Differential Diagnosis of Substance-Induced Psychosis and Schizophrenia in Patients With Substance Use Disorders

by Richard N. Rosenthal and Christian R. Miner

Abstract

We derived a statistical model that discriminates between substance-induced psychosis (i.e., DSM-III-R organic delusional disorder or organic hallucinosis; ODD-OH) and DSM-III-R schizophrenia in patients who have both DSM-III-R psychoactive substance use disorders (PSUD) and prominent delusions or hallucinations. A sample of 211 PSUD inpatients was divided by year of admission into data sets A and B, each of which was divided between those with concurrent schizophrenia and those with concurrent ODD-OH. A six-predictor discriminant function correctly classified 76.2 percent of all set A patients, including 83.1 percent with schizophrenia. Formal thought disorder and bizarre delusions significantly predict a diagnosis of schizophrenia, with odds ratios (OR) of 3.55:1 and 6.09:1, respectively. Suicidal ideation (OR = 0.32:1), intravenous cocaine abuse (0.18:1), and a history of drug detoxification (0.26:1) or methadone maintenance (0.18:1) demonstrate inverse relationships with a schizophrenia diagnosis. The model was validated in set B, correctly predicting the diagnostic status of 70.4 percent of patients (72.5% with schizophrenia). The pattern of presenting symptoms and clinical history differs in patients with psychosis due to PSUD and in those whose psychosis is due to schizophrenia. The model presented here contributes to the differential diagnosis of schizophrenia and ODD-OH among patients with PSUD.

weeks' sobriety (Widiger et al. 1993; Woody et al. 1993). This criterion is somewhat impractical for use in making definitive diagnostic decisions to guide acute inpatient treatment. In addition, standard clinical assessments often miss contributing PSUDs that are identified by research interview, even on an inpatient service devoted to comorbid PSUD and mental disorders (Rosenthal et al. 1992b). Accordingly, any additional means of acutely distinguishing organically induced from functional psychotic symptoms in patients with PSUD would improve planning of acute and longer-range treatment.

Methods

Data were derived from observations obtained during the course of routine clinical care on the Psychiatric Substance Abuse Unit, an inpatient psychiatric service at Beth Israel Medical Center (New York) during 1988 and 1989. From the time of admission until the time of discharge, patients were interviewed, observed, and treated by an interdisciplinary team. Each patient's psychosocial history, clinical symptoms, treatment parameters, and discharge planning were presented and reviewed in a daily conference. Under the direct training and supervision of the first author, 13 advanced psychiatric residents were primarily responsible for assessment and treatment, although the information they collected during the course of treatment was subject to crosschecking by other team members. The first author recorded psychiatric history, demographic data, presenting symptoms, clinical course, and DSM-III-R (American Psychiatric Association 1987) discharge diagnoses on a daily basis using a standardized format.

Over the 2-year period, data including DSM-III-R classification and information on 26 independent variables (IVs), were collected on 988 patients. Variables included (1) demographic and prior treatment information (4 IVs), (2) presenting psychiatric symptoms (14 IVs), and (3) type of PSUD (8 IVs). Subjects were divided roughly in half by year of admission. Of 457 patients admitted during the first year of the project, 65 (14.2%) met criteria for organic delusional disorder (ODD), organic hallucinosis (OH), or both in the context of co-occurring PSUD, and 106 patients (23.2%) met criteria for schizophrenia continuum disorders, in addition to co-occurring PSUD. The number of patients in the ODD–OH and schizophrenia groups was balanced by drawing a random subsample of 65 schizophrenia patients from the 106 available.

We obtained frequency counts for all demographic, symptom, and PSUD variables, as well as the presence or absence of comorbid organic mood disorder and the percentages of the two diagnostic groups that evinced each symptom or characteristic. t-Tests for independent samples were calculated for the two continuous variables: patient age and length of inpatient stay. Fisher's exact tests were conducted to assess differences in group proportions for dichotomous variables.

We also determined a discriminant function for diagnostic status (PSUD/schizophrenia vs. PSUD/ODD–OH), accomplished via logistic regression procedures. Variables yielding Fisher's exact probabilities less than 0.10 (SYSTAT 1992) were entered into a PROC LOGISTIC regression analysis (SAS 1992), and those with nonsignificant Wald chi-square values were dropped in stepwise elimination. Using the parameters of the final regression model, estimated scores for subjects' diagnostic category were generated and converted to binary form by a decision rule yielding optimal sensitivity and specificity. We then compared these estimated scores with true diagnoses across the sample.

Residual scores from the final model were submitted to a series of diagnostic checks to check for outliers, to ensure that no single observation had a disproportionate influence, and to evaluate the sample data in terms of the assumptions underlying multiple regression models generally. Specifically, these procedures ensure that (1) population errors are likely to be normally distributed, (2) the errors have constant variance, (3) the errors are independent of each other, and (4) all members of the sample are described by the same model.

Finally, we conducted a confirmatory analysis using a second sample of 81 new patients, constructed in the same manner as the first. Patients meeting criteria for PSUD/OH and/or PSUD/ODD (n = 41) were taken from the next 531 consecutive admissions to the Psychiatric Substance Abuse Unit. These patients were paired with 40 patients randomly drawn from a subset of 112 who met criteria for PSUD/schizophrenia. The regression model derived for the first sample was fit to these new data, and predicted scores were again generated, dichotomized, and compared with true diagnoses.

Results

Results of diagnostic group comparisons for the first sample of 130 patients are given in table 1. Ten tests yielded significant differences between schizophrenia and ODD–OH at values of p < 0.05, and four additional tests were significant at p < 0.10. As a group, patients diagnosed with schizophrenia had significantly longer lengths of stay than those with ODD–OH. In addition, significantly more patients with schizophrenia presented with formal thought disorders. In contrast, significantly more patients with ODD–OH were found to have nonaggressive
command auditory hallucinations, suicidal ideation, cocaine abuse (all routes of administration, combined), intravenous cocaine abuse, heroin abuse, co-occurring organic mood disorder, and a history of methadone maintenance treatment and treatment by medical detoxification.

Parameters from the logistic regression model predicting differential diagnostic status in the sample are shown in table 2. Given considerable multicollinearity among variables, many were eliminated so that the final model contains only six predictors. With the diagnosis of schizophrenia as the criterion, there are direct predictor-criterion relationships for bizarre delusions and formal thought disorder; inverse predictor-criterion relationships obtain for history of methadone maintenance, history of detoxification, intravenous cocaine abuse, and suicidal ideation. Therefore, the model performs reasonably well under the regression-diagnostic procedures described above.

The receiver operating characteristics curve derived from the final model is shown in figure 1. With a sensitiv-
ity of 83.1 percent and specificity of 69.2 percent, the optimal probability level for estimating a diagnosis of schizophrenia is 0.56. Using this as a cutoff point, estimated scores generated by the model given in Table 2 correctly classify 99 of 130 patients (76.2%)—54 PSUD/schizophrenia patients and 45 PSUD/ODD–OH patients—by diagnosis.

When the same model is fitted to a new sample of patients (n = 81) from 1988, again one that is equally divided between PSUD/schizophrenia and PSUD/ODD–OH patients, 57 patients (70.4%)—29 of 40 (72.5%) PSUD/schizophrenia patients and 28 of 41 (68.3%) PSUD/ODD–OH patients—are correctly classified by diagnosis.

Discussion

The principal limitation of this study is that the data were not collected via standardized instruments. The procedures involved in each patient's assessment were undoubtedly more heterogeneous and possibly less sensitive than would be used in formal diagnostic testing or a structured clinical interview (Rosenthal et al. 1992b). Of the several sources of noise in this data set, perhaps the most troublesome is the lack of means for assessing the reliability of judgments made by a variety of observers and interviewers.

Previous studies of the reliability of DSM-III–R diagnoses suggest the importance of extensive training on specific criteria in attaining an acceptable level of reliability. In this study, the fact that all clinical assessments were made by advanced residents trained in the same institution by the same supervisor may increase interrater reliability. In addition, the first author confirmed all discharge diagnoses, which likely added a degree of stability to the assessment process. Fenton and McGlashan (1992) reported that judgment of psychotic symptoms and schizophrenia diagnoses obtained from chart review attain acceptable reliability across several standardized assessment systems. Although the procedures used in this study were less systematic than those of structured interviews with standardized instruments, they are probably more stringent than most chart reviews.

What is lost in standardization may be partly made up for by gains in ecological validity. As is the case in most inpatient settings, observations made by one individual were checked by other treatment team members, who observed patients in a wide range of contexts on a 24-hour basis. In addition, staff had background information on many patients because of the high frequency of repeat hospitalizations among this cohort.

Table 2. Final logistic regression model predicting a diagnosis of DSM-III–R schizophrenia-continuum disorder versus organic delusional disorder or organic hallucinosis in hospitalized inpatients with psychoactive substance use disorders (n = 130)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Intercept</th>
<th>SE</th>
<th>Wald $\chi^2$</th>
<th>$p$</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>0.3028</td>
<td>0.7359</td>
<td>1.2668</td>
<td>1.389</td>
<td>6.09</td>
</tr>
<tr>
<td>Suicidal ideation</td>
<td>-1.1349</td>
<td>0.4925</td>
<td>5.56</td>
<td>0.0184</td>
<td>0.32</td>
</tr>
<tr>
<td>Formal thought disorder</td>
<td>1.2668</td>
<td>0.4925</td>
<td>6.62</td>
<td>0.0101</td>
<td>3.55</td>
</tr>
<tr>
<td>History of methadone maintenance</td>
<td>-1.7049</td>
<td>0.7359</td>
<td>5.37</td>
<td>0.0205</td>
<td>0.18</td>
</tr>
<tr>
<td>History of detoxification</td>
<td>-1.4474</td>
<td>0.8458</td>
<td>2.93</td>
<td>0.0870</td>
<td>0.26</td>
</tr>
<tr>
<td>Bizarre delusions</td>
<td>1.8069</td>
<td>0.8499</td>
<td>4.52</td>
<td>0.0335</td>
<td>6.09</td>
</tr>
<tr>
<td>Intravenous cocaine abuse</td>
<td>-1.7173</td>
<td>0.7964</td>
<td>4.65</td>
<td>0.0311</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Note.—DSM-III–R = Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association 1987). $B =$ raw score regression; SE = standard error. Goodness of fit criterion: $-2 \text{Log } L = 135.55$, $\chi^2 = 44.67$, $p < 0.0001$; sensitivity = 83.1%; specificity = 69.2%.
The regression model of table 2 has face validity when considered in the context of the wide array of patients presenting with psychotic symptoms who are admitted to an urban inpatient psychiatric unit. Certain characteristics of the model are further supported by other findings in this population. First, in contrast to the high frequency of alcohol, marijuana, and intranasal or smoked cocaine use (Tsuang et al. 1982; Fernandez-Pol et al. 1988; Casteneda et al. 1991; Rosenthal et al. 1992b), PSUD/schizophrenia patients seem consistently to show infrequent intravenous opiate or cocaine use. Accordingly, it is reasonable to expect that only a negligible percentage of patients fulfilling diagnostic criteria for schizophrenia, even those identified as PSUD/schizophrenia, will be methadone-maintained (see table 1).

Thought disorder and bizarre delusions are major criterion subsets of DSM-III-R schizophrenia, but not of DSM-III-R PSUD. Our findings echo those of Surawicz (1980) and Mendoza and Miller (1992) who described and of Cornelius et al. (1991) who demonstrated a lower rate of thought disorder in patients with OH (secondary to various causes) than in those with schizophrenia. Indeed, substance abuse has been significantly correlated with an increase in thought disorder among PSUD/schizophrenia patients compared with schizophrenia patients without PSUD (Cleghorn et al. 1991). More specifically, patients with schizophrenia are preferentially sensitive to methylphenidate-induced increases in thought disorder as compared with normals (Levy et al. 1993). Persecutory delusions occurred at the same frequency in the PSUD/schizophrenia and PSUD/ODD-OH groups (table 1) and substance-induced delusions are most frequently persecutory (Flaster 1990), therefore, bizarre delusions in the absence of a delirium state can predict a schizophrenia syndrome. Delusions with specific bizarre content are relatively uncommon in ODD-OH syndromes (Surawicz 1980; Satel et al. 1991; Mendoza and Miller 1992), where delusional themes may more often be congruent with dysphoric mood, as compared with schizophrenia (Mitchell and Vierkant 1991). Thus, as differential predictors of schizophrenia, both thought disorder and bizarre delusions have construct validity based on established diagnostic criteria.

The role of suicidal ideation in the discriminant function may not be obvious, except perhaps to those who work with substance abusers in a psychiatric setting. Suicidal ideation is a common symptom of chronic schizophrenia, and the high rate of serious suicide attempts and completion in patients with this disorder is well known (Dassori et al. 1990; Breier et al. 1991; Carone et al. 1991). Why then does the presence of this symptom help predict a nonschizophrenia diagnosis in this model?

Although this finding seems counterintuitive, a look at the specific population under study might illuminate the appropriateness of the model. Compared with PSUD/schizophrenia patients, rates of acute suicidal ideation are high among those patients who do not meet criteria for a functional psychotic disorder but who are nonetheless admitted to an inpatient acute-care psychiatric substance abuse unit (Pinkser 1981; Bunt et al. 1990). The rate of acute suicidal ideation in the current sample may be high (15%) among PSUD/schizophrenia patients, but it is more than twice as high (42%) among PSUD/ODD-OH patients admitted for acute, inpatient psychiatric care. Substance abusers who are admitted to inpatient psychiatric services, rather than medical-model detoxification services, typically complain of mood disturbance and suicidal thoughts (see Cornelius et al. 1995). In our experience, these symptoms are in keeping with the fact that a broad range of PSUD patients present with short-duration comorbid organic anxiety and mood disorders (Dorus et al. 1987; Brown and Schuckit 1988; Weiss et al. 1989; Brady et al. 1993). Indeed, such mood disorders are considerably more common than either ODD or OH, and the 43 percent comorbidity rate shown by table 1 may be largely responsible for the high incidence of suicidal ideation. Of the 457 patients admitted in 1989 to the dual-diagnosis unit from which the current study sample is derived, 30.4 percent received a DSM-III-R diagnosis of organic mood disorder, 8.3 percent met criteria for OH, and 5.9 percent had ODD (Rosenthal et al. 1992b).

It remains to be demonstrated that this six-variable model accurately distinguishes PSUD/schizophrenia patients from ODD-OH patients in environments other than inpatient psychiatric units, such as substance abuse treatment facilities, outpatient mental health clinics, or hospitals in other locations. Yet, a simple model that aids the differential diagnosis of psychotic symptoms in substance abusers could affect both on the immediate care and longer-term treatment plans for dually diagnosed patients. The recovery of psychosocial function is likely faster and the capacity to tolerate strenuous or anxiety-provoking treatment higher in patients with evanescent psychotic and mood symptoms than in patients with schizophrenia. Clearly, future research should explore the relationship of substance-induced organic mood disorder to that of ODD and OH. If cluster analysis of comorbid diagnoses suggests a more fundamental syndrome of substance-induced organic disorder that presents with various constellations of mood and psychotic symptoms, then an interesting, unresolved diagnostic issue will have been continued in DSM-IV.
References


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