

Does Recovery From Substance Use Disorder Matter in Patients With Bipolar Disorder?

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Objective: To examine the potential impact of recovery from substance use disorder (SUD) on the course of bipolar disorder among patients diagnosed with both bipolar and substance use disorders according to DSM-IV criteria.

Method: As part of the multicenter Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), we examined bipolar disorder status (i.e., whether the patient is recovering or recovered), role functioning, and quality of life in the first 1000 patients to enter the STEP-BD study. We compared patients with no history of SUD, current SUD, and past SUD (i.e., lifetime SUD, but no current SUD) on these parameters. Data were collected between November 1999 and April 2001.

Results: A current clinical status of recovering or recovered from bipolar disorder was less likely among patients with current or past SUD compared to patients with no SUD (p < .002). Recovering/recovered status did not differ significantly between patients with current SUD versus past SUD. All 3 groups differed significantly on measures of role functioning as assessed by the Longitudinal Interval Follow-Up Evaluation-Range of Impaired Functioning Tool (LIFE-RIFT), with poorest role functioning among patients with current SUD, followed by patients with past SUD (p = .0002). Patients with current or past SUD reported significantly lower quality of life as measured by the LIFE-RIFT and the Quality of Life Enjoyment and Satisfaction Questionnaire and more lifetime suicide attempts (p < .001) than patients without an SUD; patients with past versus current SUD did not differ significantly on these measures.

Conclusion: The results suggest that patients with bipolar disorder who experience sustained remission from an SUD fare better than patients with current SUD, but not as well as subjects with no history of SUD; differences among the 3 groups appear greatest in the area of role functioning.

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kipolar disorder is the Axis I psychiatric disorder associated with the highest risk for co-occurrence of substance use disorder (SUD), according to epidemiologic studies.^{1,2} Moreover, there is substantial evidence that the course of illness for patients with bipolar disorder and SUD is marked by significantly more morbidity than that for bipolar disorder alone.³⁻⁶ Current SUD has been associated with greater symptom severity and delayed recovery in bipolar disorder.⁷⁻⁹ In acutely manic subjects, those with current alcohol use disorder have been differentiated from other bipolar disorder patients by increased numbers of manic symptoms, impulsivity, and high-risk behavior, including violence.⁶ A lifetime history of SUD (past or current SUD) in bipolar patients has also been associated with more mood episodes, days ill, suicide attempts, and hospitalizations, as well as lower functioning, than no history of SUD.^{3–5}

Although the lifetime prevalence of SUD in bipolar patients is high, SUDs wax and wane in the course of bi-

polar disorder, and many patients with a lifetime history of SUD recover or have periods of recovery from their SUD.¹⁰ In one study of 288 outpatients with bipolar disorder,¹⁰ the lifetime history of SUD was 42%, whereas only 4% of subjects met criteria for current SUD at study entry. Similarly, Winokur et al.¹¹ found that although 37% of outpatients with bipolar disorder had current alcohol dependence at study entry, only 5% had current alcohol dependence at 5-year follow-up. Although clinicians treating patients with bipolar disorder and SUD often advise their patients to refrain from substance use, we are aware of no study that has examined the extent to which recovery from SUD has an impact on either the course of their bipolar disorder or their overall functioning. In this study, we examined this issue in the first 1000 patients who entered the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). We compared those patients who had experienced a sustained remission from an SUD (i.e., not meeting DSM-IV criteria for at least 1 year) to those with a current SUD diagnosis and those with no history of SUD; we sometimes use the term recovery from SUD in this article instead of sustained remission because of the importance of the concept of recovery in the substance abuse research literature¹² and clinical community.¹³ We hypothesized that patients with current SUD would have a lower level of functioning than patients with no SUD, and that patients with lifetime (but not current) SUD would have a level of functioning similar to those with no history of SUD, and significantly better than those with current SUD.

METHOD

Study Overview

The Systematic Treatment Enhancement Program for Bipolar Disorder is a multicenter, National Institute of Mental Health-supported study designed to assess optimal treatment strategies for patients with bipolar disorder, through both naturalistic and randomized controlled trials.¹⁴ Patients are eligible if they are at least 15 years old and meet DSM-IV criteria for any subtype of bipolar disorder, cyclothymia, or schizoaffective disorder, manic or bipolar subtypes. These study diagnoses are assigned by consensus following administration of the Mini-International Neuropsychiatric Interview (MINI)¹⁵ and the Affective Disorder Evaluation (ADE).¹⁶ There are few exclusion criteria: unwillingness or inability to comply with study assessments, or inability to give informed consent. All patients in STEP-BD receive the same assessments of treatment and outcome. All participants provided written informed consent after the study had been explained to them. This article reports on the first 1000 patients who entered STEP-BD.

Assessments and Procedures

The Affective Disorder Evaluation (ADE)¹⁶ includes a modification of the mood and psychosis modules from the

Structured Clinical Interview for DSM-IV (SCID).¹⁷ The ADE, which was administered by the study psychiatrist, reviews the chronology of past episodes, including recovery and treatment response. The ADE is completed at entry into STEP-BD and serves as the primary source of the history, nature, and characteristics of bipolar episodes.

The Mini-International Neuropsychiatric Interview (MINI Plus Version 5.0)¹⁵ is a semistructured interview designed to identify both current and lifetime major Axis I psychiatric disorders, including SUDs. The MINI has been compared to the SCID-P for DSM-III-R and has been found to be acceptably valid and reliable¹⁵; it has also recently been used in other studies of patients with mood disorders.^{18,19} For the current study, the MINI was administered by master's- or doctoral-level staff; they were trained using the MINI originator's training tape, with subsequent on-site supervision. The MINI was used to confirm the bipolar-spectrum diagnosis and to identify comorbid psychiatric disorders at study entry.

The Clinical Monitoring Form (CMF)²⁰ is an assessment instrument administered by study clinicians at study entry to document the patient's clinical status. The CMF consists of 9 parts, including modified versions of the SCID current mood modules, associated symptoms, stressors, and comorbid conditions; current medication adherence and adverse effects; laboratory data; and summary scores (i.e., clinical status, Clinical Global Impressions, Global Assessment of Functioning). Based on the presence or absence of DSM-IV-based criteria, 1 of 8 operationally defined clinical states was assigned at study entry. Four clinical states correspond to the DSM-IV definitions for major depression, mania, hypomania, or mixed episodes. Patients achieving relative euthymia (≤ 2 moderate symptoms) for at least a week are assigned a status of recovering or recovered, depending on whether this status has been sustained for at least 8 weeks. Two subsyndromal states $(\geq 3 \text{ moderate symptoms, but not full criteria for a mood})$ episode) categorize patients as either continued symptomatic (a subsyndromal state following an acute episode without an intervening full recovery) or roughening (a subsyndromal state occurring after recovery from the last full mood episode). These bipolar state categories and interrater reliability training are further discussed by Sachs et al.²⁰ All STEP-BD staff had to complete a standardized training and meet certification requirements for establishing interrater agreement in order to use the CMF.

Quality of life and functional impairment were assessed with 2 questionnaires: the short form of the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q)²¹ and the Longitudinal Interval Follow-Up Evaluation– Range of Impaired Functioning Tool (LIFE-RIFT).²² The short form of the Q-LES-Q is a well-validated, 16-item, self-report measure of life satisfaction and enjoyment of general activities. The LIFE-RIFT is a 4-item, clinicianadministered, semistructured interview that assesses 4 domains (work, recreation, interpersonal relations, and global satisfaction) that are rated from 1 (no impairment) to 5 (severe impairment). The total scale score thus ranges from 4 to 20, with higher scores indicating more impairment. The reliability and validity of LIFE-RIFT have been examined in bipolar I disorder with excellent interrater agreement (r = 0.94) and internal reliability over time, with coefficient α ranging from 0.78 to 0.84.²²

Data Analysis

Differences between patients with a current SUD diagnosis, a lifetime diagnosis but no current diagnosis ("past" diagnosis), and no diagnosis were evaluated for categorical variables with Pearson χ^2 tests, and for continuous variables with Kruskal Wallis tests appropriate to the unequal sample sizes for these groups. In all cases, we completed follow-up tests of pairwise comparisons among the 3 groups, with α set at .05 for these analyses. When potential confounding variables were identified, differences between patients based on SUD characteristics were reexamined, using logistic and linear regression analyses and treating the potential confounding variables as covariates.

RESULTS

Characteristics of Participants

The sample consisted of 1000 STEP-BD participants assessed between November 1999 and April 2001. The population was 59% female, with a mean \pm SD age of 40.6 \pm 12.7 years and a mean \pm SD duration of bipolar illness of 23.1 \pm 12.9 years. The majority of the sample (71%) met DSM-IV criteria for bipolar I disorder; 24% met criteria for bipolar II, 4% bipolar NOS, and 1% schizoaffective, cyclothymic, or unspecified. At study entry, 39.8% of the sample were married or living as married, 82.3% had at least some college education, and 47.0% had a college degree. Regarding occupational status, 34.5% reported full-time work outside the home; 20.0% reported part-time or homemaker status; 38.8% reported unemployment, disability, or leave of absence; and 5.0% and 1.8% reported retired or "other" status, respectively. The majority of the sample was white (92.6%), with 3.4% of the sample identifying themselves as black or African American, 1.1% as Asian, 0.4% as Native American or Alaskan, and 2.8% as mixed race or other; 3.7% of the sample identified themselves as Hispanic or Latino.

Diagnostic comorbidity data were missing for 3.8% of the sample, and data collection procedures for an additional 4.5% of subjects failed to meet project quality assurance standards. Data from these participants were excluded from analyses. Current SUDs were present in 11.5% of the available sample (8.3% alcohol use disorders and 5.2% non–alcohol use disorders), and an additional 36.2% met criteria for lifetime but not current SUD (33.3% alcohol and 22.0% non–alcohol use disorders), leaving 52.3% of patients with no SUD diagnosis. Alcohol and non–alcohol use disorders tended to co-occur; 8.3% of patients with a current alcohol use disorder and 39.6% of those with a current non–alcohol use disorder met criteria for the other disorder. Similarly, 33.3% of patients with past alcohol use disorder met criteria for a past non– alcohol use disorder, and 66.3% of patients with a past non–alcohol use disorder met criteria for a past alcohol use disorder.

Entry Characteristics of Patients With Current, Past, or No SUD

Table 1 presents the sociodemographic, diagnostic, and severity characteristics of patients at study entry. The presence of a past or current SUD differentiated patients from those with no SUD on a number of sociodemographic and severity variables. Patients with a current SUD were significantly more likely to be male than those with no SUD. Moreover, patients with a current SUD were significantly younger than those with a past SUD or no history of the disorder, and were significantly less likely to be a college graduate or married/living as married.

To identify whether differences between diagnostic groups in education and marital status were dependent upon differences in age, we statistically controlled for age in a reanalysis of these variables. Under these conditions, patients with current SUD continued to be significantly less likely to be married/living as married than each of the other groups of patients (p < .05), and were significantly less likely to have graduated from college than patients with no SUD (p < .001). Those with a past history of SUD were also significantly less likely to have completed college than patients with no SUD (p < .04).

Concerning clinical characteristics, no significant differences in bipolar diagnostic status (I vs. II) were found for the 3 groups of patients defined by SUD diagnoses. A current clinical status of recovering or recovered from bipolar disorder was less likely among patients with current or past SUD compared to patients with no SUD. Recovering/recovered status did not differ significantly between patients with current SUD compared to past SUD. Current anxiety disorders and attention-deficit/hyperactivity disorder (ADHD) were each more prevalent among both current and past SUD patients when compared with non-SUD patients. In contrast, current eating disorders were significantly more common among patients with current SUD, with the past SUD group more closely resembling those with no SUD history. On measures of role functioning, all 3 groups differed significantly, with poorest role functioning among patients with current SUD, followed by patients with past SUD. On the Q-LES-Q, patients with current or past SUD reported significantly lower quality of life than patients without an SUD diagnosis. Patients with a past SUD and those with a current SUD did not differ significantly on this measure. Finally, both current and

	Current SUD	Past SUD	No SUD	Significance of Differences
Patient Characteristic	(N = 105)	(N = 332)	(N = 480)	Between Groups
Sex (male [‡]), %	53.3 ^b	41.9	38.7 ^a	$\chi^2 = 7.6$, df = 2; p = .0222
Age, mean ± SD, y	34.3 ± 12.3^{b}	41.3 ± 11.5^{a}	41.5 ± 13.5^{a}	$KW\chi^2 = 28.6, df = 2; p < .0001$
Education (college graduate), %	38.8 ^b	55.1 ^a	62.7 ^a	$\chi^2 = 20.5$, df = 2; p < .0001
Marital status (married or living as married), %	24.3 ^b	43.7 ^a	40.9 ^a	$\chi^2 = 12.6$, df = 2; p < .002
Bipolar I subtype, %	81.2	73.7	70.8	$\chi^2 = 4.7$, df = 2; p = .10
Bipolar disorder status (recovering/recovered), %	40.0 ^b	45.2 ^b	55.4 ^a	$\chi^2 = 12.9$, df = 2; p < .002
Current anxiety disorder, %	48.6 ^b	38.3 ^b	24.0 ^a	$\chi^2 = 33.5$, df = 2; p < .0001
Current eating disorder, %	8.6 ^b	1.8^{a}	0.6^{a}	$\chi^2 = 28.3$, df = 2; p < .0001
Current ADHD, %	9.5 ^b	9.3 ^b	2.5 ^a	$\chi^2 = 19.9$, df = 2; p < .0001
Lifetime history of suicide attempt, %	46.6 ^b	38.0 ^b	29.1 ^a	$\chi^2 = 14.7$, df = 2; p < .001
LIFE-RIFT, mean ± SD score	$12.6 \pm 3.8^{\circ}$	11.5 ± 3.9^{b}	10.9 ± 3.8^{a}	$KW\chi^2 = 17.0, df = 2; p = .0002$
Q-LES-Q, mean ± SD score	47.3 ± 18.2^{b}	52.2 ± 18.6^{b}	58.0 ± 19.8^{a}	$KW\chi^2 = 19.9, df = 2; p < .0001$

Table 1. Characteristics at Entry Into STEP-BD for Bipolar Disorder Patients (N = 1000) With Current, Past, or No Substance Use Disorder (SUD) Diagnoses*†

*Superscripts (a, b, or c) differing from each other indicate significant differences in pairwise comparisons.

*Diagnostic comorbidity data were missing for 3.8% of the sample, and data collection procedures for an additional 4.5% of subjects failed to meet project quality assurance standards. Data from these participants were excluded from analysis.

[‡]Two transgendered participants were deleted from this analysis.

Abbreviations: ADHD = attention-deficit/hyperactivity disorder, KW = Kruskal Wallis, LIFE-RIFT = Longitudinal Interval Follow-Up Evaluation–Range of Impaired Functioning Tool, Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire,

STEP-BD = Systematic Treatment Enhancement Program for Bipolar Disease.

past SUD patients were significantly more likely to have made a suicide attempt than those with no SUD.

To ensure that differences in sociodemographic characteristics among the SUD groups did not account for the clinical findings, we reexamined the associations between SUD status and recovering/recovered status, LIFE-RIFT scores, and Q-LES-Q scores, statistically controlling for differences in age, gender, education, and marital status. This statistical control did not alter the pattern of significance for recovering/recovered status or quality of life for the 3 SUD groups. However, when sociodemographic factors were statistically controlled, the difference in LIFE-RIFT scores between the past SUD and no SUD groups was no longer significant.

DISCUSSION

To our knowledge, this is the first large-scale study to examine the relationship between recovery from SUDs and the course of bipolar disorder. The results partially confirm our hypothesis that bipolar patients who experience a sustained remission from an SUD fare better than patients with current SUD but not as well as subjects with no history of SUD, although differences among the 3 groups appeared greatest in the area of role functioning.

The proportion of the STEP-BD population of 1000 patients with a lifetime history of SUD was quite large; nearly half of the sample had either current or past SUD, consistent with the prevalence of SUD found in large epidemiologic studies.^{1,2} Our study reinforces the observation from previous studies¹¹ that SUDs in bipolar patients are intermittent. A quarter of the patients with lifetime SUD met criteria for a current SUD diagnosis at the time of study entry, although it is not known how long, on average, the patients with past SUD had been in recovery.

The course of bipolar disorder tends to be more difficult in younger patients, with more suicide attempts associated with younger age.²³ The patients in our study with current SUD were significantly younger than those with either no SUD or past SUD. They also had lower educational attainment, were less likely to be married, and were more likely to be male, but these effects were not dependent on differences in age. When age was statistically controlled, patients in recovery from SUDs also had lower educational attainment than those with no SUDs, although at a level that was significantly better than that of individuals with a current SUD. No differences between individuals with no SUD and past SUDs were found for marital status.

It is noteworthy that recovery from SUD was linked to significantly better role functioning as compared to individuals with current SUD and was not discriminable from individuals with no SUD. In contrast, those who had remitted from a past SUD continued to have lower life satisfaction than those with no SUD, at a level that was not significantly different from patients with current SUD. An identical pattern of findings was evident for current clinical status; patients with past SUD had a lower likelihood of being in recovering/recovered status than those with no history of SUD, at a level that was not significantly different from patients with current SUD. The improvement in functioning, but not course of illness, is consistent with findings from studies of patients with schizophrenia who achieve recovery from SUD.²⁴ It is possible that patients who work hard to recover from their SUD are disappointed when their mood symptoms improve less than they had hoped, and their lack of significant improvement in life satisfaction may reflect the gap between their actual improvement (e.g., their increased role functioning) and the gains that they had hoped to achieve with SUD recovery. Life satisfaction in SUD patients may also be lower because they achieve less during their substance-using years and may not be able to catch up to their peers. For example, patients with past SUD were less likely than those with no SUD to be college graduates (when controlling for age), so they may have lagged behind their peers in some career areas, thus potentially lowering overall life satisfaction.

The co-occurrence of an anxiety disorder in bipolar patients is associated with poorer role functioning and quality of life and a greater likelihood of suicide attempts.²⁵ However, the lack of a significant difference between the current and past SUD patients in the prevalence of anxiety disorders makes it unlikely that anxiety disorders were responsible for the lower life satisfaction among the current SUD patients than among those with past SUD. Current eating disorders were more prevalent in the current SUD patients, although these were uncommon in all 3 groups; it is possible that the presence of an eating disorder makes recovery from SUD more difficult in patients with bipolar disorder. Finally, the increased lifetime history of suicide attempts among the SUD patients corroborates results from previous studies showing the high rate of suicidality among bipolar patients with SUD.26,27

One limitation of this study is that current SUD status was obtained through self-report and lifetime diagnoses were obtained retrospectively. Although SUDs may be underreported²⁸ or overreported¹⁰ by bipolar research subjects, Weiss et al.²⁹ found that self-reports of substance use by bipolar patients in a treatment research setting can be highly valid. Another possible limitation, as Frye et al.²⁸ have suggested, is that more severely ill bipolar patients, including those with SUD, may be less likely to participate in research; our study might thus underestimate the actual prevalence of SUD in bipolar patients. However, since the rates of SUDs in our study are similar to those found in both the Epidemiologic Catchment Area Study¹ and the National Comorbidity Survey,² this is not likely the case.

It is possible that longitudinal analysis may provide a different perspective from our cross-sectional study. Over time, we expect to collect such prospective data. It is also not possible to know from this study whether treatment for SUD in bipolar patients had an impact on mood outcome. These findings are consistent, however, with the multidimensionality of outcomes reported by Drake et al.³⁰ for this population. These results also corroborate data from Weiss et al.,³¹ who found that a specialized group therapy for patients with bipolar disorder and substance dependence had greater impact on substance use than on mood during a 6-month period. Since the proxy we used for severity, current mood state, may not adequately differentiate between more and less severe forms of bipolar disorder, it is not possible to conclude from our data whether the poorer clinical status, functioning, and quality of life in the 2 SUD groups are due to the severity of their mood disorder rather than to their substance use. In the NIMH Collaborative Depression Study sample, for example, SUD did not predict a more chronic course for bipolar II subjects compared to subjects with no SUD, leading the authors to conclude that the course of that disorder was influenced more by the bipolar disease process than the co-occurring condition.³²

Despite the size of our sample, one additional limitation is that our study group was not sociodemographically representative of the general population. The study cohort was overwhelmingly white, with few minority subjects. Since approximately one third of the United States population is non-white or Hispanic,³³ our results may not accurately represent non-white bipolar patients. Educational attainment was also much higher for this cohort than would be expected in the general population, and it is possible that this would affect our study results, as educational attainment appears to influence course of alcohol use disorders.³⁴

In spite of these limitations, several conclusions can be drawn from this study. Overall, as a group, bipolar patients with a history of SUD fare worse than their bipolar counterparts with no history of SUD. Experiencing periods of recovery from SUD, however, is more the rule than the exception in bipolar disorder, and in several dimensions, recovery from SUD is associated with lower severity than current SUD. It remains unclear, however, whether SUDs are more prevalent in a subgroup of patients with a more severe bipolar disease process or whether SUDs themselves have a deleterious impact on bipolar disorder course. It is likely that some part of the severity in the course of patients with current or past SUD is due to both effects of the SUD itself and the severity of the cooccuring bipolar disease. Prospective data from a large sample will help clarify this question. This study reiterates the importance of recognizing SUDs in bipolar patients; SUD is associated with greater disorder severity and disability, but helping patients to achieve SUD recovery may be associated with improvement in their functioning.

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