

Evaluating Dependence Criteria for Caffeine

Catherine L.W. Striley,¹ Roland R. Griffiths,² and Linda B. Cottler¹

Background: Although caffeine is the most widely used mood-altering drug in the world, few studies have operationalized and characterized Diagnostic and Statistical Manual IV (DSM-IV) substance dependence criteria applied to caffeine. **Methods:** As a part of a nosological study of substance use disorders funded by the National Institute on Drug Abuse, we assessed caffeine use and dependence symptoms among high school and college students, drug treatment patients, and pain clinic patients who reported caffeine use in the last 7 days and also reported use of alcohol, nicotine, or illicit drugs within the past year ($n=167$). **Results:** Thirty-five percent met the criteria for dependence when all seven of the adopted DSM dependence criteria were used. Rates of endorsement of several of the most applicable diagnostic criteria were as follows: 26% withdrawal, 23% desire to cut down or control use, and 44% continued use despite harm. In addition, 34% endorsed craving, 26% said they needed caffeine to function, and 10% indicated that they talked to a physician or counselor about problems experienced with caffeine. There was a trend towards increased caffeine dependence among those dependent on nicotine or alcohol. Within a subgroup that had used caffeine, alcohol, and nicotine in the past year, 28% fulfilled criteria for caffeine dependence compared to 50% for alcohol and 80% for nicotine. **Conclusion:** The present study adds to a growing literature suggesting the reliability, validity, and clinical utility of the caffeine dependence diagnosis. Recognition of caffeine dependence in the DSM-V may be clinically useful.

Introduction

CAFFEINE IS THE MOST WIDELY USED drug in the world. In the United States, it is estimated that 80% to 90% of children and adults consume caffeine regularly, with a mean daily consumption of 280 mg in male consumers 35 to 54 years of age.¹ Although moderate intake has sometimes been considered to be safe or even beneficial, caffeine use has been implicated in several medical concerns including hypertension, cardiac problems, pregnancy risk, anxiety disorders, and insomnia²⁻⁵

It is difficult to accurately assess caffeine consumption because the number of servings or doses per day varies widely by individual, and because the amount of caffeine in each serving differs greatly across caffeine-containing products (e.g., 107–420 mg/12 oz. cup of brewed coffee; 50–505 mg/can of energy drink; 50–300 mg/dose of dietary supplement).¹ Caffeine is a mild stimulant drug with pharmacological actions mediated primarily through a blockade of endogenous adenosine. Caffeine is thought to produce stimulant motor effects and reinforcing effects by releasing the presynaptic and postsynaptic inhibition that adenosine exerts on striatal dopaminergic neurotransmission.⁶ At usual dietary doses caffeine produces a range of positive subjective effects including increased well-being, happiness, energy, and

sociality.⁷ Such effects are most likely to be observed in response to the first caffeine dose of the day in daily caffeine users who abstain from consumption overnight⁷ and are likely due to reversal of overnight withdrawal effects.⁸

Caffeine withdrawal has also been documented in laboratory animals and humans.³ In humans, the withdrawal syndrome is comprised of headache, fatigue, dysphoric mood, difficulty concentrating, and flu-like somatic symptoms.⁹⁻¹¹ In experimental studies the incidence of headache was 50% and clinically significant distress or impairment of daily functioning was 13%.¹¹ Severity of symptoms has been found to increase as the daily dose of caffeine increases. Abstinence from doses as low as 100 mg/d has been found to produce symptoms.¹¹ In survey studies in the general population the prevalence of withdrawal based on Diagnostic and Statistical Manual IV Text Revision (DSM-IV-TR) research criteria was 24%.^{12,13}

The reinforcing effects of caffeine (e.g., the ability to maintain self-administration, place preference, or choice behavior) have been shown in studies in laboratory animals and humans.⁷ Studies in humans also show that caffeine can produce conditioned flavor preferences, an effect likely to play a role in the development of strong consumer preferences for specific types or brands of caffeine-containing beverages.¹

¹Department of Epidemiology, College of Public Health and Health Professions, College of Medicine, University of Florida, Gainesville, Florida.

²Department of Psychiatry and Behavioral Sciences, Department of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, Maryland.

Human studies show that alleviation of withdrawal symptoms increases both caffeine reinforcement and conditioned taste preference.^{10,14,15}

Tolerance refers to an acquired decrease in responsiveness to a drug as the result of drug exposure. Caffeine tolerance has been shown in laboratory animals and humans.^{7,16,17} In humans, tolerance to subjective effects has been shown at high caffeine doses (400–1200 mg/d).^{16,18} At lower doses, tolerance does not occur.⁷ Kendler and Prescott¹³ found that 15% to 16% of caffeine users self-reported symptoms sufficient to fulfill DSM-IV-TR criteria for tolerance.

Although withdrawal and tolerance have been shown, there is debate about whether or not caffeine can produce a clinical syndrome of substance dependence.^{19–21} The two most widely used psychiatric diagnostic systems, International Classification of Diseases (ICD) and DSM, differ in regard to recognizing a caffeine dependence syndrome. DSM-IV-TR states, "A diagnosis of Substance Dependence can be applied to every class of substances except caffeine."²² In contrast, a diagnosis of substance dependence applied to caffeine is recognized by ICD-10.^{23,24}

Even though the caffeine dependence diagnosis does not exist in the DSM, several studies have documented DSM caffeine dependence using the generic dependence criteria.^{25–27} Strain and colleagues²⁵ reported a compelling case series evaluation on 16 individuals who met criteria for caffeine dependence using the Structured Clinical Interview for DSM-III-R.²⁸ Subjects met 3.4 of 4 criteria for caffeine dependence that were evaluated: 75% met tolerance, 94% met withdrawal, 81% reported having a persistent desire or unsuccessful efforts to cut down or control caffeine use, and 94% reported continued caffeine use despite knowledge of a persistent or recurrent physical or psychological problem likely to have been caused or exacerbated by caffeine use. Those who met criteria for caffeine dependence had high rates (63%) of past substance use disorders, with 57% reporting past alcohol abuse or dependence.²⁵

Survey studies also show that DSM-IV criteria for substance dependence could be applied to caffeine users. In structured telephone interviews with current caffeine users in Vermont, Hughes and colleagues¹² found that 30% were dependent on caffeine by using DSM-IV criteria adopted for caffeine. Although the sample size was quite small, Svikis *et al.*²⁹ reported that 57% of 44 women seeking prenatal care from a private obstetrician fulfilled DSM-IV criteria for dependence on caffeine sometime during their lifetime.

The case reports and survey studies point to a further need for assessing caffeine dependence. For decades, our team has been involved in the operationalization and assessment of dependence criteria. As part of a recent study, we developed questions to assess dependence on caffeine in order to assess the feasibility and the appropriateness of this category for the DSM. The data using this assessment were collected among a diverse sample (students, drug treatment patients, and pain clinic patients) to provide the opportunity to characterize the prevalence of adopted criteria for caffeine dependence. The pattern of endorsement of DSM-IV criteria applied to caffeine among the sample in St. Louis was compared with rates of endorsing DSM-IV criteria for alcohol and nicotine among the subsample who endorsed using all three drugs. Criteria were also compared with those reported by Hughes *et al.*¹² in a random-digit dialing sample in Vermont.

Methods

Samples

A nosological study of the classification of substance use disorders funded by National Institute on Drug Abuse was conducted from 1997 to 2001 (Cottler, L.B., PI). Questions were added to assess adopted diagnostic criteria for caffeine dependence and ecstasy and prescription pill misuse. One of the present authors (LBC) was a member of the DSM-IV Workgroup for Substance Abuse and Dependence, which was just beginning to discuss these substances in more detail. The sample was recruited via flyers in an adolescent inpatient substance abuse treatment facility and in a major teaching hospital pain clinic and through recruiting at local high schools and universities. These populations were selected for their expected high rates of drug use and drug abuse/dependence. Participants were required to have a recent history of alcohol or illicit drug misuse. Informed consent was obtained from adult participants and parents, and assent was obtained from adolescents. Interviews were conducted in private by trained interviewers in convenient, private locations. Respondents in treatment received \$15, and those from the community received \$30 for the time and effort involved. All protocols were reviewed and approved by the Washington University Human Research Protection Office. A Certificate of Confidentiality provided additional protection.

Assessments

All respondents were assessed with the Composite International Diagnostic Interview-Substance Abuse Module (SAM, DSM-IV version),³⁰ including adopted generic criteria for substance dependence applied to caffeine. To our knowledge, the SAM³⁰ is the only widely available structured interview that assesses caffeine dependence.^{31,32} Caffeine dependence was operationalized in the SAM according to criteria for substance dependence using DSM-IV criteria. The diagnostic algorithms used by the SAM to create DSM-IV categories for dependence on caffeine, nicotine, alcohol, and other abused substances were developed by the Washington University team and checked by members of the DSM-IV Field Trials as the analyses got underway. The data gathered in St. Louis by the Washington University group are referred to as St. Louis data hereafter. The St. Louis data were compared with data collected by Hughes and colleagues,¹² who assessed for caffeine dependence in coffee, tea, and soda consumers in a sample of 162 residents of Chittenden County, Vermont, by using an instrument created for their study. In that study, one household member over 18 years of age was recruited by random-digit dialing. Throughout the remainder of this paper, data from the Hughes *et al.*¹² study are referred to as the Vermont data.

Data analysis

SAS version 9.2 was used for analyses of data from the St. Louis sample. Bivariate analysis was conducted using PROC FREQ to calculate the rates of fulfilling substance dependence criteria and nondiagnostic symptoms for caffeine use in this sample. Chi-square analysis was used to analyze differences in criteria and symptom rates between the St. Louis and Vermont data. The data collected in the St. Louis sample permitted comparison of the rates of fulfilling

substance dependence criteria between caffeine, alcohol, and nicotine among the subsample of 148 people who had used all three substances in the last 12 months. We also compared the rates of dependency for those who endorsed caffeine dependence and used another substance using chi-square analysis.

Results

One hundred sixty-seven people in the St. Louis sample had a recent history of alcohol, nicotine, or illicit drug misuse and reported caffeine use in the last 7 days; these individuals comprised the sample. They ranged in age from 13 to 82 years (with a mean age of 28.7 years [SD=15.8]; 54% were female, and 12% were currently married). Seventy-four percent identified themselves as white or Caucasian; 13% as African American; 4% as Asian American; and the remaining 9% as Hispanic, Native American, biracial, Middle Eastern, or other (see Table 1). As shown in Table 1, the St. Louis sample tended to be younger, more racially diverse, and more likely to be unemployed than the Vermont sample study.¹² The St. Louis sample was generally in excellent to fair health. They were recruited from groups expected to have high rates of drug use; the drugs most likely to be reported included alcohol, nicotine, and cannabis.

Past weekly caffeine users were asked "In the past 7 days, on average, how many drinks containing caffeine have you had in one 24-hour period?" Responses ranged from 1 (37%) to 30 drinks (1%), with a mean of 2.9 drinks (SD=3.4).

Table 2 presents the proportion of users who met each of the seven DSM-IV criteria for a diagnosis of substance dependence applied to caffeine for the St. Louis sample. (For comparison, data from Vermont study¹² are provided in the far right column of Table 2). In the St. Louis sample, the criteria most likely to be reported were "continued use despite knowledge of physical or psychological problems caused or exacerbated by caffeine use" (44%) and "taking in larger amounts or for longer time than intended" (40%), while in the Vermont sample, the most commonly endorsed criteria were "persistent desire or unsuccessful efforts to cut down caffeine" (56%) and "larger amounts or longer time than intended time" (50%). In both samples, giving up important activities to use caffeine was rarely reported (1% or less).

Table 2 also shows that the rates of caffeine dependence (endorsing three or more of the seven dependence criteria) were similar (35% St. Louis versus 30% Vermont). When the three most applicable criteria were considered (i.e., withdrawal, a persistent desire or unsuccessful efforts to cut down or control substance use, and continued use despite knowledge of having a persistent or recurrent physical or psychological problem likely to have been caused or exacerbated by the substance), 20% of the St. Louis sample continued to meet diagnostic criteria.

Several nondiagnostic questions about caffeine use were added to the SAM, including questions about caffeine craving, needing caffeine to function, and talking to a doctor about use or problems from caffeine. As shown in Table 3, 34% said they craved caffeinated beverages, 26% said they needed caffeine to function, and 10% indicated that they talked to a physician or counselor about problems experienced with caffeine.

Next we considered caffeine dependence among those who were dependent or not dependent on other drugs—nicotine, al-

TABLE 1. DEMOGRAPHICS OF ST. LOUIS STUDY SAMPLE AND, FOR COMPARISON, THE VERMONT STUDY SAMPLE

	St. Louis sample (n=167)	Vermont sample (n=162) ^a
Female	54%	62%
Education		
> High school graduate	42%	65 ^b
Age (mean, SD)	28.6 (15.8)	38.4
13–17	16%	
18–21	41%	
22–64	39%	
65–82	4%	
Race/ethnicity		
White	74%	94%
African American	13%	
Other	13%	
No full-time work past year	57%	25% ^c
General health		Not reported
Excellent	19%	
Good	40%	
Fair	25%	
Poor	26%	
Drug use in last year		Not reported
Alcohol	85%	
Nicotine (cigarettes)	72%	
Cannabis	62%	
Amphetamines	25%	
Cocaine	23%	

^aData from Hughes *et al.*¹²

^bSome college.

^cNot employed.

cohol, marijuana, cocaine, and amphetamines—among those who had used that specific drug in the past 12 months. As shown in Table 4, although there were no statistical differences in caffeine dependence among those who did or did not meet criteria for other drugs, there was a trend ($p < 0.10$) for nicotine and for alcohol users, with greater caffeine dependence in those who were dependent on nicotine or alcohol compared with those who were not dependent on nicotine or alcohol.

Lastly, we considered the subsample of 148 persons who had exposure to caffeine, alcohol, and nicotine in the last 12 months. As shown in the right-most set of columns in Fig. 1, 28% were dependent on caffeine, half were alcohol dependent (50%), and 80% were nicotine dependent. The proportion of persons who met each the individual criteria was generally similar to that for dependence on the drug, with the highest rates for nicotine, and the lowest for caffeine. Two criteria, withdrawal symptoms and using despite harm, were somewhat higher for caffeine than for alcohol.

Discussion

This study characterized caffeine dependence according to DSM-IV. The study extends the telephone survey of caffeine dependence in the general population in Vermont by Hughes *et al.*¹² to a more heterogeneous sample that was recruited from groups that were expected to have high rates of drug use. The present study conducted face to face interviews and asked more questions, including questions about comorbid drug use. In our sample of 167 past weekly caffeine users, 35% met criteria for dependence when all seven of the adopted DSM dependence criteria were used. More conservatively,

TABLE 2. PAST YEAR RATES OF ENDORSEMENT OF CRITERIA FOR SUBSTANCE DEPENDENCE APPLIED TO CAFFEINE FOR THE ST. LOUIS STUDY SAMPLE AND, FOR COMPARISON, A VERMONT STUDY SAMPLE^a

<i>Adopted DSM-IV substance dependence criteria for caffeine</i>	<i>St. Louis data (n = 167)</i>	<i>Vermont data (n = 162)^b</i>
1. Tolerance	13% (14, 26)	8% (5, 14)
Need to drink more caffeine to get same effect	17% (12, 23)	17%
2. Withdrawal	26% (32, 47)	18% (14, 27)
Used a caffeinated product to avoid withdrawal symptoms ^c	24% (18, 31)	17%
After 12 or 24 hours without caffeine, ^d felt tired or drowsy ^c	27% (20, 34)	20%/47% ^e
After 12 or 24 hours without caffeine, ^d felt anxious or depressed ^c	13% (20, 33)	7%/18% ^{e, f}
After 12 or 24 hours without caffeine, ^d had trouble concentrating ^c	13% (8, 18)	4%/35% ^e
3. Caffeine often taken in larger amounts or for longer time than intended	17% (18, 31)	28% (21, 35)
4. Persistent desire or unsuccessful efforts to cut down or control caffeine use	23% (54, 68)	56% (48, 63)
Tried to cut down on or quit caffeinated beverages	21% (15, 28)	42% ^g
5. Great deal of time is spent in activities necessary to obtain caffeine or recover from effects	40% (37, 52)	50% (42, 58)
Made a special trip/planned ahead so wouldn't run out	40% (37, 52)	28%
6. Important social, occupational, or recreational activities are given up or reduced because of caffeine use	1% (0, 3)	<1% (0, 4)
7. Continued use of caffeine despite knowledge of physical or psychological problems caused or exacerbated	44% (46, 61)	14% (9, 21%)
Continued to drink caffeinated beverages after knew medical problem could be made worse by caffeine ^c	11% (6, 16)	Not given
Fast or irregular heartbeat or chest pain ^c	11% (6, 16)	17% racing 9% irregular
Stomach problems ^c	16% (10, 21)	18%
Trouble falling or staying asleep ^c	36% (29, 43)	39%
Feeling very anxious due to caffeine use ^c	19% (13, 25)	30%
Feeling irritable or angry due to caffeine use ^c	10% (5, 14)	Not given
Caffeine dependence diagnosis		
3 or more of the 7 substance dependence criteria	35% (28, 42)	30%
3 or more of 6 criteria (excluding criterion 6)	35% (28, 42)	Not given
3 or more of 4 criteria (excluding criteria 3, 5, and 6)	25% (19, 32)	9%
3 of 3 criteria (excluding criteria 1, 3, 5, and 6)	20% (14, 26)	Not given

^aData in columns show the prevalence of endorsement of criteria or symptom expressed as a percentage of the study sample; numbers in parentheses show 95% confidence intervals; absence of a confidence interval indicates that it was not provided in the Hughes *et al.* (1998) paper.

^bData from Hughes *et al.*¹²

^cQuestions asked for lifetime use only in St. Louis data.

^d12 hours without caffeine for St. Louis data; 24 hours for Hughes *et al.* (1998) data.

^eTwo values are reported: the first value is those who tried to stop temporarily and the second value is those who tried to stop permanently

^fAnxiety only.

^g42% tried to cut down, 11% to quit.

TABLE 3. PAST YEAR RATES OF ENDORSEMENT OF NONDIAGNOSTIC SYMPTOMS FROM CAFFEINE USE FOR THE ST. LOUIS STUDY SAMPLE AND, FOR COMPARISON, A VERMONT STUDY SAMPLE^a

<i>Nondiagnostic symptoms</i>	<i>St. Louis data (n = 167)</i>	<i>Vermont data (n = 162)^b</i>
Intoxication or withdrawal symptoms interfered with functioning ^c	13% (8,18)	15% (10,22)
Use produced hazard	Not asked	<1% (0, 4)
Unchangeable pattern of use	Not asked	15% (10, 22)
Craved or had strong desire for caffeinated beverages	34% (26, 40)	19% (13, 26)
Needed caffeine to help function ^d	26% (25, 39)	33% (26, 40)
Physician consultation ^e	10% (0.06, 15)	13%

^aData in columns show the prevalence of endorsement of symptom expressed as a percentage of the study sample; numbers in parentheses show 95% confidence intervals.

^bData from Hughes *et al.*¹²

^cFor the St. Louis sample this was defined as withdrawal causing severe anxiety, depression, or inability to concentrate.

^dFor the St. Louis sample this question was: "Has there ever been a period in your life when you felt you needed caffeinated beverages to help you function that is, you felt you could not do your work well unless you had had a caffeinated beverage".

^eFor the St. Louis sample, this question was "Have you *ever* talked to a doctor or health professional about any problems from your use of caffeinated beverages?" while in the Hughes *et al.*¹² study users reported if a physician or counselor advised them to stop or reduce caffeinated beverages in the *last year*. Confidence interval was not provided.

TABLE 4. CAFFEINE DEPENDENCE AMONG PERSONS WITH AND WITHOUT OTHER DRUG DEPENDENCE (n = 167)^{a,b}

Drug	Nicotine** (n = 120)		Alcohol** (n = 142)		Marijuana (n = 103)		Cocaine (n = 38)		Amphetamines (n = 42)	
	Did not meet dependence criteria (n = 27)	Met dependence criteria (n = 93)	Did not meet dependence criteria (n = 76)	Met dependence criteria (n = 66)	Did not meet dependence criteria (n = 57)	Met dependence criteria (n = 46)	Did not meet dependence criteria (n = 27)	Met dependence criteria (n = 11)	Did not meet dependence criteria (n = 30)	Met dependence criteria (n = 12)
% who met adopted criteria for caffeine dependence	19	37	28	42	30	41	26	18	23	33

^aThe top row indicates the number of persons reporting past year use of the indicated drug; the second row shows the number persons who were or were not dependent

^bIn second and third rows, dependence is based on all seven DSM-IV-TR dependence criteria

**p < 0.10 (chi-square from 2x2 table with drug dependence and no drug dependence vs. caffeine dependence and no caffeine dependence).

when only three DSM criteria were used that are most unambiguously relevant to commonly held ideas about of “addiction” (persistent desire or unsuccessful efforts to cut down or control substance use; substance use is continued despite having a persistent or recurrent physical or psychological problem likely to have been caused or exacerbated by the substance; withdrawal or use to avoid withdrawal), 20% of the sample continued to fulfill criteria for dependence. Overall, these data clearly document that caffeine dependence exists among community-sampled caffeine users.

It is interesting to note that although the prevalence of fulfilling the caffeine diagnosis was similar in our drug-using population (35%) and in the general population study⁷ (30%), a larger proportion of the drug-using sample reported craving for caffeinated beverages (34% vs. 19%), tolerance (13% vs. 8%), withdrawal (26% vs. 18%), and continued use of caffeine despite knowledge of a physical or psychological problem (44% vs. 14%). These data suggest that the drug-using sample may be more vulnerable than the general population to these aspects of caffeine dependence. Given this, it is noteworthy that the drug using sample has a lower proportion fulfilling the criteria of having a persistent desire or unsuccessful efforts to cut down or control caffeine use (23% vs. 56%). Thus, even though individuals with histories of drug or alcohol abuse or dependence have more symptoms of dependence than the general population, they are less motivated to quit caffeine. It is possible that this reflects general difference in dispositional tendencies between these two groups. Drug users may have more vulnerability to develop drug dependence to a wide variety of drugs, while concurrently being less motivated to cut back or quit substance use.

Caffeine use can produce a number of unpleasant symptoms such as anxiety and insomnia and has been implicated in various adverse health effects including hypertension, myocardial infarction, urinary incontinence, spontaneous abortion, reduced fetal growth, and possibly gastroesophageal reflux.⁵ In the present study 10% of the sample had talked to a doctor or health professional about problems from their use of caffeinated beverages. Sleep disturbance, anxiety, stomach problems, and cardiac symptoms were reported by 36%, 19%, 16%, and 10% of the sample, respectively. These rates of receiving medical consultation and experiencing symptoms are roughly similar to those reported by Hughes *et al.*¹² in their general population sample.

As expected based on the populations from which subjects were recruited, our study sample had high rates of use of alcohol and other drugs. The majority of caffeine users in our study sample had past year use of alcohol (85%), nicotine (72%), and/or marijuana (62%). There was a trend towards increased caffeine dependence among those dependent on nicotine or alcohol (Table 4). This is consistent with several lines of evidence suggesting a relationship between caffeine use or dependence and dependence on other drugs. Twin studies suggested a common genetic factor underlies the use of caffeine, alcohol and nicotine,^{33,34} although other recent twin studies found that caffeine and nicotine use and dependence were substantially influenced by genetic factors unique to these drugs.^{35,36} Also, in a study of pregnant caffeine-using women,²⁹ those who had a caffeine dependence diagnosis were almost nine times more likely to report a history of daily cigarette smoking, compared with women without the diagnosis. Furthermore, women with both

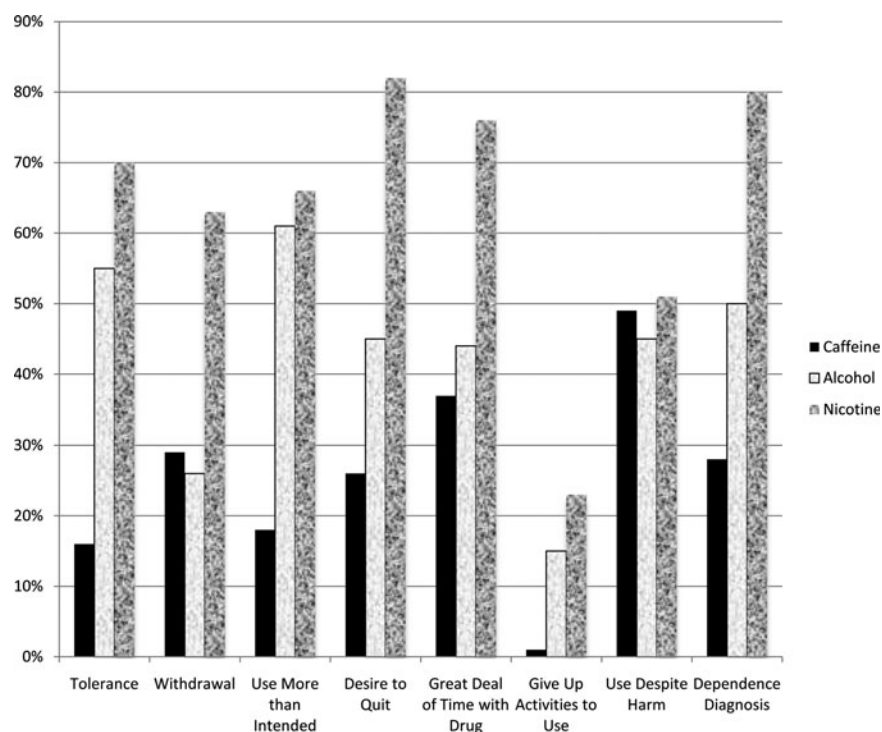


FIG. 1. Among those who used caffeine, alcohol, and tobacco in the last 12 months ($n = 148$), the percentage that fulfilled each of the seven individual criteria for caffeine, alcohol, and tobacco dependence criteria (DSM-IV-TR) and fulfilled full criteria for dependence diagnosis (i.e., rightmost columns; those who fulfilled three or more of the individual criteria).

caffeine dependence and a family history of alcoholism were six times more likely to have a lifetime diagnosis of alcohol abuse or dependence.

The present study supplements a growing number of small-scale survey and case series studies^{12,25–27,29} documenting that caffeine can produce a caffeine dependence syndrome. Although large-scale epidemiology studies have not been conducted, various observations suggest the reliability, validity, and utility of the diagnosis. Hughes and Howard³⁷ found high test-retest reliability for caffeine dependence. In a prospective study of caffeine quitting during pregnancy, Svikis *et al.*²⁹ reported that women with caffeine dependence consumed significantly more caffeine than those without the diagnosis both before and throughout pregnancy. Liguori *et al.*³⁸ showed that individuals who fulfilled criteria for caffeine dependence tended to be more likely to demonstrate reliable reinforcement (75%) than those who did not (20%). With regard to the utility of the diagnosis, recognition of a caffeine dependence diagnosis would call clinician's attention to a disorder that may be causing patients significant distress,^{20,24} and that patients may not be compliant with medical instructions to cut back or quit for medical conditions such as pregnancy²⁵ or for medical procedures. In addition, since caffeine dependence is associated with dependence on other drugs, the caffeine dependence diagnosis might be a useful clinical and research tool to identify a general vulnerability to substance dependence.

Overall, the present study, which examined caffeine use within a population with high rates of other drug use, provides additional data supporting the applicability of a dependence diagnosis for caffeine. A growing literature now suggests that the diagnosis is biologically plausible, reliable, and valid and has clinical utility. We propose that Caffeine

Dependence be included in the DSM Fifth Edition. Recognition of the diagnosis can also be expected to spur large-scale epidemiological research as well as additional studies on clinical relevance, comorbidity, and associated impairment across representative samples of treatment and clinical settings.

Acknowledgments

Support for the study "Reliability and Validity of DSM and ICD Substance Use Disorders" and Linda Cottler's involvement was provided by R01 DA05585 from the National Institute on Drug Abuse, (Cottler, L.B., PI) and from grant R01 DA 02791. Support for Catherine Striley's involvement was provided in part by grant R01 DA 02791 from the National Institute on Drug Abuse. Support for Roland Griffiths' involvement was provided in part by grant R01 DA03889 from the National Institute on Drug Abuse. All authors contributed in a significant way to the manuscript and have read and approved the final manuscript. We gratefully acknowledge the participants in the Nosology study.

Author Disclosure Statement

No competing financial interests exist.

References

1. Juliano LM, Ferré S, Griffiths RR. Caffeine: pharmacology and clinical effects. In: Principles of Addiction Medicine. R.K. Ries, D.A. Fiellin, S.C. Miller, R. Saitz (Eds). Philadelphia, PA: Lippincott Williams & Wilkins; 2009:159–178.
2. James JE. Caffeine and Health. San Diego, CA: Academic Press, Inc., 1991

3. Higdon JV, Frei B. Coffee and health: a review of recent human research. *Crit Rev Food Sci Nutr.* 2006;46:101–123.
4. Nawrot P, Jordan S, Eastwood J, *et al.* Effects of caffeine on human health. *Food Addit Contam.* 2003;20:1–30.
5. Juliano LM, Anderson BL, Griffiths RR. Caffeine. In: Lowinson & Ruiz's Substance Abuse: A Comprehensive Textbook, Fifth Edition. P. Ruiz, E. Strain (Eds.) Philadelphia: Lippincott Williams & Wilkins; 2011:335–353.
6. Ferré S. An update on the mechanisms of the psychostimulant effects of caffeine. *J Neurochem.* 2008;105:1067–1079.
7. Griffiths RR, Juliano LM, Chausmer AL. Caffeine pharmacology and clinical effects. In: Principles of Addiction Medicine. A.W. Graham, T.K. Schultz, M.F. Mayo-Smith, R.K. Reis (Eds.) Chevy Chase, MD: American Society of Addiction Medicine; 2003:193–224.
8. James JE, Rogers PJ. Effects of caffeine on performance and mood: withdrawal reversal is the most plausible explanation. *Psychopharmacology (Berl).* 2005;182:1–8.
9. Silverman K, Evans SM, Strain EC, Griffiths RR. Withdrawal syndrome after the double-blind cessation of caffeine consumption. *N Engl J Med.* 1992;327:1109–1114.
10. Hughes JR, Oliveto AH, Bickel WK, Higgins ST, Badger GJ. Caffeine self-administration and withdrawal: incidence, individual differences and interrelationships. *Drug Alcohol Depend.* 1993;32:239–246.
11. Juliano LM, Griffiths RR. A critical review of caffeine withdrawal: empirical validation of symptoms and signs, incidence, severity, and associated features. *Psychopharmacology (Berl).* 2004;176:1–29.
12. Hughes JR, Oliveto AH, Liguori A, Carpenter J, Howard T. Endorsement of DSM-IV dependence criteria among caffeine users. *Drug Alcohol Depend.* 1998;52:99–107.
13. Kendler KS, Prescott CA. Caffeine intake, tolerance, and withdrawal in women: a population-based twin study. *Am J Psychiatry.* 1999;156:223–228.
14. Garrett BE, Griffiths RR. Physical dependence increases the relative reinforcing effects of caffeine versus placebo. *Psychopharmacology.* 1998;139:195–202.
15. Tinley EM, Yeomans MR, Durlach PJ. Caffeine reinforces flavour preference in caffeine-dependent, but not long-term withdrawn, caffeine consumers. *Psychopharmacology (Berl).* 2003;166:416–423.
16. Evans SM, Griffiths RR. Caffeine tolerance and choice in humans. *Psychopharmacology.* 1992;108:51–59.H
17. Holtzman SG. Complete, reversible, drug-specific tolerance to stimulation of locomotor activity by caffeine. *Life Sci.* 1983;33:779–787.
18. Sigmon SC, Herning RI, Better W, Cadet JL, Griffiths RR. Caffeine withdrawal, acute effects, tolerance, and absence of net beneficial effects of chronic administration: cerebral blood flow velocity, quantitative EEG, and subjective effects. *Psychopharmacology.* 2009; 204:573–585.
19. Hughes JR, Oliveto AH, Helzer JE, Higgins ST, Bickel WK. Should caffeine abuse, dependence, or withdrawal be added to DSM-IV and ICD-10? *Am J Psychiatry.* 1992;149:33–40.
20. Satel S. Is caffeine addictive?—A review of the literature. *Am J Drug Alcohol Abuse.* 2006;32:493–502.
21. Ogawa N, Ueki H. Clinical importance of caffeine dependence and abuse. *Psychiatry Clin Neurosci.* 2007;61:263–268.
22. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Revised Fourth Edition. Washington DC: American Psychiatric Association; 2000.
23. World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva, Switzerland: World Health Organization; 1992.
24. World Health Organization. International statistical classification of diseases and related health problems, 10th revision. Geneva, Switzerland: World Health Organization; 1992.
25. Strain EC, Mumford GK, Silverman K, Griffiths RR. Caffeine dependence syndrome. Evidence from case histories and experimental evaluations. *JAMA.* 1994;272:1043–1048.
26. Oberstar JV, Bernstein GA, Thuras PD. Caffeine use and dependence in adolescents: one-year follow-up. *J Child Adolesc Psychopharmacol.* 2002;12:127–135.
27. Jones HA, Lejuez CW. Personality correlates of caffeine dependence: the role of sensation seeking, impulsivity, and risk taking. *Exp Clin Psychopharmacol.* 2005;13:259–266.
28. Spitzer RL, Williams JBW. Structured clinical interview for DSM-III-R. New York, NY: New York State Psychiatric Institute, Biometrics Research; 1985.
29. Svikis DS, Berger N, Haug NA, Griffiths RR. Caffeine dependence in combination with a family history of alcoholism as a predictor of continued use of caffeine during pregnancy. *Am J Psychiatry.* 2005;162:2344–2351.
30. Cottler LB, Robins LN, Helzer JE. The reliability of the CIDI-SAM: a comprehensive substance abuse interview. *Br J of Addict.* 1989;84:801–814.
31. Griffiths RR, Ressig CJ. Substance abuse: Caffeine use disorders. In: Psychiatry. A. Tasman, J. Kay, J. Lieberman, M.B. First, M. Maj. (Eds.) Chichester, UK: John Wiley & Sons; 2008:1019–1040.
32. Compton WM, Cottler LB, Dorsey KB, Spitznagel EL, Mager DE. Comparing assessments of DSM-IV substance dependence disorders using CIDI-SAM and SCAN. *Drug Alcohol Depend.* 1996;41:179–187.
33. Swan GE, Carmelli D, Cardon LR. Heavy consumption of cigarettes, alcohol and coffee in male twins. *J Stud Alcohol.* 1997;58:182–190.
34. Hettema JM, Corey LA, Kendler KS. A multivariate genetic analysis of the use of tobacco, alcohol, and caffeine in a population based sample of male and female twins. *Drug Alcohol Depend.* 1999;57:69–78.
35. Kendler KS, Myers J, Prescott CA. Specificity of genetic and environmental risk factors for symptoms of cannabis, cocaine, alcohol, caffeine, and nicotine dependence. *Arch Gen Psychiatry.* 2007;64:1313–1320.
36. Kendler KS, Schmitt E, Aggen SH, Prescott CA. Genetic and environmental influences on alcohol, caffeine, cannabis, and nicotine use from early adolescence to middle adulthood. *Arch Gen Psychiatry.* 2008;65:674–682.
37. Hughes JR, Howard TS. Nicotine and caffeine use as confounds in psychiatric studies. *Biol Psychiatry.* 1997;42:1184–1185.
38. Liguori A, Hughes JR, Grass JA. Absorption and subjective effects of caffeine from coffee, cola and capsules. *Pharmacol Biochem Behav.* 1997;58:721–726.

Address correspondence to:
Catherine L.W. Striley, PhD, MSW, MPE
Department of Epidemiology
College of Public Health and Health Professions
College of Medicine
University of Florida
101 S. Newell Drive
P.O. Box 100231
Gainesville, FL 32611-0231
E-mail: cstriley@ufl.edu