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Measuring principal substance of abuse in comorbid patients for clinical research

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Abstract

Few individuals with substance use disorders limit their intake to one substance of abuse; however, many studies focus on a single substance. Unfortunately, the optimal method to determine the principal substance is unclear. In particular, this issue is problematic in patients with co-occurring psychiatric illness, who commonly use multiple substances. Hence we compared three methods for assessing the principal substance of abuse in 150 subjects with bipolar disorder and substance dependence: 1) the Addiction Severity Index interview, 2) a self-administered questionnaire, and 3) the most frequently used substance.

While most subjects were concordant on the interview and the other two methods, we found substantial disagreement (9.3% between the interview and the questionnaire, and 12.7% between the interview and the most frequently used substance) and partial agreement (14.0%). These findings from a comorbid population demonstrate that different methods to assess principal substance of abuse could lead to different conclusions about treatment outcomes. Hence studies of comorbid patients may benefit from 1) using more than one method to assess principal substance and 2) reporting use of all substances as well as a targeted substance.

Keywords

treatment; comorbidity; group treatment; diagnosis; methodology; assessment

1. Introduction

Few individuals with substance use disorders limit their intake of alcohol and drugs to a single substance. A recent national probability study examined 12-month prevalence rates and found that 55.2% of respondents with a drug use disorder also had an alcohol use disorder (Stinson et al., 2005); these data are similar to earlier reports from the Epidemiologic Catchment Area Study (Helzer and Pryzbeck, 1988). A study of cocaine-dependent subjects found that most had a lifetime alcohol use disorder, regardless of treatment-seeking status (62% of treatment-seekers and 68% of non-treatment-seekers; Carroll et al., 1993). Conversely, studies of clinical samples show that most alcohol-dependent patients also use drugs: 64% use both (Tsuang et al., 1994), 61% use alcohol and drugs on the same day (Martin et al., 1996), about half are

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regular drug users (Schmitz et al., 1991), and half (49%) have a drug use disorder (Ross, 1993).

Polysubstance use among patients with substance use disorder and co-occurring serious psychiatric illness is also common (Swartz et al., 2006; Weiss et al., 2007). Therefore, when conducting studies of populations with co-occurring substance use disorders and psychiatric illness, recruiting patients with a specific psychiatric disorder and a single principal drug of abuse (e.g., patients with posttraumatic stress disorder and cocaine dependence) may be unwieldy, and such a restriction could reduce generalizability. For studies of behavioral treatment, which typically focus on use of all substances (as opposed to a medication that may target a specific drug), the argument for including psychiatrically ill patients with different substances of abuse is even stronger. Comorbid patients who use multiple drugs may identify one particular substance that they want to stop using, rather than wanting to become abstinent from all substances. For example, a patient with bipolar disorder may want to stop using cocaine, but not marijuana; marijuana use may be viewed as “self-medication” for the mood disorder. In such a case, it would be important to identify the principal substance of abuse in order to determine the effectiveness of a treatment intervention.

In a review of the issues involved in studying single vs. multiple drugs, Rounsaville and colleagues (2003) have advocated moving away from research focused on a single drug, particularly when evaluating behavioral treatments; they suggest routinely assessing use of a wide variety of drugs and including subjects who use multiple substances in studies. When analyzing data from such studies, they suggest focusing on a “principal substance of abuse” for each study subject, and examining improvement in use of that substance as a primary outcome measure.

Unfortunately, identifying the principal substance of abuse in comorbid patients is not always straightforward. Indeed, the heterogeneity in terminology and method of assessment of principal substance can potentially lead to the identification of different “principal” substances. For example, a patient may express a preference for opioids, experience the most problems from cocaine, and use marijuana and alcohol most often. We are aware of no previous research, however, that has empirically examined the issue of how to reliably identify a principal substance of abuse.

In fact, terminology used to describe this varies across studies, including “primary” drug (e.g., Lejuez et al., 2005; Pirard et al., 2005; Zhang et al., 2003), “preferred” drug (e.g., Fry & Dwyer, 2001; Kirby & Petry, 2004; Winters et al., 2000), “drug of choice” (e.g., Conway et al., 2003; Sumnall et al., 2004), “goal drug” (Bellack et al., 2006), and the “primary substance problem” (e.g., Blanchard et al., 2003). These terms refer to a variety of operational definitions of the principal substance, including 1) the most frequently used drug (Lejuez et al., 2005; Winters et al., 2000); 2) the drug responsible for the current treatment episode (Lawrinson et al., 2005; Zhang et al., 2003); and 3) level of severity, as measured by a) a clinical rating of lifetime substances of dependence (Conway et al., 2003), b) number of dependence symptoms (Blanchard et al., 2003), c) the substance causing the most problems (Kirby & Petry, 2004), and d) a clinical rating of greatest subjective distress or functional impairment (Crits-Christoph et al., 1999). Some researchers (e.g., Blanchard et al., 2003; Conway et al., 2003; Crits-Christoph et al., 1999; Pirard et al., 2005) employ standardized instruments, such as the Structured Clinical Interview for DSM-IV (First et al., 1996), the Anxiety Disorders Interview Schedule (DiNardo et al., 1988), or the Addiction Severity Index (McLellan et al., 1992) to determine principal substance. However, studies often use unique self-report items or do not clearly specify how the determination of principal substance is made. Further, laboratory data suggest that those who abuse multiple substances may vary their purchase and use of drugs

based on price, availability, and purity, rather than expressed preference (Sumnall et al., 2004).

As part of an ongoing study of a new group treatment for patients with bipolar disorder and substance dependence, we therefore compared several methods for assessing principal substance of abuse in 150 patients with bipolar disorder and substance dependence to illustrate the problem.

2. Illustrative example: methods

At intake, patients enrolling in a comparison study of two group treatments had current diagnoses of bipolar disorder and substance dependence, based on the Structured Clinical Interview for DSM-IV (First et al., 1996), and had used alcohol or other drugs within the past 60 days. The McLean Hospital Institutional Review Board approved this project.

Information on principal substance of abuse was obtained in three different ways at the intake assessment. We used the Addiction Severity Index (ASI, 5th edition; McLellan et al., 1992), a widely employed and empirically validated (Kosten et al., 1983) multidimensional structured interview of substance-related problems. As prescribed, trained research assistants administered this interview to subjects at intake. The ASI asks, "Which substance is the major problem?" Possible answers are 1) alcohol or a specific drug, 2) "alcohol and drug" (i.e., alcohol plus one or more drugs), or 3) "polydrug" (i.e., more than one drug). While the ASI interview may be inappropriate for severely mentally ill patients (Zanis et al., 1997), our low rates of missing data and misunderstood interview items suggest that this measure was appropriate for our particular sample, given extensive interviewer training. Subjects also completed a self-administered questionnaire that we have used in multiple studies (Weiss et al., 2004), which asks, "What is the primary substance (drug or alcohol) that you use?" Only one substance could be named. Finally, we used data from the ASI interview to determine the most frequently used substance in the past 30 days; this measure has been used as a criterion for principal drug in some studies (e.g., Lejeuz et al., 2005; Winters et al., 2000). If two or more substances were used equally often, cases were counted as agreement if any of the substances matched the primary substance on the ASI interview.

3. Illustrative example: Results

3.1. Subjects

The study sample (N=150) was 51.3% male and 90.7% white. The mean age was 38.8 (sd=10.5 years). Most subjects were not currently married or cohabitating (71%), about half were unemployed (54%), and half had graduated from college (49%). The median family income was \$35,001–50,000. Most subjects (79.2%) were diagnosed with bipolar I disorder, 14.1% had bipolar II disorder, and 6.7% had bipolar disorder not otherwise specified. About half (56.7%) were currently diagnosed with both drug and alcohol use disorders, 31.3% with alcohol use disorders only, and 12.0% with drug use disorders only. Among those with drug use disorders, the most common drug dependence diagnoses were marijuana (n=62) and cocaine (n=59), followed by sedative/hypnotics (n=30), opioids (n=27), amphetamines (n=26), hallucinogens (n=11), and more than one drug (n=6). During the month prior to study entry, subjects reported a mean of 11.9 (sd=10.3) days of any substance use: 8.3 (sd=9.3) days of alcohol use and 6.8 (sd=10.1) days of drug use.

3.2. Prevalence

Comparison of the *major problem* substance named on the ASI interview to the *primary* substance named on the self-administered questionnaire yielded similar results, with both

measures showing alcohol to be the most common principal substance (56.0% vs. 63.3% respectively; see Table 1). Next most common were cocaine (14.0% on the ASI vs. 14.7% on the questionnaire) and marijuana (10.7% on the ASI vs. 14.7% on the questionnaire), then “alcohol and drug” (10.7% on the ASI; not applicable on the questionnaire), followed by six or fewer subjects on either assessment reporting polydrug use, opioids, sedative-hypnotics, amphetamines, hallucinogens, and other stimulants. Similarly, alcohol was the substance used most frequently (61.3%) in the past 30 days at baseline, with marijuana and cocaine a distant second and third at 12.7% and 8.7% respectively.

3.3. Concordance

Three-quarters of subjects (76.7%, $n=115$) were concordant on the ASI interview and the questionnaire, primarily due to agreement that they were abusing alcohol (80/115 cases of agreement). Another 14.0% ($n=21$) showed partial agreement: “alcohol and drug” ($n=16$) or “polydrug” ($n=5$) was listed on the ASI interview, whereas only one substance could be selected on the questionnaire. The remaining 9.3% ($n=14$) of the subjects disagreed on the two assessments altogether, with different substances listed on the two measures (see Table 2a). As shown in Table 2b, disagreement between the principal substance named on the ASI interview and the substance used most frequently was similar (12.7%, $n=19$). As above, partial agreement occurred for the same 14.0% of subjects.

4. Discussion

There is no gold standard method to measure substance use outcomes in patients who use a variety of different substance of abuse; indeed, most patients with a co-occurring psychiatric illness abuse more than a single substance. For comorbid populations, a variety of treatment outcome measures have been used, including days of alcohol use, days of drug use, alcohol severity score, drug severity score, and an SUD recovery rating (Drake et al., 1998); a composite score for days using several substances (Hien et al., 2004); the proportion of negative urine toxicology screens (Bellack et al., 2006); and the proportion of positive urines for each drug and overall (Hien et al., 2000). Measuring improvement in principal drug of abuse is a potentially useful method of assessing outcome in this population (Rounsaville et al., 2003); patients often enter treatment using multiple substances, but may identify one specific substance as the one that they would like to stop or reduce. However, as shown here, the “principal substance” can be defined and assessed in a variety of ways, and those different definitions and assessment methods can yield varied responses. To call attention to this issue, we report here that asking about the “major problem” yielded a different principal substance than asking about the “primary substance” for 9.3% of study subjects; and measuring the substance used most frequently yielded a principal substance different from the “major problem” for 12.7% of subjects. It is notable that, while 39.3% of patients received a SCID diagnosis of cocaine dependence, only 14.0–14.7% identified cocaine as the principal substance. This discrepancy demonstrates the need for an assessment in addition to the SCID to determine principal substance, since the SCID is not designed for this purpose.

One possible explanation for the discrepancies we found is the method of data collection: subject responses may vary between an interview and a self-administered questionnaire. Moreover, reliability over time in determining principal substance of abuse is unclear, and may change as a result of treatment. For example, patients in an abstinence-oriented treatment program may be persuaded that their use of all substances is problematic, not just their initially targeted principal substance.

These findings suggest that apparently minor differences in the methodology of assessing principal substance of abuse can yield different results, as it did here for 1 out of 10 patients. Hence, studies of patients with heterogeneous substance use disorders, such as those with co-

occurring psychiatric illness, may benefit from particularly careful consideration of the identification of the principal substance abused. In studies targeting alcohol, the criteria used by Greenfield and colleagues (1998) might be useful: subjects using more than one substance were asked to name the substance causing the most difficulties, the substance they used most frequently, and their primary substance. To be included in the sample, subjects had to answer alcohol for each question. This method would also be appropriate for a pharmacotherapy study targeting a specific substance, but such strict exclusion criteria in a behavioral therapy study would likely result in an unrepresentative sample. A study designed to recruit subjects with different principal substances of abuse might ask those same questions to identify the principal substance; if the responses varied, then one solution would be to report use of all substances, as well as the principal substance.

Since there is some evidence that amounts of alcohol use that might not otherwise be viewed as harmful may adversely affect the course of patients with bipolar disorder (Goldstein et al., 2006), reporting on all substance use could yield valuable information. However, the current report is designed to raise awareness of the issue that developing a consistent definition in the field for commonly used terms such as “principal substance of abuse” will help facilitate cross-study comparisons and thus strengthen our confidence in research findings.

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Table 1

Prevalence of principal substance use problems by measure (N=150)

Substance	ASI interview	Questionnaire	Used most frequently
Alcohol	56.0% (84)	63.3% (95)	61.3% (92)
Cocaine	14.0 (21)	14.7 (22)	8.7 (13)
Marijuana	10.7 (16)	14.7 (22)	12.7 (19)
Sedatives	1.3 (2)	3.3 (5)	4.0 (6)
Opioids	2.0 (3)	2.6 (4)	1.4 (2)
Amphetamines	1.3 (2)	0.7 (1)	1.3 (2)
Other stimulants	0.0 (0)	0.7 (1)	0.0 (0)
Hallucinogens	0.0 (0)	0.7 (1)	0.7 (1)
Alcohol & drugs	10.7 (16)	n.a.	8.0 (12)
Polydrug	4.0 (6)	n.a.	2.0 (3)

n.a.=not applicable

Table 2**Table 2a. Cases of disagreement on principal substance of abuse between the ASI interview and the self-administered questionnaire (n=14/150)**

ASI interview	Questionnaire (n)
Cocaine	alcohol (3); heroin (1); marijuana (1)
Alcohol	cocaine (3); marijuana (1)
Marijuana	alcohol (1); sedative-hypnotics (1)
Opioids	sedative-hypnotics (1)
Amphetamines	other stimulant (1)
Polydrug	alcohol (1)

Table 2b. Cases of disagreement on principal substance of abuse between the ASI interview and the substance used most frequently (n=19/150)

ASI interview	Most frequently used (n)
Cocaine	alcohol (6); marijuana (4)
Marijuana	alcohol (3); sedative-hypnotics (1); cocaine (1)
Alcohol	marijuana & cocaine (1); inhalant (1); sedative-hypnotics (1)
Opioids	sedative-hypnotics (1)