Substance Use Disorder and the Early Course of Illness in Schizophrenia and Affective Psychosis

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Abstract

The relationship between a history of substance use disorder and the early course of psychotic illness was examined in 96 subjects with schizophrenia and 106 subjects with affective psychosis followed in the Suffolk County Mental Health Project, a longitudinal study of first-admission psychosis. Subjects received a structured diagnostic interview and clinical ratings at baseline assessment and again 6 months later. The 6-month assessment included information about treatment received during the interval. A lifetime history of substance use disorder was associated with worse clinical functioning at 6 months for schizophrenia subjects, but not for those with affective psychosis. There were no significant associations of substance use disorder with type of treatment during the interval or with self-reported compliance with medication. Schizophrenia subjects were more likely than subjects with affective psychosis to report cannabis use during the interval and to meet criteria for cannabis use disorder.

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Concomitant substance abuse in patients with psychotic illness is of concern to providers of mental health services because it often complicates the picture both diagnostically and therapeutically. However, most existing studies have examined this problem cross-sectionally in a sample of subjects who have been ill for varying amounts of time and who are entering treatment at a single facility.

The Suffolk County Mental Health Project is an ongoing epidemiological study of subjects with newly identified psychotic illness who are admitted to a wide variety of facilities in a large, diverse county encompassing the eastern two thirds of Long Island, New York. Because subjects are experiencing their first hospitalization for psychosis, it is possible to examine variables surrounding the early course of illness. The methods and initial characteristics of the sample have been described elsewhere (Bromet et al. 1992).

In a previous analysis of comorbid substance abuse at the time of entry into this longitudinal study, little difference was found in demographic variables and initial clinical presentation between subjects with and without a lifetime history of *DSM–III–R* (American Psychiatric Association 1987) substance abuse or dependence, except that comorbid substance use disorder was less common among women and somewhat more frequent in patients with affective psychosis (Kovasznay et al. 1993). These data thus suggested that substance use disorder did not have much influence on the onset of psychotic illness. Nevertheless, clinical experience suggests that substance abuse does influence the course of illness, and several cross-sectional studies (Mueser et al. 1990, 1992) have supported this concept.

The current study examines the relationship between substance use disorder and course of psychotic illness during the first 6 months of observation for participants in the Suffolk County Mental Health Project. Because followup assessments are not linked to treatment, subjects who were noncompliant with treatment or not enrolled in treatment were still included. In addition, the availability of information from two full assessments 6 months apart, interviews with family members, and a review of medical records made it possible to classify a subject's substance use disorder status with greater confidence than might be possible in a cross-sectional study.

The current study addresses these four questions: (1) Among patients with schizophrenia, is the history of a substance use disorder associated with differences in background characteristics? (2) Among patients with schizophrenia, is a history of substance use disorder asso-

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ciated with treatment experience and clinical presentation at 6 months? (3) What is the pattern of substance use at index admission and during the interval, and what is its relationship to substance use history, treatment experience and clinical presentation? (4) Do the above variables have the same relationship for subjects with affective psychosis or are they diagnosis specific?

Methods

Selection of Sample. The selection of the sample for the Suffolk County Mental Health Project and the method for determining a longitudinal best estimate diagnosis have been described elsewhere (Bromet et al. 1992; Fennig et al. 1994). The sample reported in this article was selected from the first 309 subjects participating in the study. Seventy-two percent of the subjects agreed to undergo a baseline assessment. Those who refused consent were more likely to be older and female. Six-month followup information was available for 278 subjects (90%), with no significant demographic differences between those with and without such information. Face-to-face interviews were obtained at 6 months for 238 of the 278 subjects (85.6%), telephone interviews for 31 subjects (11.1%), and information from a significant other only for 9 subjects (3.2%).

The sample for this article included individuals assessed at both the baseline and the 6-month point, with a longitudinal best estimate diagnosis of schizophrenia (including schizophreniform and schizoaffective disorder) or affective psychosis (bipolar or major depressive disorder with psychotic features). Subjects with other primary diagnoses were excluded.

Baseline Interview. Consenting subjects participated in the Structured Clinical Interview for *DSM–III–R* (SCID; Spitzer et al. 1992), and additional assessment measures to facilitate completion of clinical ratings, including the Brief Psychiatric Rating Scale (BPRS), an 18-item scale covering a wide range of psychiatric symptoms (Overall and Gorham 1962); the Schedule for Assessment of Negative Symptoms (SANS), an instrument with five subscales assessing negative symptoms (Andreasen 1982); the Schedule for Assessment of Positive Symptoms (SAPS), an instrument with five subscales assessing positive psychotic symptoms (Andreasen 1984); and the Global Assessment of Functioning (GAF), a summary scale that assigns a single score for the worst level of functioning in the past month and another single score for the highest level of functioning in the past year (American Psychiatric Association 1987). In addition, with the subject's permission, medical records were reviewed, and a family or household member was interviewed regarding events surrounding the onset of illness. All interviews were conducted by rigorously trained master's-level mental health professionals. A project psychiatrist accompanied the interviewer on approximately every 10th interview and rated all items in the SCID and clinical ratings independently, with good interrater agreement (Bromet et al. 1992).

Six-Month Interview. The SCID and clinical rating assessments listed above were repeated at the 6-month interview, with a modification of the GAF to rate the highest level of functioning for the past 6 months only. The interview also included questions about treatment experience and questions from the National Institute on Drug Abuse household survey instrument on drug use. A family member was interviewed regarding the patient's course over the interval. Consent was requested to obtain medical records for all hospitalizations since the onset of illness, and a one-page treatment summary was requested from providers of outpatient care. When face-to-face interviews could not be arranged, information was obtained by telephone or letter.

Diagnosis. Two psychiatrists made a longitudinal best estimate diagnosis for each subject at 6 months, and all diagnoses were reviewed by a consensus panel including at least two additional psychiatrists. All applicable *DSM–III–R* diagnoses were included, and a primary diagnosis was specified. For substance use disorders, subjects received lifetime *DSM–III–R* diagnoses, based on all available interview information and medical records. The frequencies of individual substance diagnoses are shown in table 1.

Analysis. Two groups were studied: (1) subjects with schizophrenia, including schizophreniform disorder and schizoaffective disorder (n = 96); and (2) subjects with affective psychosis (n = 106), including bipolar disorder with psychosis (n = 64) and major depression with psychosis (n = 42). These two latter diagnoses were compared with each other on study variables to ensure that combining them would not result in the loss of important differences, and no such differences were found, except for higher (worse) mean BPRS score and higher (worse) mean SAPS score in the major depression group. However, the mean BPRS and SAPS scores for the combined group were still significantly lower (better) than for the schizophrenia group.

The schizophrenia and affective psychosis groups were then subdivided based on the presence or absence of a lifetime history of substance use disorder (the individual

Table 1. Frequencies of individual substance diagnoses by primary psychotic diagnosis using *DSM–III–R* criteria

	Schizophrenia		Affective psychosis		
Substance	*n* = 42	(%)	*n* = 52	(%)	*p*[1]
Alcohol	35	(83.3)	47	(90.4)	NS
Alcohol only	10	(23.8)	20	(38.5)	NS
Drug only	7	(16.7)	5	(9.62)	NS
Cannabis	29	(69.1)	24	(46.2)	0.03
Cocaine	10	(23.8)	16	(30.8)	NS
Hallucinogens	8	(19.1)	4	(7.69)	NS
Stimulants	5	(11.9)	8	(15.4)	NS
Opiates	4	(9.52)	2	(3.85)	NS
Sedative/hypnotics	1	(2.38)	4	(7.69)	NS
Other drugs	1	(2.38)	0	(0.0)	NS
Polydrug dependence	2	(4.76)	1	(1.92)	NS

Note.—DSM–III–R = Diagnostic and Statistical Manual of Mental Disorders. 3rd ed., revised (American Psychiatric Association 1987). Categories are not mutually exclusive. NS = not significant.

[1]Chi-square test used except for variables with small cells; Fisher's exact test used for small cells.

met *DSM–III–R* criteria for alcohol or drug abuse or dependence). Demographic and outcome variables were analyzed separately for the two main diagnostic groups, as it was expected that many variables would differ considerably between diagnosis, and the analysis of interest was the relationship of substance use disorder to outcome. Demographic variables were compared using logistic regression analysis to calculate odds ratios and maximum likelihood estimates. Clinical ratings at the 6-month assessment, including the GAF best and worst, BPRS, SAPS, and SANS, were compared for subjects with and without lifetime substance abuse, using analysis of covariance and adjusting for gender and previous score on the same rating scale at index admission. Other course variables were also examined, including number of mental health contacts during the interval, employment status during the interval, and whether the subjects were taking medications at the 6-month point. Maximum likelihood estimates were used for these variables. For comparison of medians, the Wilcoxon rank-sum test was used. Substance use during the interval was examined using chi-square analysis or Fisher's exact test, depending on the size of the cell.

Results

Forty-two of the schizophrenia subjects (43.8%) and 52 of the subjects with affective psychosis (49.1%) had a lifetime history of substance use disorder. Demographic variables are described in table 2. Gender was the only demographic characteristic that differed significantly between subjects with and without a substance use disorder, with men being more common among those with a substance use disorder. This difference was highly significant for subjects with affective psychosis ($p < 0.0003$) and marginal ($p = 0.072$) for those with schizophrenia.

Clinical rating scores, psychotic symptoms, and employment status at 6 months are summarized in table 3. Lower (worse) GAF scores and higher (worse) BPRS score at 6 months were associated with having a substance use disorder for subjects with schizophrenia, but not for those with affective psychosis. SANS and SAPS scores did not differ significantly by substance abuse history.

Treatment experience during the 6-month interval is summarized in table 4. There were no significant associations between substance use disorder and rehospitalization,

Table 2. Demographic characteristics of subjects by primary diagnosis and lifetime history of substance use disorder (SUD) using *DSM–III–R* criteria

	Schizophrenia				Affective psychosis			
Characteristic	Lifetime SUD (*n* = 42)	No SUD (*n* = 54)	Odds ratio	*p*	Lifetime SUD (*n* = 52)	No SUD (*n* = 54)	Odds ratio	*p*
Median age in years	27.0	28.5	—	NS	27.5	28.0	—	NS
Male (%)	66.7	48.2	2.16	0.072	65.4	29.6	4.48	0.0003
Nonwhite (%)	28.6	27.8	0.96	NS	11.5	22.2	2.19	NS
High school graduate (%)[1]	72.5	80.8	1.55	NS	81.6	91.3	2.33	NS
Ever married (%)[1]	20.0	32.7	0.477	NS	49.0	39.1	2.18	NS
Working or in school before index admission (%)[2]	31.0	44.4	0.560	NS	65.4	59.7	1.29	NS

Note.—DSM–III–R = Diagnostic and Statistical Manual of Mental Disorders. 3rd ed., revised (American Psychiatric Association 1987). NS = not significant.

[1]Excluding 15 subjects under age 18.
[2]Excluding two subjects with missing data.

Table 3. Clinical ratings, psychotic symptoms, and occupational functioning at 6 months by primary diagnosis and lifetime history of substance use disorder (SUD) using *DSM–III–R* criteria

	Schizophrenia			Affective psychosis		
	Lifetime SUD	No SUD	*p*	Lifetime SUD	No SUD	*p*
Mean GAF worst in past month (SE)[1]	35.5 (2.0)	42.2 (1.77)	0.015	56.7 (2.13)	56.9 (2.11)	NS
Mean GAF best in past 6 months (SE)[1]	42.0 (1.79)	47.3 (1.59)	0.031	63.8 (1.69)	63.1 (1.67)	NS
Mean BPRS total score (SE)[2]	34.7 (1.37)	30.2 (1.22)	0.017	25.2 (1.19)	26.7 (1.18)	NS
Mean SAPS global score (SE)[2]	5.70 (0.45)	4.15 (0.39)	NS	8.50 (0.35)	1.45 (0.35)	NS
Mean SANS global score (SE)[3]	5.00 (0.39)	8.05 (0.36)	NS	3.15 (0.45)	4.30 (0.45)	NS
Current hallucinations or delusions, *n* (%)[4]	20 (51.3)	17 (34.7)	NS	2 (4.44)	7 (15.6)	NS
Working or in school at 6 mo, *n* (%)[5]	8 (19.5)	17 (32.08)	NS	29 (58.0)	32 (64.0)	NS

Note.—DSM–III–R = Diagnostic and Statistical Manual of Mental Disorders. 3rd ed., revised (American Psychiatric Association 1987). Each clinical rating was adjusted for gender and rating at index hospitalization using linear regression analysis. SANS and SAPS global scores are each the sum of five global ratings. NS = not significant; SE = standard error; GAF = Global Assessment of Functioning (American Psychiatric Association 1987); BPRS = Brief Psychiatric Rating Scale (Overall and Gorham 1962); SAPS = Schedule for the Assessment of Positive Symptoms (Andreasen 1984), SANS = Schedule for the Assessment of Negative Symptoms (Andreasen 1982).

[1]Excludes 23 subjects with missing information, of whom 8 had schizophrenia and 15 had affective psychosis.
[2]Excludes 25 subjects with missing information, of whom 8 had schizophrenia and 17 had affective psychosis.
[3]Excludes 26 subjects with missing information, of whom 8 had schizophrenia and 18 had affective psychosis.
[4]Excludes 24 subjects with missing information, of whom 8 had schizophrenia and 16 had affective psychosis.
[5]Excludes 8 subjects with missing information, of whom 2 had schizophrenia and 6 had affective psychosis.

Table 4. Treatment experiences during the 6-month interval by primary diagnosis and lifetime history of substance use disorder (SUD) using *DSM–III–R* criteria

	Schizophrenia			Affective psychosis		
	Lifetime SUD (*n* = 42)	No SUD (*n* = 54)	*p*	Lifetime SUD (*n* = 52)	No SUD (*n* = 54)	*p*
Rehospitalized or never discharged during 6-month interval, %[1]	31.0	17.3	NS	20.0	17.7	NS
Median No. days in hospital during interval[2]	22	13	NS	0	5.5	NS
Median No. mental health visits per 100 days in community[3]	3.95	3.82	NS	8.33	6.55	NS
Median No. medication visits in interval[4,5]	2.5	4.5	NS	6	5	NS
Medications at 6 months, *n* (%)[6]	28 (68.3)	39 (73.6)	NS	36 (69.2)	42 (82.4)	NS

Note.—DSM–III–R = Diagnostic and Statistical Manual of Mental Disorders. 3rd ed., revised (American Psychiatric Association 1987). NS = not significant.

[1]Includes 5 subjects who were never discharged from the hospital, all of whom had schizophrenia; also excludes 6 subjects with missing data, of whom 2 had schizophrenia and 4 had affective psychosis.
[2]Excludes 25 subjects with missing data, of whom 12 had schizophrenia and 13 had affective psychosis.
[3]Excludes 51 subjects with missing data, of whom 32 had schizophrenia and 19 had affective psychosis.
[4]Excludes 29 subjects with missing data, of whom 14 had schizophrenia and 15 had affective psychosis.
[5]Not adjusted for days in community.
[6]Excludes 5 subjects with missing data, of whom 2 had schizophrenia and 3 had affective psychosis.

amount or type of outpatient treatment, or medication compliance.

Use of selected substances during the 6-month interval is described in table 5. Cannabis and alcohol were the only substances for which use patterns differed significantly between the groups. Schizophrenia patients with a history of substance use disorder were more likely to have used cannabis during the interval ($p = 0.002$) and were marginally more likely to be using cannabis at least weekly ($p = 0.085$), but the numbers were very small. Among subjects with affective psychosis, those with a history of substance use disorder were more likely to be drinking alcohol at least weekly ($p = 0.040$). For all other substances, including cocaine, the number of patients admitting use during the interval was very small and did not reach statistical significance.

Discussion

Several studies have shown a worse outcome in schizophrenia patients with a history of substance use disorder when compared with patients without such a history (Drake and Wallach 1989; Test et al. 1989). However, most studies have examined samples of chronically ill patients. To our knowledge, no studies have examined the early course of illness for schizophrenia patients in parallel with patients with affective psychosis. We found that a lifetime history of substance use disorder does seem to influence the course of illness at 6 months for subjects with a diagnosis of schizophrenia, but not for those with affective psychosis. The schizophrenia subjects with a history of substance use disorder had poorer functioning at 6 months, as reflected by the GAF scores both for worst functioning in the past month and for best functioning during the 6-month interval. In addition, this group had worse BPRS scores, suggesting more symptomatology, although this increase in symptoms was not reflected in differences in either the SAPS global score or the percentage with hallucinations or delusions at 6 months. This higher level of symptomatology was found despite the lack of significant differences in treatment experience during the interval.

Our findings are at odds with those of Zisook et al. (1992), who found that lifetime history of substance use disorder had no effect on the level of functioning in an outpatient sample. However, that sample consisted of 51 individuals attending a single clinic, whereas ours included individuals receiving treatment in a wide variety of settings, as well as those who received little or no treatment. Therefore, our sample may be more representative of the full spectrum of patients with schizophrenia and affective psychosis.

The schizophrenia group with a history of substance use disorder was also more likely to be using cannabis during the interval. Cannabis use disorder was the only lifetime substance use diagnosis that occurred more frequently in subjects with schizophrenia than in those with affective psychosis. Several studies have suggested an association between cannabis use and a subsequent diagnosis of schizophrenia (Andreasson et al. 1987, 1989; Mathers and Ghodse 1992; Allebeck et al. 1993). Others have found an association between cannabis use and severity of schizophrenia symptoms (Negrete et al. 1986), exacerbation of psychotic symptoms (Knudson and Vilmar 1984), and relapse (Linszen et al. 1994), whereas other studies have suggested that cannabis use is associated with attenuation of negative symptoms (Peralta and Cuesta 1992). Our study suggests that cannabis may exacerbate overall symptoms, as represented by the BPRS score, while showing little effect on the negative symptoms, as represented by the SANS. However, Peralta and Cuesta (1992) studied an inpatient sample, whereas our subjects, although originally a first-admission sample,

Table 5. Substance use during the 6-month interval by primary diagnosis and lifetime history of substance use disorder (SUD) using *DSM-III-R* criteria

	Schizophrenia			Affective psychosis		
	Lifetime SUD $n = 39$ (%)	No SUD $n = 48$ (%)	p	Lifetime SUD $n = 45$ (%)	No SUD $n = 44$ (%)	p
Any alcohol use	22 (56.4)	19 (39.6)	NS	31 (68.9)	26 (59.1)	NS
Drinking alcohol at least weekly	7 (18.0)	4 (8.33)	NS	13 (28.9)	5 (11.4)	0.040
Any cannabis use	11 (28.2)	2 (4.17)	0.002	5 (11.1)	1 (2.27)	NS
Using cannabis at least weekly	5 (12.8)	1 (2.08)	0.085	2 (4.44)	0 (0.00)	NS
Any cocaine use	4 (10.3)	2 (4.17)	NS	3 (6.67)	0 (0.00)	NS

Note.—DSM-III-R = Diagnostic and Statistical Manual of Mental Disorders. 3rd ed., revised (American Psychiatric Association 1987). Based on numbers with complete face-to-face interviews at 6 months. NS = not significant.

were then assessed 6 months later when most were not experiencing an acute episode of illness. In fact, in our previous assessment of subjects at the time of entry into the Suffolk County study, we found little difference in positive symptoms and less negative symptoms associated with substance abuse, but we did not stratify by diagnosis at that time (Kovasznay et al. 1993).

Alcohol was by far the most popular drug used by subjects in the sample. Eighty-three percent of the schizophrenia subjects with a substance use disorder history had a lifetime diagnosis of alcohol abuse or dependence, although only 24 percent of these patients had limited their substance abuse to alcohol. Noordsy et al. (1991), interviewing 75 outpatients with schizophrenia, found that they used alcohol to relieve social anxiety, tension, dysphoria, apathy, anhedonia, and insomnia, although relatively few subjects reported an improvement in specific psychotic symptoms. Drake and Wallach (1993), studying 187 severely and persistently mentally ill subjects, 61 percent of whom had schizophrenia, found that they had difficulty sustaining moderate alcohol use and were likely either to develop alcohol-related difficulties or become abstinent at a 7-year followup. This picture of a sample with chronic illness illustrates the likely later course of our subjects, who are early in their illness. Drake et al. (1990) have suggested that schizophrenia patients are more vulnerable to the negative effects of alcohol, and our findings support this concept.

The majority of subjects with a history of substance use disorder met criteria for more than one substance use disorder. For example, only 12.8 percent of subjects with cannabis abuse had abused only cannabis; over half (54.7%) had also abused alcohol and at least one additional drug as well. Therefore, it is especially difficult to draw conclusions about the effects of specific drugs. Common sense would suggest that concurrent abuse of multiple substances is more toxic than that of a single drug.

We found no difference in compliance with outpatient treatment or medication among those with and without substance abuse. This finding is consistent with the results of Pristach and Smith (1990), who found no difference in self-reported compliance during the period immediately preceding inpatient admission for 42 schizophrenia subjects with and without substance abuse, although others have found poorer compliance (Drake et al. 1989) in substance-abusing patients.

Nevertheless, individuals with schizophrenia seem to be more vulnerable to the adverse effects of substances than subjects with affective psychosis. Even though many of the individuals with a history of substance use disorder were currently either not using or using small amounts, prior substance abuse seems to have lasting effects. If in fact there is underlying structural brain pathology in schizophrenia, it is not surprising that repeated exposure to toxic substances, such as occurs in substance abuse or dependence, might lead to damage that lasts beyond the active phase of substance abuse.

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