p = .08), a trend favored the IGT cohort over the non-IGT group; actual effect sizes (1-tailed) in these 2 instances were 0.67 and 0.47, respectively. With this small sample, statistical significance was not achieved for these 2 outcomes. However, it is important to note that the power to detect between-group differences on these measures with these effect sizes and sample sizes was only 0.60 and 0.38, respectively.

Another substance use measure, months of abstinence from both drugs and alcohol, was evaluated in 2 ways: (1) percentage of months abstinent and (2) number of consecutive months abstinent. First, the percentage of months abstinent was compared between the IGT and non-IGT cohorts, with adjustment for missing data by dividing the number of abstinent months by the number of months in which data were collected. Generalized estimating equation-based probit analysis revealed that IGT patients achieved a significantly greater percentage of months abstinent from both drugs and alcohol than did the non-IGT patients (59.4% for IGT vs. 34.1% for non-IGT patients; p < .01). IGT patients also achieved a greater percentage of months abstinent from drugs (69.9% vs. 38.5% for the 34 patients who did not have ASI drug composite scores of 0 throughout the study; p < .009) and alcohol (62.9% vs. 49.6% for the 42 patients who did not have ASI alcohol composite scores of 0 throughout the study) than the non-IGT patients, although the latter difference was not statistically significant.

Figure 1. Mean ASI (A) Drug and (B) Alcohol Composite Scores by Month, IGT Versus Non-IGT Patients[a]



[a]Abbreviations: ASI = Addiction Severity Index, IGT = Integrated Group Therapy.

Next, the number of consecutive months of abstinence from both alcohol and drugs was examined. To assure a conservative count, missing assessments were counted as months of drug or alcohol use. Again, IGT patients fared better than non-IGT patients. Significantly more IGT patients than non-IGT patients maintained abstinence for 3 or more consecutive months (61.9% [N = 13] vs. 20.8% [N = 5]; $\chi^2 = 8.10$, df = 1, p < .004); more IGT than non-IGT patients also achieved abstinence for at least 2 consecutive months (81.0% [N = 17] vs. 41.7% [N = 10]; $\chi^2 = 7.52$, df = 1, p < .006). Eighty-six percent (N = 18) of IGT patients achieved at least 1 month of abstinence, compared to only 70.8% of non-IGT patients (N = 17), although this contrast did not attain statistical significance.

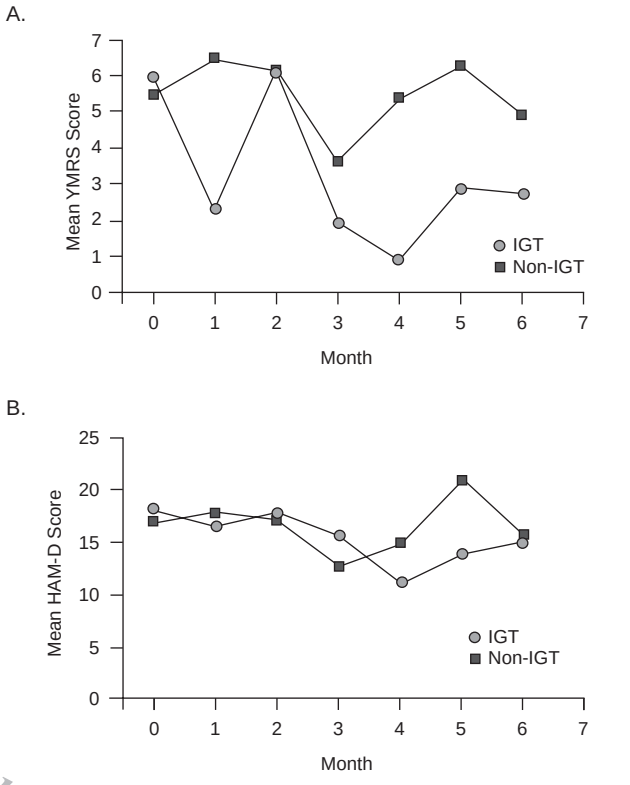
Mood. Regression modeling conducted with mood rating scale change-from-baseline outcome measures revealed that IGT patients had a significantly greater improvement in YMRS scores than did the non-IGT patients

($p < .04$; Figure 2A). Standard deviations ranged from 1.9 to 5.5 for the IGT patients and from 4.3 to 9.5 for the non-IGT patients. However, no differences by IGT status were found for change in HAM-D scores over time (Figure 2B).

Medication compliance. Patients reported quite high medication compliance, with monthly means ranging from 3.8 to 4.1 on a 5-point scale. The median was 4 every month ("more than two-thirds compliant, but not 100%") and the mode each month was the maximum score of 5. Although IGT patients reported greater compliance than non-IGT patients every month, no statistically significant difference by IGT status was found for change in medication compliance scores over time.

Hospitalization. Eighteen patients were hospitalized for either psychiatric or substance-related reasons during the study period: 8 IGT patients (38.1%) for a mean of 14.1 days per hospitalization and 10 non-IGT patients (41.7%) for a mean of 8.8 days. These differences were not statistically significant. One non-IGT patient committed suicide during the study period.

Figure 2. Mean (A) YMRS and (B) HAM-D Scores by Month, IGT Versus Non-IGT Patients[a]



[a]Abbreviations: HAM-D = Hamilton Rating Scale for Depression, IGT = Integrated Group Therapy, YMRS = Young Mania Rating Scale.

Adjustment for Age

Because subjects were not randomly assigned to treatment groups, it is possible that those with clinical or sociodemographic characteristics associated with good outcomes were more likely to enter IGT. Comparison of IGT and non-IGT subjects showed that age was, in fact, nonrandomly distributed between the 2 groups, as described above. Thus, treatment condition and age were entered together in multivariate regression analyses with the outcome measures in which there were statistically significant treatment group differences. For change in ASI drug composite score and months abstinent from both alcohol and drugs, age was not a significant predictor, and treatment group (i.e., IGT vs. non-IGT) remained significant. However, for change in ASI alcohol composite score and change in YMRS score, neither statistically significant treatment group difference was sustained after age was added to the model.

Group Attendance

IGT subjects had a high rate of group attendance, attending a mean of 71.6% of groups offered. Moreover, attendance increased with each successive group therapy cohort. Patients in the first group cohort attended 55.9% of sessions offered, whereas the second and third cohorts of patients attended 74.4% and 82.6% of sessions, respectively. Only 2 (9.5%) of 21 patients dropped out of treatment (although both continued to complete assessments): both were in the first group cohort, and each dropped out after attending 2 sessions.

Participation in Other (Nonstudy) Treatments

Although we did not limit coexisting treatment in our initial study of IGT, we monitored subjects' use of other treatment with the Treatment Services Review[24] and the Treatment Summary. In the first month after hospitalization, 37 patients (82.2%) saw an individual therapist, attending a mean ± SD of 4.9 ± 2.4 sessions. Engagement in most other treatments was less common. Family or couple treatment and group therapy were each attended by 4 subjects (8.9%), and only 2 subjects (4.4%) saw an individual drug counselor. Twenty-eight patients (62.2%) attended at least 1 self-help group. Twenty-two subjects (48.9%) engaged in partial hospital treatment during their first post-discharge month. No significant differences were found between the IGT and non-IGT cohorts in the amount of non-study psychosocial treatment received. Since it was a required inclusion criterion, all 45 subjects saw a pharmacotherapist.

IGT Groups 1 and 2 (12 weeks) Versus IGT Group 3 (20 weeks)

As described above, we extended the third IGT group from 12 to 20 weeks, as part of the iterative developmental process. Since the number of patients in each group cohort was so small, we expected no statistically significant outcome differences for groups 1 and 2 versus group

3 and did not find them. The group 3 outcome data, however, supported the decision to lengthen the treatment: all of the patients in group 3 abstained from drugs and alcohol during month 5 (the last month of treatment) and at the 3-month posttreatment follow-up.

DISCUSSION

We have developed a form of group therapy for patients with bipolar disorder and substance dependence that integrates treatment by focusing on similarities in the recovery and relapse processes between the 2 disorders.[13] To our knowledge, this is the first empirical study of a psychotherapeutic treatment specifically designed for this commonly seen patient population, which has generally had a poor prognosis.[2–5] Our results are quite promising, in that patients who received IGT had significantly greater improvement in the ASI drug composite score (a measure of drug-related problem severity) and significantly more months of abstinence from drugs and alcohol than did the comparison group of patients who did not receive IGT. IGT patients also had significantly greater improvement in manic symptoms and a greater improvement in severity of alcohol-related problems, although these differences were not sustained when we controlled for age. Moreover, the level of treatment attendance was quite high.

With the limited sample size in this pilot study (21 IGT patients and 24 non-IGT patients), the achievement of significant differences between the 2 groups in major outcome measures is quite promising. Even nonsignificant differences (e.g., change in the number of days of drug use and alcohol use) showed moderate-to-large effect sizes.

It is important to note that this was an open study, not a randomized, controlled trial; patients were recruited for only one condition (i.e., IGT or non-IGT) at a time, and we cannot know whether this biased the study results in favor of IGT. For example, it is possible that some patients who were less motivated for treatment may have agreed to participate in monthly evaluations, whereas only patients with some interest in treatment entered IGT. However, the lack of a significant difference between those recruited for the 2 patient cohorts in their reasons for not participating mitigates somewhat against this argument. In addition, patients were not offered a choice of treatment versus no treatment. Rather, they were recruited in blocks at different times, depending on the phase of the study. We believe that this block selection design, intermediate between naturalistic and randomized study designs, can yield data that do not unduly suffer from self-selection bias. At least one available study report provides support for this belief. McKay et al.[28] reported similar outcomes among alcohol-dependent patients who were randomly assigned to particular treatment modalities (specifically, day hospital or inpatient treatment) when compared with patients who self-selected these treatments.

It is noteworthy that IGT had a greater impact on drug use than on alcohol use and a stronger effect on manic symptoms than on depressive symptoms. It is possible that these 2 phenomena are related; some authors have pointed to specific drugs of abuse, particularly stimulants, as triggers for mania.[29] It is also possible that although IGT promoted complete abstinence from both drugs and alcohol, some patients did not accept that concept and stopped or reduced use of the drug that had caused them the most problems while not substantively changing their alcohol use.

It is unclear how much of the improvement experienced by IGT patients can be attributed to the specific content of the group therapy as opposed to the nonspecific but potentially important therapeutic value of gathering a group of diagnostically homogeneous patients together each week to share their experiences. While we hypothesize that a key therapeutic element in IGT is its integration of the treatment of bipolar disorder and substance dependence into a coherent, unified approach, this needs to be tested in randomized trials. As the next logical step in investigating that question, we are undertaking a randomized controlled study in which we are comparing IGT with a group therapy that focuses on drug use but does not attempt to integrate the treatment of the 2 disorders. In this way, we plan to continue in the process of developing and testing specific effective treatment protocols for this challenging patient population.

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