

*The American Journal of Drug and Alcohol Abuse*, 32:493-502, 2006

Informa Healthcare

ISSN: 0095-2990 print /1097-9891 online

DOI: 10.1080/00952990600918965

# Is Caffeine Addictive?—A Review of the Literature

Sally Satel, M.D.\*<sup>1</sup>

<sup>1</sup>Oasis Clinic, American Enterprise Institute.

\*Correspondence: Sally Satel, M.D., 1150 17th St. NW, Washington, DC, 20036; E-mail: slsatel@aol.com

## Abstract

The common-sense use of the term addiction is that regular consumption is irresistible and that it creates problems. Caffeine use does not fit this profile. Its intake does no harm to the individual or to society and its users are not compelled to consume it. Though cessation of regular use may result in symptoms such as headache and lethargy, these are easily and reliably reversed by ingestion of caffeine. Some have argued that continued caffeine use is an attempt to suppress low grade withdrawal symptoms such as sleepiness and lethargy. In some moderate users, this is possible; however, in experimental contexts, the phenomenon is too inconsistent to constitute a reliably valid syndrome.

---

## INTRODUCTION

In July 2005, the Center for Science in the Public Interest, a Washington-based consumer advocacy group, called for the Food and Drug Administration (FDA) to mandate warning labels on caffeinated soda. The group's main concern was not only the association between soda and childhood obesity; it also judged caffeine to be a potentially dangerous substance. The Center suggested that "[C]affeinated drinks should bear a notice that reads 'This drink contains x grams of caffeine, which is a mildly addictive stimulant drug. Not appropriate for children' [1].

Is caffeine addictive? Is it a harmful substance that compels the consumer to use at the risk of his wellbeing and despite a stated desire to refrain? Is it a "model drug of abuse" as the National Institute on Drug Abuse put it? [2]. The answer is no. This paper summarizes evidence justifying this conclusion.

## IMPAIRMENT AND REINFORCEMENT

How does caffeine use fit into the DSM-IVR drug abuse schema? [3]. A significant level of impairment is rarely a consequence of its consumption. Caffeine can be a factor in poor sleep, jitteriness, and arrhythmias in adults. Its effects on children, especially hyperactive ones, are not well known. However, in adults, too much caffeine produces sensations that are unpleasant (e.g., tremulousness, jitteriness) and may put a break on its consumption. Moreover, if caffeine were so intensely desirable, some individuals would likely self-administer caffeine supplements—available in 200 mg tablets—in doses exceeding the average caffeine intake of about 200–300 mg/day.

What about DSM IV-R dependence criteria? [4]. Caffeine consumers do not display an inability to control consumption. Coffee drinking is weakly reinforcing, but this is not the same as saying that caffeine, as a substance, is reinforcing. Nehlig states that "the conditions under which caffeine functions as a reinforcer still are not clearly understood" [5].

First, the possible reinforcing effects of coffee may not be the caffeine per se, but rather the pleasurable aroma and taste of coffee as well as the social environment that usually accompanies coffee consumption. Second, the desire to use repeatedly is most marked in heavy caffeine consumers (>1000 mg/day) who also had histories of alcohol or drug abuse. For moderate caffeine users (130–600 mg/day), caffeine reinforcement occurs in a smaller subset of consumers [6].

The author could find no reports of use that bear analogy to alcoholic-style drinking or chain smoking. Theoretically, an individual might be exquisitely sensitive to the effects of caffeine and be at risk for a more classical addiction, but if so, his sensitivity to caffeine would make the stimulating effects of the drug itself (e.g., jitteriness) too unpleasant to tolerate. Case reports of toxic levels involve deliberate or accidental overdoses of caffeine pills, not compulsive consumption of those pills or of coffee. In short, coffee drinking resembles more a dedicated habit than a compulsive addiction [7].

Animal studies permit analysis of the effects of caffeine on the brain. Nehlig has examined this question in depth and discovered that caffeine levels approximating human consumption do not activate brain reward circuits as do classic stimulants [8]. Amphetamines, cocaine, and nicotine stimulate the release of dopamine in the shell of the nucleus accumbens, the key structure in the brain for reward, motivation, and addiction. However, caffeine has no effect on the shell of the nucleus accumbens. Moreover, the experimental rats received caffeine intravenously, a route well known to

be more reinforcing than oral use.

An important question about the reinforcing properties of caffeine is whether ongoing use is a function of a drinker's enjoyment of caffeine-containing beverages—in which case, it is more like a loyal, pleasurable habit than a compulsion—or whether users consume it to avoid subtle withdrawal effects.

## CAFFEINE TOLERANCE AND WITHDRAWAL

People use caffeine in a regular pattern—every morning or after dinner—but there is little evidence that such behavior is of a compulsive nature. Rather, caffeine drinkers are often dedicated to their coffee—they seek its warmth, flavor, aroma, and, sometimes, mildly stimulating benefits. They do not feel intense distress if it is unavailable; though, some will drink it in order to suppress withdrawal symptoms.

*Tolerance.* Daily caffeine drinkers quickly develop tolerance to the jitteriness, anxiety, and edginess occasionally reported by first time users of the substance. Rather than becoming tolerant to caffeine's desirable effects (wakefulness, alertness), most drinkers become tolerant to the negative ones. Notably, with standard drugs of abuse it generally takes additional drugs to achieve the desired effect of a high or a feeling of tranquility.

*Withdrawal.* Also called discontinuation syndroms, withdrawal occurs upon abruptly stopping the use of a drug (including some prescribed medications). This phenomenon occurs because the user's central nervous system has adapted to regular exposure to the substance.

Such physical dependence is a product of “neuroadaptation”—that is, central nervous system neurons adapt to compensate for the continuous presence of a substance in the brain tissue. In the case of opiate addiction, when the level drops below a certain point, the neurons “rebound” and the user experiences physical symptoms such as chills, shakes, stomach cramps, or vomiting. After a period of regular use, a person might “crave” opiates simply to stop the sickness, and not because he desires the high. By contrast, the essence of addiction (psychological dependence) is a craving for the drug and its compulsive use.

Caffeine withdrawal includes headache, lethargy, irritability, and mental fuzzy-headedness. Some or all can occur among many daily caffeine consumers who abruptly stop their intake [9]. Sometimes doses as low as 100 mg/d can provoke these symptoms, though daily caffeine consumption among Americans is estimated at about 280 mg/d or the equivalent of 2–3 cups of coffee [10, 11]. Symptoms begin twelve to twenty-four hours after sudden cessation of continuous use, reach a peak at twenty to forty-eight hours, and resolve after ingesting caffeine [12, 13, 14].

Thus, physical dependence denotes the need for a substance to achieve physiological homeostasis; the classic signs of this phenomenon are tolerance and withdrawal. It differs from addiction (also called psychological dependence or just “dependence” in DSM IV) in that the latter entails compulsive engagement in a behavior with negative consequences.

*Studies on Withdrawal.* Researchers use two standard techniques to assess the nature and frequency of withdrawal. One is to ask daily caffeine consumers whether they have ever stopped use abruptly and the effects of cessation. However, the problem with retrospective surveys is that recall is often unreliable and difficult to validate.

The second kind of study entails observation of regular consumers of caffeine who are switched, without their knowledge or the awareness of the rater, to a caffeine-free diet during a study period. Such double-blinded, prospective clinical studies assess experience in real-time by objective observers.

*Survey Studies.* There are ten published random surveys of caffeine withdrawal, with four of them involving hospitalized patients. Of the remaining six, two specifically recruited subjects who identified themselves as experiencing caffeine-withdrawal while two others simply recruited coffee drinkers [15, 16]. In the first, Goldstein and Kaiser reported that 58 percent of the eighteen people in their survey who drank 5–10 cups of coffee per day felt “half awake” when they stopped and another 8 percent reported headaches after stopping [17]. Hughes and colleagues found that 11 percent of those who had given up or reduced caffeine use in the past year experienced headache plus one other symptom which together produced “significant distress or impairment in social, occupational, or other important areas of functioning” [18].

The remaining two of the six surveys were both random samples of over 1000 participants who were not surveyed specifically for their caffeine use. Dews and colleagues reported on 11,112 subjects who responded to an ad unrelated to caffeine consumption. Sixty-one percent (6,815) claimed to be daily caffeine consumers and of these, 11 percent reported that they experienced symptoms such as headaches, irritability, and sleepiness when they stopped using caffeine abruptly [19]. In the second survey, Kendler and Prescott reported on 1,642 women in a twin-registry study of genetic aspects of various conditions. Twenty-four percent claimed that in stopping or decreasing use, they developed a headache and at least one other symptom [20].

*Experimental studies.* In 2004, Juliano and Griffiths summarized forty-two double-blind trials [21]. In these trials, subjects typically underwent placebo replacement for caffeine for various periods of time. The researchers then compare

withdrawal symptoms in those who received a placebo versus those who continued to receive caffeine. The bulk of the studies showed that caffeine abstinence resulted in the placebo group reporting higher rates of lethargy, fuzziness, and headache.

Three studies made a special effort to recruit subjects who were naïve to the purpose of the study.

Hughes and colleagues recruited moderate to heavy coffee drinkers (about 5–7 cups/d) to participate in a study of the effects of different coffee strengths on mood, general performance, and preference for each beverage [22]. The study was administered over a four-day period. Twenty-two subjects with no history of substance abuse or mental illness participated. Subjects consumed either 4 cups of decaf coffee only on Day 1 or caffeinated coffee only on Day 2 or vice versa. On Days 3 and 4, subjects were allowed to choose between decaf and caffeinated coffees. There were six 4-day sessions total. Overall, subjects preferred caffeinated coffee on the days they could choose. On experimental days when they were given decaf, 41 percent reported drowsiness, fatigue, and headache, though baseline levels of these symptoms were not reported.

Silverman and coworkers recruited sixty-two adults through ads promoting a study of the effect of foods—including caffeine—on behavior and mood [23]. The participants' average daily intake of caffeine was 235 mg/d. No participants with a history of psychiatric disorder were enrolled. The subjects participated in 2 two-day study periods that were one week apart. During each two-day period, they received either their usual caffeine dose in pill form or placebo pills. Fifty-two percent of those in the placebo condition reported moderate or severe headaches (2 percent baseline), while 8–11 percent complained about depression and anxiety.

Dews and his team used subjects who responded to an ad for various medical studies [24]. Over half [6]815) of the 11,112 subjects were daily caffeine drinkers and of these, fifty-seven said they experienced difficulty in the past when they stopped use. Subjects for an experimental phase were selected from the fifty-seven; subjects with a psychiatric disorder within the last twelve months were excluded.

The fifty-seven subjects consumed an average of 200–300 mg caffeine/day with a maximum consumption of 550 mg. They were divided, randomly, into three experimental groups. The first (n = 18) was kept on a constant dose of caffeine throughout the observation period. In the second (n = 18), coffee was replaced with decaf, without their knowledge, after the first five days of the fourteen day study. Only six reported any symptoms within the first forty-eight hours of caffeine abstinence (one of them specifically reporting a “caffeine deprivation headache” on the first four days of withdrawal). Five others reported headache and lethargy on days 10 and 11.

Members of the third group (n = 20) were given progressively lower concentrations of caffeine (80 percent, 60, 40, 20, 0) on days 6–12. In that group, no consistent pattern of symptoms could be discerned. In many instances, the magnitude of the change registered was one-third of a point on a scale in which a single point indicated the change from “same as usual” to “slightly less than usual.”

In Dews' study, three of seven subjects who claimed to experience “severe” withdrawal during the interview portion of the study, did not report any discomfort during the experimentally induced withdrawal segment of the trial. As the authors state: “It would appear that self-reports are an unreliable indicator of what is recognized by the same subject under double-blind conditions” [25]. They conclude that caffeine withdrawal is not a clinically significant phenomenon and that many of the symptoms appear because subjects expect them to do so.

## METHODOLOGICAL PROBLEMS

A number of methodological issues, in addition to the relatively small samples routinely used, complicate interpretation of clinical trials data. Foremost is whether the blind can be maintained, given the ability of drinkers to detect the presence of caffeine [26]. Because blinding requires that neither the tester nor the participant know which drinks contain the active ingredient, the distinctive taste may make it impossible to preserve a blind. Additionally, there is evidence that research subjects will report in the desired direction of the person administering the study if it is known to them thus making it very difficult to obtain accurate data about caffeine effects and especially when reported withdrawal symptoms cannot be verified through a physical exam [27].

Second, it is important for studies to examine subjects who are representative of normal caffeine consumers. Particularly, a 1994 study by Strain and others, published in the prestigious *Journal of the American Medical Association* and one of the most widely cited studies on caffeine withdrawal, is problematic in this regard [28].

Not only was the study's sample size of eleven very small, the individuals were recruited through a newspaper ad specifically seeking subjects who deemed themselves “psychologically or physically dependent” upon caffeine. Therefore, the researchers chose an unrepresentative sample. Furthermore, the subjects' consent-to-participate form laid out the specific withdrawal symptoms, thus contaminating the blind and introducing expectation bias. In short, when the authors report that eight of the eleven subjects displayed “functional impairment” during the course of 2 two-day

abstinence periods which were separated by one week, the finding is not obviously applicable to most caffeine consumers.

In addition, almost half of the subjects in the Strain study consumed their caffeine in the form of soft drinks. Given an average caffeine consumption of 300 mg/d, this means the subjects drank about *ten* cans of soda per day.

Additionally, the majority of the subjects had previous psychiatric problems, either alcohol or drug abuse and/or mood disorders. Such subjects may use caffeine to self-medicate depression-related lethargy and thus could experience an exaggerated withdrawal. They are more sensitive to the effects of caffeine, and may be prone to experience distress, to find strong emotional states hard to manage, and to act impulsively.

Lastly, the nature of a caffeine withdrawal syndrome is highly variable. For example, two studies examining the cardiovascular effects of abrupt caffeine cessation elicited reports of no symptoms [29, 30]. In another study from Johns Hopkins, Suzette Evans and Roland Griffiths noted that twenty-four hours after cessation of high doses of caffeine (900 mg/d), subjects reported no withdrawal [31]. Numerous other studies yield inconsistent observations and self-report [32]–40).

## CLINICAL RELEVANCE: SHOULD WE BE WORRIED?

The American Psychiatric Association does not recognize caffeine dependence. Only caffeine withdrawal is mentioned in the *Diagnostic and Statistical Manual*; not as a formal diagnosis but rather as a diagnosis worthy of further study. However, the 5th edition of the manual is under construction—the final text is not expected until at least 2010—and some researchers such as Griffiths claim that dependence is a valid diagnosis and presumably seek its inclusion (41). Nonetheless, clinical indicators of dependence, such as difficulty curtailing or stopping the use of caffeine intake and consumption despite harm, have not been demonstrated—let alone replicated (42).

The prevalence of caffeine withdrawal syndrome is unknown. Nonetheless, a clinician should keep in mind that the symptoms can appear in a patient who has abruptly stopped intake of food and fluids. The symptoms can be mistaken for depression or tension headache. Better yet, he can advise patients how to avoid symptoms by tapering caffeine before an elective procedure. If withdrawal has begun and is unpleasant, the clinician can administer caffeine tablets.

## CONCLUSION

Caffeine is a mild stimulant that restores mental alertness or wakefulness during fatigue or drowsiness. Its use is widely acceptable because caffeine is rarely medically harmful (except perhaps in people who have particular physical conditions) and does not lead to social disruption of any kind. Abrupt discontinuation of a moderate amount (generally at least 3 cups of coffee per day; 7 cans of cola soft drink per day) can lead to bothersome symptoms, most notably headache, in some but not all people (43). These effects can be readily avoided by tapering the amount consumed. The only study in which withdrawal-related impairment appeared to be problematic was conducted using a small sample of patients chosen specifically because they believed they were dependent on caffeine and had high rates of remitted substance abuse and mood disorders. In short, these subjects did not represent a random sample of caffeine drinkers and it is not possible to infer typical discontinuation symptoms from them.

Some have argued that continued caffeine use represents an attempt to suppress low grade withdrawal symptoms such as sleepiness and lethargy. In some moderate users, this is possible; however, in experimental contexts, the phenomenon is too inconsistent to constitute a reliably valid syndrome.

The common-sense use of the term addiction is that regular consumption is irresistible and that it creates problems. Caffeine use does not fit this profile. First, there is no harm to individuals or to society. Second, there is rarely a strong compulsion to use; more correctly the pattern of use can be described as a dedicated habit. Cessation of regular use may result in symptoms such as headache and lethargy. These are easily and reliably reversed by ingestion of caffeine. Avoidance of such symptoms, when they do occur, is easily accomplished by ingesting successively smaller doses of caffeine over about a week-long period.

Thus, caffeine use meets neither the common sense nor the scientific definitions of an addictive substance.

## ACKNOWLEDGEMENT

This research was supported by a grant from the American Beverage Association.

## REFERENCES

1. Center for Science in the Public Interest. CSPI Calls on FDA to Require Health Warnings on Sodas. <http://www.cspinet.org/new/200507131.html>.
2. Caffeine: A Model Drug of Abuse. National Institute on Drug Abuse, Research Monograph 1996; 162:73–75.
3. American Psychiatric Association. Diagnostic and Statistical Manual. 4th ed. 199.
4. American Psychiatric Association. Diagnostic and Statistical Manual. 4th ed. 197.
5. Nehlig A. Does caffeine lead to psychological dependence? *Chemtech* 1999; 29:30–35.
6. Nehlig A. Are we dependent upon coffee and caffeine? A review on human and animal data. *Neuroscience and Biobehavioral Reviews* 1999; 23:563–576.
7. Daly JW. Caffeine has weak reinforcing properties, but with little or no evidence for upward dose adjustment possible because of the adverse effects of higher doses. *Drug and Alcohol Dependence* 1998; 51:199–206.
8. Juliano LM, Griffiths RR. A critical review of caffeine withdrawal: Empirical validation of symptoms and signs, incidence, severity, and associated features. *Psychopharmacology* 2004; 176:1–29.
9. Griffiths RR, Evans SM, Heishman SJ, Preston KL, Sannerud CA, Wolf B, Woodson PP. Low dose caffeine physical dependence in humans. *Journal of Pharmacology and Experimental Therapeutics* 1990; 255:1123–32.
10. Barone JJ, Roberts HR. Caffeine consumption. *Food Chem Toxicol* 1996; 34:119–129.
11. Dreisbach RH, Pfeiffer C. Caffeine-withdrawal headache. *The Journal of Laboratory and Clinical Medicine* 1943; 28:1212–19.
12. Goldstein A, Kaiser S, Whitby O. Psychotropic effects of caffeine in man, IV: Quantitative and qualitative differences associated with habituation to coffee. *Clinical Pharmacology and Therapeutics* 1969; 10:489–97.
13. Strain EC, Mumford GK, Silverman K, Griffiths RR. Caffeine dependence syndrome: Evidence from case histories and experimental evaluations. *The Journal of the American Medical Association* 1994; 272:1043–48.
14. Oberstar JV, Bernstein GA, Thuras PD. Caffeine use and dependence in adolescents: One year follow-up. *Journal of Child & Adolescent Psychopharmacology* 2002; 109:85–91.
15. Goldstein A, Kaizer S. Psychotropic effects of caffeine in man: A questionnaire survey of coffee drinking and its effects in a group of housewives. *Clinical Pharmacology and Therapeutics* 1969; 10:477–88.
16. Hughes JR, Oliveto AH, Liguori A, Carpenter J, Howard, T. Endorsement of DSM-IV dependence criteria among caffeine users. *Drug and Alcohol Dependence* 1998; 52:99–107.
17. Dews PB, Curtis G, Hanford K, O'Brien, CP. The frequency of caffeine withdrawal in a population-based survey and in a controlled, blinded pilot experiment. *Psychopharmacology* 1999; 39:1221–32.
18. Kendler KS, Prescott, CA. Caffeine intake, tolerance, and withdrawal in women: A population-based twin study. *American Journal of Psychiatry* 1999; 156:223–228.
19. Hughes J, Higgins S, Bickel WW, Hunt K, Fenwick JW, Gulliver SB, Mireault GC. Caffeine self-administration, withdrawal, and adverse effects among coffee drinkers. *Archives of General Psychiatry* 1991; 48:611–17.
20. Silverman K, Evans SM, Strain EC, Griffiths RR. Withdrawal syndrome after the double-blind cessation of caffeine consumption. *New England Journal of Medicine* 1992; 327:1109–1114.
21. *Ibid.*, 1230.
22. Rosenthal R. Covert communication in the psychological experiment. *Psychological Bulletin* 1967; 67:356–67.
23. Robertson D, Wade D, Workman R, Woolsey R, Oates JA. Tolerance to the humoral and hemodynamic effects of caffeine in man. *Journal of Clinical Investigation* 1981; 67:1111–1117.
24. Ammon H, Bieck P, Mandalaz D, Verspohl E. Adaptation of blood pressure to continuous heavy coffee drinking in young volunteers. A double-blind crossover study. *British Journal of Clinical Pharmacology* 1983; 15:701–706.
25. Evans SM, Griffiths RR. Caffeine tolerance and choice in humans. *Psychopharmacology* 1992; 108:51–59.
26. Hughes JR, Oliveto AH, Higgins ST. Caffeine self-administration and subjective effects in adolescents. *Experimental Clinical Psychopharmacology* 1995; 3:364–70.
27. Liguori A, Hughes JR, Oliveto AH. Caffeine self-administration in humans: 1. Efficacy of cola vehicle. *Experimental and Clinical Psychopharmacology* 1997; 5:286–94.
28. Dews PB, O'Brien CP, Bergman J. Behavioral effects of caffeine: Dependence and related issues. 1998. (Unpublished version)
29. Hughes JR, Oliveto AH, Bickel WK, Higgins ST, Badger GJ. Caffeine self-administration and withdrawal:

Incidence, individual differences and interrelationships. *Drug and Alcohol Dependence* 1993; 32:239–46.

30. *Ibid.*, 614.

31. Juliano LM, Griffiths RR. Is caffeine a drug of dependence? *Psychiatric Times* 2001; 18(2).

32. Hughes JR, Oliveto AH, Helzer JE, Higgins ST, Bickel WK. Should caffeine abuse, dependence, or withdrawal be added to DSM-IV and ICD-10? *American Journal of Psychiatry* 1992; 149:33–40.