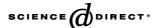
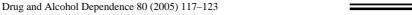


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Co-occurring DSM-IV drug abuse in DSM-IV drug dependence: Results from the National Epidemiologic Survey on Alcohol and Related Conditions

Deborah S. Hasin a,c, Mark Hatzenbueler, Sharon Smith, Bridget F. Grant b,*

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Abstract

The extent to which dependence occurs with or without abuse is important because of the potential for underestimation and biased estimates of drug dependence in surveys that rely on abuse as a screening method for dependence. The purpose of this paper was to present the prevalence of DSM-IV drug dependence with and without drug abuse in a nationally representative sample, as well as in subgroups defined by sex, age and race/ethnicity. Among all respondents with current drug dependence, 22.0% did not additionally meet criteria for abuse (19.5% among males and 27.8% among females). Current drug dependence without abuse was especially common among females age 45–64 (52.6% of all cases). Among those with lifetime diagnoses of drug dependence, a small proportion overall, 5.0% had no symptoms of abuse, with the highest proportion again found among females aged 45–64 (19.5% of all cases). The use of drug abuse as a screening method for drug dependence in large epidemiologic studies will differentially underestimate the prevalence of dependence by subgroup, affecting many types of research. Dependence with and without abuse may represent heterogeneous phenotypes for genetic and gene-environment research, which should be explored.

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1. Introduction

When the signs and symptoms of two mental disorders appear related, questions often arise about their relationship to each other. This has been the case for substance abuse and dependence since substance use disorders were divided into these two conditions in Diagnostic and Statistical Manual of Mental Disorders, third edition (DSM-III: American Psychiatric Association, 1980). Much of the work on the relationship of abuse and dependence has focused on alcohol use disorders, addressing whether alcohol abuse should be dropped from the nomenclature (Rounsaville, 1987), whether alcohol

abuse usually develops into dependence (Grant and Dawson, 1997; Hasin et al., 1990, 1997d; Schuckit et al., 1994, 2001), whether alcohol abuse and dependence are interchangeable (Prescott et al., 1999; Hasin et al., 1997c; Hasin and Paykin, 1999) and whether symptoms of alcohol abuse always accompany dependence (Hasin and Grant, 2004). These questions have largely been answered in the negative. However, much less is known about the relationship of dependence and abuse symptoms for drug use disorders, including whether symptoms of drug abuse always accompany drug dependence. The question is important for several reasons. First, in population surveys relying on drug abuse symptoms as a screening method for drug dependence, cases of drug dependence without abuse will be missed, resulting in underestimated dependence prevalence. This method was used in several surveys

^{*} Corresponding author. Tel.: +1 301 443 7370; fax: +1 301 443 1400. E-mail address: bgrant@willco.niaaa.nih.gov (B.F. Grant).

including the NIMH National Comorbidity Survey replication (NCS-R), the follow-up survey (NCS-2), the adolescent (NCS-A) survey and the world mental health (WMH) comorbidity surveys (Kessler and Walters, 2002; World Health Organization, 2003). Further, if DSM-IV drug dependence without abuse is unequally distributed across population subgroups, then prevalence estimates and results of risk factor analyses may be biased. Second, in genetics research, the presence or absence of abuse among individuals with dependence may introduce unrecognized heterogeneity into the diagnostic phenotype of dependence. Third, case recognition of drug dependence in clinical practice may be affected if abuse symptoms are used (informally or in a structured manner) as a screening method for dependence.

The conceptual background of abuse and dependence suggests examination of this issue because the final structure of abuse and dependence in DSM, fourth edition (DSM-IV: American Psychiatric Association, 1994) is inconsistent with the theoretical background of the dependence and abuse concepts. The DSM-IV division between abuse and dependence was based (Rounsaville et al., 1986) on the formulation of the alcohol dependence syndrome (ADS) of Edwards and Gross (1976), later generalized to drug disorders by the World Health Organization. The ADS was described as a combination of physiological and psychological processes reflecting impaired control over use, constituting what is now recognized as a "complex" disorder. Consistent with this, DSM-IV dependence criteria reflect both physiological and psychological symptoms. The dependence syndrome was considered one "axis" of problems, differentiated from another axis consisting of problems resulting from drug use such as substancerelated injuries, social, or legal problems (Edwards, 1986). This second axis corresponds to DSM-IV drug abuse. Importantly, the two axes in the "bi-axial" dependence syndrome distinction were not considered "orthogonal". Instead, they were defined as different types of substance-related problems expected to co-occur in some but not all cases. While the separation of dependence and abuse criteria in DSM-III-R and DSM-IV was based on the bi-axial distinction (Edwards, 1986), DSM-III-R and DSM-IV departed from the dependence syndrome concept by creating a hierarchy between dependence and abuse. This left abuse undiagnosed among individuals with dependence. Due to this hierarchy, little is known about the co-occurrence of drug abuse and dependence, or whether knowledge about dependence is affected by failing to note the co-occurrence of abuse.

Our previous investigation of this issue for DSM-IV alcohol abuse and dependence in the U.S. general population revealed that a substantial proportion of those with alcohol dependence did not manifest symptoms of alcohol abuse, and that this varied considerably by population subgroup (Hasin and Grant, 2004). Due to important biochemical and social/legal differences between alcohol and drug use disorders, we have now examined the occurrence of drug dependence with and without abuse. In doing so, we addressed these questions: (1) what is the prevalence of DSM-IV drug dependence

with and without DSM-IV drug abuse in the general population, and what proportion of DSM-IV drug dependence cases are not accompanied by abuse? (2) Does the co-occurrence of drug abuse with dependence differ in sex-, race- and agespecific subgroups of the population?

2. Methods

2.1. Sample

Subjects were participants in the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a nationally representative face-to-face survey of 43,093 respondents aged 18 years and older conducted by the NIAAA in 2001-2002. The target population of the NESARC was the civilian non-institutionalized population residing in the United States and District of Columbia, including Alaska and Hawaii. African-Americans and Hispanics were oversampled, as were young adults. The NESARC also included a group quarters sampling frame. Details of the sampling frame are provided elsewhere (Grant et al., 2003b, 2004). The overall survey response rate was 81%. The NESARC sample was weighted to adjust for probabilities of selection of a housing unit or equivalent, household- and person-level nonresponse, the selection of one person per household and oversampling of young adults. Once weighted, the data were adjusted to represent the United States population on a variety of sociodemographic variables including region, age, sex, race and ethnicity based on the 2000 Decennial Census. For this analysis, we included all NESARC respondents except Native Americans, a distinct group too small to analyze, leaving a sample of 42,392. Among these, 47.9% were male, 70.9% white, 11.1% African-American, 11.6% Hispanic, and 4.36% Asian. By age, 21.8% were 18-29, 30.9% were 30-44, 31.1% were 45-64 and 16.2% were 65 or older.

2.2. Measures

DSM-IV drug abuse and dependence were assessed with the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule—DSM-IV Version (AUDADIS-IV) (Grant et al., 2001), a fully-structured diagnostic interview for non-clinician interviewers. The AUDADIS-IV includes an extensive list of symptom questions that operationalize each DSM-IV criterion for drug abuse and dependence separately. To indicate whether criteria were met for a diagnosis of DSM-IV drug dependence or abuse, responses were combined across drug categories, following procedures published previously (Grant et al., 2004). Each criterion for DSM-IV substance abuse was rated independently of whether or not dependence was present, allowing identification of drug dependent individuals with and without abuse. The high reliability and validity of the AUDADIS drug dependence diagnosis has been demonstrated in numerous clinical and general population studies in the U.S. and abroad (Canino et al., 1999; Chatterji et al., 1997; Cottler et al., 1997; Grant et al., 1995, 2003a; Hasin et al., 1996, 1997a, 1997b; Pull et al., 1997; Üstün et al., 1997; Vrasti et al., 1997). The reliability of DSM-IV drug abuse is also adequate when diagnosed non-hierarchically (independent of dependence) (Canino et al., 1999; Chatterji et al., 1997; Vrasti et al., 1997), as done here.

In this study, we addressed both current (last 12 months) and lifetime dependence. A variable was also created to indicate whether participants had been in treatment and/or a 12-step group for drug problems in the previous 12 months. This provided parallel information about substance abuse among individuals treated in a variety of settings, including drug and alcohol inpatient and outpatient settings, mental health settings, outpatient physicians, other health care providers, and human service agencies as well as 12-step groups.

2.3. Interviewers, training and field quality control

Approximately, 1800 professional interviewers from the U.S. Bureau of the Census administered the AUDADIS-IV using laptop computer-assisted software with built-in skip logic and consistency checks. The interviewers had an average of 5 years experience on census and other health-related national surveys. All interviewers across the Census Bureau's 12 regional offices completed 10 days of standardized training through centralized training sessions directed by NIAAA and census headquarters staff. For quality control, regional supervisors re-contacted a random 10% of all respondents and re-asked a subset of the interview questions to verify the accuracy of the interviewer's performance. This careful process showed that the interviewers performed at a high level, as indicated by the high reliability of the instrument (Grant et al., 2003a, 2003b). In the very few cases when the accuracy of the interviews was uncertain, the interview data were discarded and the interview re-done by a supervising interviewer.

2.4. Statistical analysis

The prevalence of DSM-IV drug dependence with and without abuse is shown in percentages weighted for characteristics of the sample design. Thus, the figures are representative of the U.S. general population. In addition, the percent of dependence cases without abuse is presented, for the total sample and by gender-, race- and age-specific subgroups of the population.

3. Results

3.1. Current dependence and abuse

For the full sample, the total prevalence of current (last 12 months) DSM-IV drug dependence was 0.58% (S.E. 0.05). When broken down by the presence of abuse, the prevalence of drug dependence with abuse was 0.45% and the prevalence of dependence without abuse was 0.13%. Thus, about one-fifth (22.4%) of those with current diagnoses of DSM-IV drug dependence did not also have drug abuse.

The results for current disorders by race/ethnic and age groups are shown separately for males and females in Table 1. Among all males, the prevalence of dependence cases with and without abuse was 0.66 and 0.16, respectively; thus, about 19.5% of DSM-IV drug dependence cases among males did not also have abuse. While we previously reported that the proportion of cases of alcohol dependence without abuse was much higher in some minority groups, (Hasin and Grant, 2004), this was not the case for drug dependence, as the proportions were similar across race/ethnic groups (Table 1). There was, however, about a 29% graded increase across male age groups from respondents aged 18-29 to aged 45-64, much of which was contributed by the African-American subgroup. Estimates became unstable in the oldest subgroups due to the smaller proportion of dependent respondents in the oldest groups.

Table 1
Prevalence of current (last 12 months) DSM-IV drug dependence with and without abuse and percentages of total dependence cases without abuse

Sex and age	White			African-American			Asian			Hispanic			Total		
	With abuse	Without abuse	%	With abuse	Without abuse	%	With abuse	Without abuse	%	With abuse	Without abuse	%	With abuse	Without abuse	%
Men															
18-29	2.01	0.51	20.24	1.92	0.00	0.00	1.04	0.00	0.00	1.71	0.51	22.97	1.88	0.42	18.26
30-44	0.45	0.12	21.05	0.84	0.29	25.66	0.00	0.00	0.00	0.46	0.00	0.00	0.47	0.12	20.34
45-64	0.31	0.06	16.22	0.09	0.24	72.73	0.00	0.34	100.00	0.13	0.00	0.00	0.26	0.08	23.53
65+	0.00	0.03	100.00	0.00	0.29	100.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	100.00
Total	0.63	0.16	20.25	0.82	0.20	19.61	0.31	0.09	22.50	0.81	0.18	18.18	0.66	0.16	19.51
Women															
18-29	0.60	0.11	15.49	0.83	0.16	16.16	0.53	0.70	56.91	0.62	0.07	10.14	0.63	0.14	18.18
30-44	0.35	0.15	30.00	0.51	0.06	10.53	0.00	0.00	0.00	0.05	0.00	0.00	0.32	0.11	25.58
45-64	0.06	0.06	50.00	0.24	0.22	47.83	0.26	0.00	0.00	0.16	0.37	69.81	0.09	0.10	52.63
65+	0.04	0.02	33.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.02	33.33
Total	0.24	0.08	25.00	0.45	0.12	21.05	0.22	0.18	45.00	0.26	0.11	29.73	0.26	0.10	27.78

Among females, the prevalence of DSM-IV drug dependence with and without abuse was 0.26 and 0.10%, respectively. Thus, among females, about 27.8% of current DSM-IV drug dependence cases did not also have abuse. Similar to the pattern just described among males, the proportion of females with current DSM-IV drug dependence who did not also have current abuse did not vary much between race/ethnicity groups. The only exception to this was among Asian females, where small numbers may have led to instability. Among females, age differences in the proportion of those with dependence who did not also have current abuse were apparent, and more striking than among males, with a 190% increase across female age groups aged 18-29 to aged 45-64. This pattern of decreasing proportions of current dependence cases with abuse as age increased was not found previously for alcohol dependence/abuse for either gender.

The number of individuals in the sample who received any treatment or participated in 12-step programs for drug problems in the previous twelve months was small (N = 273), so we combined genders to examine the treated group. Of these, 21.87% met full criteria (3 + criteria in the prior 12 months) for dependence with abuse, while 5.01% met current criteria for dependence without abuse. Thus, 18.64% of those with any dependence had current dependence without accompanying abuse. Specific population subgroups are not presented due to small numbers. These results for treated individuals did not show the marked differences from the total sample that was previously found for alcohol (Hasin and Grant, 2004). The small proportion of individuals with current dependence who were in treatment is consistent with the previous epidemiologic literature, while the relatively low proportion of those in treatment meeting full criteria for current dependence is accounted for by the fact that nearly all had past diagnoses of drug dependence.

3.2. Lifetime dependence and abuse

For the full sample, the total prevalence of lifetime DSM-IV drug dependence was 2.49 (0.12). When broken down by

the presence of abuse, the prevalence of drug dependence with abuse was 2.27% and the prevalence of dependence without abuse was 0.22%. Thus, about 8.8% of those with lifetime diagnoses of DSM-IV drug dependence never met the criteria for drug abuse. Table 2 shows the results for lifetime disorders for males and females.

For lifetime DSM-IV drug dependence diagnoses among males, the prevalence of dependence cases with and without abuse was 2.93 and 0.23%, respectively. Thus, about 7.3% of males with a lifetime DSM-IV drug dependence diagnosis did not also have abuse. Unlike the results previously found for alcohol (Hasin and Grant, 2004), minority males did not show a distinctively higher proportion of lifetime drug dependence cases without abuse than whites, since some race/ethnic groups were higher than whites and some were lower. When lifetime disorders were examined across age groups among males from 18 to 65, no increasing gradient for dependence cases was found—in fact, the highest proportion of dependence cases without abuse in an ethnic by age group was found among Hispanic males aged 18–29, 17.18%.

For lifetime DSM-IV drug dependence diagnoses among females, the prevalence of dependence cases with and without abuse was 1.67 and 0.21%, respectively. Thus, about 11.2% of females with a lifetime DSM-IV drug dependence diagnosis did not also have abuse. Once again, no consistently higher proportion was found among minorities, with some race/ethnic groups higher than whites and some lower. However, a striking 131% increase in the proportion of lifetime dependence cases without abuse was seen across female age groups aged 18–29 to aged 45–64. This age-related pattern was not found among females for lifetime alcohol dependence/abuse.

In the sample, 720 respondents had been in treatment or a self-help group for a drug problem at some point in their lives. Of these, 51.99% met criteria for lifetime dependence with abuse, while only 2.86% met criteria for lifetime dependence without abuse. Thus, 5.21% of those with any dependence had dependence without abuse, a

Table 2
Prevalence of lifetime DSM-IV drug dependence with and without abuse and percentages of total dependence cases without abuse

Sex and age	White			African-American			Asian			Hispanic			Total		
	With abuse	Without abuse	%	With abuse	Without abuse	%	With abuse	Without abuse	%	With abuse	Without abuse	%	With abuse	Without abuse	%
Men															
18-29	5.55	0.56	9.17	2.44	0.00	0.00	2.57	0.00	0.00	2.70	0.56	17.18	4.43	0.46	9.41
30-44	4.12	0.21	4.85	4.85	0.13	2.61	0.60	0.00	0.00	2.60	0.21	7.47	3.80	0.19	4.76
45-64	2.30	0.21	8.37	2.91	0.24	7.62	1.88	0.00	0.00	1.04	0.00	0.00	2.24	0.19	7.82
65+	0.17	0.03	15.00	0.00	0.29	100.00	0.00	0.00	0.00	0.00	0.00	0.00	0.14	0.04	22.22
Total	3.13	0.25	7.40	3.13	0.14	4.28	1.47	0.00	0.00	2.15	0.28	11.52	2.93	0.23	7.28
Women															
18-29	3.50	0.18	4.89	1.46	0.20	12.05	0.53	0.78	59.54	2.20	0.42	16.03	2.82	0.26	8.44
30-44	2.97	0.35	10.54	1.95	0.15	7.14	0.11	0.12	52.17	1.69	0.17	9.14	2.52	0.29	10.32
45-64	0.88	0.26	22.81	1.73	0.11	5.98	0.26	0.00	0.00	0.91	0.22	19.47	0.95	0.23	19.49
65+	0.14	0.02	12.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.12	0.02	14.29
Total	1.80	0.22	10.89	1.52	0.13	7.88	0.25	0.24	48.98	1.52	0.25	14.12	1.67	0.21	11.17

smaller proportion than was found in the general population.

4. Discussion

Our previous report on the occurrence of DSM-IV alcohol dependence with and without abuse in the U.S. general population indicated that dependence occurred without abuse in a substantial proportion of alcohol dependence cases, with important variability between race/ethnic population subgroups. Because drug use disorders differ in many respects from alcohol use disorders, it was important to examine this issue for drugs as well. The large, nationally representative NE-SARC sample and completeness of the measures made it possible to address the question for the first time. Results clearly demonstrate that a considerable proportion of individuals with current DSM-IV drug dependence do not have accompanying abuse symptoms. This phenomenon occurred more commonly in older drug dependent individuals, especially among females. When lifetime diagnoses were considered, we also found that some individuals with dependence did not meet criteria for lifetime abuse symptoms, although the proportion was somewhat smaller than for current cases. While there was little difference in prevalence of lifetime diagnoses of drug dependence without abuse by age in males, females did show a sharp age gradient for lifetime diagnoses: over twice as many lifetime diagnoses of dependence were unaccompanied by abuse among females aged 45-64 as among females aged 18–29.

The study findings are consistent with the bi-axial conceptualization of substance use disorders that served as the basis for the DSM-IV distinction between dependence and abuse symptoms. This conception placed dependence on one axis and related problems or consequences of substance use on another (Edwards, 1986). As was shown previously for alcohol (Hasin and Grant, 2004), the findings support the idea that conditions on these two axes co-occur in some but not all cases of drug dependence, information that is lost with DSM-IV because it does not indicate abuse when dependence is present.

The results for drug dependence and abuse showed some similarities to the previously reported results for alcohol dependence and abuse (Hasin and Grant, 2004) but differed in important ways as well. For both alcohol and drugs, more females than males had diagnoses of dependence without abuse. In addition, the proportion of dependence cases without abuse was greater for current than for lifetime diagnoses.

In terms of differences from previous results for alcohol dependence, the occurrence of drug dependence without abuse was somewhat less common. Also, results were quite similar for whites and minorities in the present drug results, while an ethnic contrast had been striking in the previous report on alcohol. Whether this finding generalizes to other minority groups with prevalences too low to be examined here (e.g. Native Americans) requires further research. An-

other important difference between the above findings and the previous findings on alcohol was the age gradient found for current diagnoses for males and for both current and lifetime diagnoses for females. This gradient was not found at all in the alcohol results. Yet another discrepancy between the results for alcohol and for drugs was the lack of a sharp difference in the occurrence of drug dependence without abuse between treated and total samples, while a strong difference between the treated and total samples was found previously for alcohol dependence.

Several factors could give rise to the contrasting results for drug and alcohol dependence. One factor is that the specific abuse symptoms (hazardous use, irresponsibility in main social roles, legal problems related to substance use etc.) giving rise to the diagnoses of alcohol or drug abuse may differ, a possibility that should be investigated. Another is the fact that for NESARC respondents aged 21 and over, use of alcohol was legal, while drug use at any age is not. Since abuse symptoms all have an element of irresponsibility or unlawful behavior (e.g. driving while intoxicated or high), these might be expected to accompany dependence on an illegal substance more commonly than dependence on a legal one.

Different biopsychosocial processes may give rise to the symptoms of drug dependence and drug abuse. For example, genes affecting reward, craving, or withdrawal (characterizing dependence) may differ from genes affecting noveltyseeking or behavioral undercontrol (characterizing abuse). Since a subset of drug dependence cases did not have accompanying abuse, this type of heterogeneity should be explored. Furthermore, the heterogeneity was not evenly distributed across major subgroups of the population. Rather, dependence without abuse was more likely among females than males, and among older individuals, especially older females. If this had occurred only for current drug dependence, it could have been straightforward to explain the phenomenon as indicating a late stage of dependence, with abuse symptoms of an early phase no longer present. However, the similarity in findings on an age gradient for lifetime as well as current dependence among females is inconsistent with this explanation, and is more consistent with an explanation that includes an age cohort-related environmental effect, or gene-environment interaction. This also warrants further investigation.

Because a sizable proportion of drug dependence cases do not also have symptoms of abuse, the use of DSM-IV drug abuse as a screening method will result in missed cases and an underestimation of the prevalence of DSM-IV drug dependence. Because the underestimation will vary by gender and by age, inferences about the relationship of drug dependence to important characteristics such as comorbidity (e.g. major depression, which is more common among females) are likely to be altered. These issues are also likely to affect time trend studies, especially when time trends in prevalence, age at onset or longitudinal course differ by gender or age. Statistical modeling cannot adjust for the loss of information due to this method of screening in epidemiologic studies.

Future general population studies that involve assessment of drug use disorders should pretest and validate screening techniques in appropriate samples before applying the techniques in full-scale surveys.

A widely-used screening instrument for mental disorder in primary care (Spitzer et al., 1995) and its variants (Spitzer et al., 1999) uses the DSM-IV alcohol abuse criteria as a method to screen for DSM-IV alcohol dependence. While drug disorders were not included in the original version of this screening instrument, many published versions as well as unpublished versions currently being used to collect data have adopted a parallel format to screen for drug dependence via drug abuse questions. Our results indicate that relying on current DSM-IV drug abuse symptoms to screen for current drug dependence will result in undetected cases, especially among older females. For this purpose, a screening method that works more effectively across age and gender groups should be developed. There is also a need to develop efficient screening methods for specific drugs, an issue that cannot be addressed in population surveys like the NESARC, due to the low prevalence of dependence on specific drugs in the general population.

Finally, as noted above, many types of study designs have been utilized to understand the relationship of alcohol abuse to dependence symptoms. Far fewer such studies have been done with drug use disorders. With the development of large data sets such as the NESARC that will eventually incorporate a longitudinal as well as cross-sectional component, these relationships can further be investigated for drug dependence and abuse. A better understanding of the epidemiologic relationships of drug abuse to dependence should suggest improved phenotypes to use in investigations of both genetic and environmental vulnerability factors for drug use disorders.

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