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CLINICAL REVIEW

Caffeine: Sleep and daytime sleepiness

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Summary Caffeine is one of the most widely consumed psychoactive substances and it has profound effects on sleep and wake function. Laboratory studies have documented its sleep-disruptive effects. It clearly enhances alertness and performance in studies with explicit sleep deprivation, restriction, or circadian sleep schedule reversals. But, under conditions of habitual sleep the evidence indicates that caffeine, rather then enhancing performance, is merely restoring performance degraded by sleepiness. The sleepiness and degraded function may be due to basal sleep insufficiency, circadian sleep schedule reversals, rebound sleepiness, and/or a withdrawal syndrome after the acute, over-night, caffeine discontinuation typical of most studies. Studies have shown that caffeine dependence develops at relatively low daily doses and after short periods of regular daily use. Large sample and population-based studies indicate that regular daily dietary caffeine intake is associated with disturbed sleep and associated daytime sleepiness. Further, children and adolescents, while reporting lower daily, weight-corrected caffeine intake, similarly experience sleep disturbance and daytime sleepiness associated with their caffeine use. The risks to sleep and alertness of regular caffeine use are greatly underestimated by both the general population and physicians.

Introduction

Caffeine is one of the most commonly consumed psychoactive substances in the world. It is available in a variety of dietary sources such as coffee, tea, coca, candy bars, and soft drinks. It also is an ingredient in various over-the-counter drugs (OTCs) including headache, cold, allergy, pain relief, and alerting drugs. The caffeine content of some of the various beverages, foods, and OTCs is provided in Table 1. The table is not to be considered exhaustive. The caffeine content of foods, commercially prepared beverages, and OTCs is constant and documented, but the caffeine content of brewed beverages can vary depending on the bean

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Table 1 Caffeine content of drinks and foods.

Product	Serving size	Caffeine (mg)
Coffees[49]		
Brewed-graved	8 oz	80–135
Instant	8 oz	40–108
Drip	7 oz	115–175
Espresso	2 oz	100
Starbucks regular	16 oz	259
Decaffeinated	8 oz	5–6
Teas		
Leaf teas	7 oz	50–60
Instant	7 oz	30
Bottles	8 oz	40–80
Soft drinks[50]		
Jolt	12 oz	71
Mountain dew	12 oz	58
Mellow yellow	12 oz	53
Coca-Cola	12 oz	45
Dr. Pepper	12 oz	41
Pepsi Cola	12 oz	37
RC Cola	12 oz	36
Candies & desserts[51]		
Chocolate baking	28 g (10 oz)	25
Chocolate chips	43 g (1/4 cup)	15
Chocolate bar	28 g	15
Jello choc fudge	86 g	12
Energy drinks[52]		
Red devil	8.4 oz	42
SoBe no fear	16 oz	141
Red bull	8.3 oz	67

used and the method of brewing. This variability requires that investigators estimate the caffeine content of brewed beverages when assessing self-reported caffeine consumption and introduces error variance when relating caffeine doses to any outcome variables.

Caffeine's effects on laboratory assessed sleep in double-blind placebo controlled studies have been well documented. Laboratory studies have also documented its alerting and performance-enhancing effects. However, the extent to which regular dietary caffeine intake affects sleep and daytime function in the population is not fully known. Such information is important since there is evidence suggesting the use of caffeine in society is expanding, both in terms of increased daily dosages and earlier ages for the initiation of regular daily caffeine use.

To understand the effects of caffeine and its discontinuation on sleep and daytime alertness and its tolerance and dependence liability we will first review its pharmacology. After reviewing the pharmacology of caffeine and the well-documented sleep disruptive effects of caffeine and studies suggesting that caffeine's performance-enhancing effects are for the most part restoring performance degraded by sleepiness, this review will evaluate the degree to which caffeine dependence interacts with its sleep–wake effects. Finally, evidence from population-based studies on the role of daily dietary caffeine in disturbed sleep and impaired daytime function will be assessed and the risks of caffeine associated sleep disruption and daytime sleepiness in children and adolescents will be reviewed.

Caffeine pharmacology

Orally ingested caffeine is absorbed rapidly, reaching peak plasma concentrations in 30–75 min.[1] It is estimated that 80% of plasma caffeine levels are present in human brain, based on animal studies that have compared plasma to brain concentration.[2] Caffeine is metabolized to paraxanthine (80%) and to theobromine and theophylline (16%). With higher caffeine doses, and the repeated consumption typical of regular caffeine users, the plasma levels of paraxanthine accumulate and this paraxanthine accumulation reduces caffeine clearance. Paraxanthine shares many of the effects of caffeine and consequently regular caffeine consumption leads to both accumulated caffeine and paraxanthine levels, both of which are biologically active. The half-life of single dose caffeine is 3–7 h, but with higher levels of intake the duration of action is extended, likely due to the accumulated paraxanthine and retarded caffeine clearance.[2]

Caffeine's primary mode of action is adenosine receptor blockade. The A_1 and A_{2A} adenosine receptors are those primarily involved in caffeine's central effects. A_1 receptors are distributed widely throughout the brain including hippocampus, cerebral and cerebellar cortex, and thalamus, while A_{2A} receptors are located in striatum, nucleus accumbens and olfactory tubercle. Adenosine receptors are also present in blood vessels, kidneys, heart and the GI tract. Adenosine decreases neural firing rate and inhibits most neurotransmitter release. The mechanism(s) by which adenosine inhibits neurotransmitter release have not been resolved. The putative role of adenosine in sleep homeostasis has been outlined in a recent review.[3] One postulated mechanism for adenosine's role in sleep homeostasis is inhibition of cholinergic neurons in the basal forebrain which normally produce arousal.

Thus, adenosine promotes sleep and caffeine blocks adenosine's sleep promoting effects.

The extent of tolerance development to caffeine's effects is controversial and not clearly established.[4–8] In part, the equivocal results are due to methodological limitations. Studies compare caffeine naïve to habitual caffeine consumers, or habitual consumers before and after caffeine abstinence. Given that 80% or more of the population report regular use of caffeine, non-caffeine consumers are a very self-selected, atypical subpopulation. Response differences may merely reflect genetic or other trait differences between non-caffeine and habitual consumers, or an atypical response to caffeine that led to the non-consumer's caffeine avoidance. Very few studies have directly administered caffeine repeatedly with parallel placebo controls. The available data do suggest that caffeine tolerance development is partial and may differ with regard to caffeine's peripheral versus central effects.

As to central effects, a study measured human brain metabolic response to caffeine using rapid proton echo-planar spectroscopic imaging in regular caffeine users.[4] Brain lactate during 1 h following caffeine (10 mg/kg) was elevated in caffeine naive relative to regular caffeine users. In the regular caffeine users after a 4–8 weeks abstinence, caffeine re-exposure raised brain lactate to a level similar to that of the caffeine naïve subjects. A study of caffeine (400 mg administered three times a day) effects on nocturnal sleep and daytime alertness attempted to model the physiological arousal of chronic insomnia in healthy normals.[5] The caffeine was administered for 7 days and over the 7 days partial tolerance to the sleep disruptive and daytime alerting effects of caffeine was observed. It is possible that more clearly defined pharmacological tolerance occurred, but that was offset by the increase in homeostatic drive resulting from the nightly sleep disruption. The hypothalamic-pituitary-adrenocortical axis (HPA) is activated by caffeine administration and cortisol secretion has been used to mark this HPA activation. Salivary cortisol response to a caffeine challenge (250 mg) was assessed before and after 5 days of 0, 300, or 600 mg daily caffeine.[6] On day 1 relative to placebo cortisol was elevated in a dose-related manner. By day 5 partial tolerance developed in the daily 300 mg group and complete tolerance in the daily 600 mg group. Thus, most of the evidence suggests either complete or partial tolerance to caffeine's central effects.

The peripheral effects of caffeine and possible tolerance development to its peripheral effects have received more attention because of concerns regarding dietary caffeine intake and cardiovascular health.[7] Peripheral pressor responses to caffeine were assessed in the cortisol study cited above using the same caffeine administration methodology.[8] Caffeine elevated blood pressure relative to placebo and the blood pressure response was not abolished after 5 days of 600 mg daily. The sympathetic nervous system has an important role in regulating blood pressure. A study assessed sympathetic nerve activity and blood pressure in habitual and non-habitual caffeine drinkers.[9] Relative to placebo, caffeine (250 mg) increased blood pressure in the non-habitual drinkers, but not the habitual drinkers. In contrast, sympathetic system activity was similarly increased in both groups. Importantly, plasma caffeine concentrations did not differ between the two groups. Thus, tolerance to the peripheral effects of caffeine may be differential, depending on the response system assessed, but appears to be less consistent than the tolerance to its central effects.

Caffeine effects on sleep in controlled laboratory studies

A number of polysomnographic studies have assessed the sleep effects of caffeine administered within 1 h of sleep. An early study administered 0, 1.1, 2.3, or 4.6 mg/kg (77–322 mg for a 70 kg person) caffeine 30 min before sleep to healthy normals with a reported average daily 3-cup caffeine consumption history.[10] Caffeine reduced total sleep time, increased latency to sleep, and reduced percent stage 3–4 sleep in a dose-related manner. REM sleep was not affected.

In a study of the hypnotic effects of temazepam, methylphenidate (10 mg) and caffeine (150 mg) were used to model insomnia.[11] To establish the insomnia model, healthy young adults with an unspecified caffeine history received each drug alone 30 min before sleep. Compared to placebo both drugs prolonged sleep onset and reduced total sleep time, but did not affect sleep stages. Caffeine 150 mg had a greater effect on sleep latency and total sleep time than methylphenidate 10 mg.

Another study of young adults (21–31 yr) with an unspecified caffeine drinking history compared the effects of 000, 100, 200, and 300 mg of caffeine taken at "lights-out".[12] In a dose-related manner all caffeine doses reduced total sleep time and percentage of stage 3+4 sleep. Sleep onset was not affected, probably because of the "lights-out" drug administration used in the study and caffeine's

30–70 min time to plasma peak. In a second study, done with the same participants, the sleep effects of caffeine 300 mg were compared to methylphenidate 10 and 20 mg and pemoline 20 and 40 mg.[12] Caffeine and the high doses of methylphenidate and pemoline reduced total sleep time relative to placebo, with no differences in total sleep time among the drugs. Sleep onset and percent stage 3+4 sleep were not affected by any of the drugs. The high dose of methylphenidate prolonged REM latency and reduced REM percent, which was not found with caffeine or pemoline.

A study attempting to model the physiological arousal of insomnia in healthy young men administered 400 mg caffeine three times a day (800, 1600, and 2300 h) for 7 consecutive days.[5] Relative to baseline, total sleep time was reduced and sleep latency was increased. The percentage of stage 4 sleep was reduced, but the percentage and latency of REM sleep was not affected. As cited above, this study showed partial tolerance development over the 7 days of caffeine.

Given adenosine's putative role in sleep homeostasis several studies have assessed EEG slow wave activity during sleep after caffeine administration. Caffeine (100 mg) or placebo was administered to young men with a caffeine drinking history of 1–3 cups daily.[13] Caffeine or placebo was administered at bedtime and relative to placebo it prolonged sleep latency and reduced sleep efficiency and visually scored stage 4 sleep. EEG spectral power density in the 0.75–4.5 Hz band was reduced. Salivary caffeine was 7.5 μmol/l and declined to 3.5 μmol/l by the seventh hour of sleep. A parallel study administered placebo or caffeine 200 mg at 0700 h and assessed its effect on the subsequent night of sleep (2300–0700 h).[14] Immediately prior to sleep at 2300 h salivary caffeine levels were 3.1 μmol/l and relative to placebo sleep efficiency was reduced and EEG spectral power density in the 0.75–4.5 Hz band was suppressed. As degree of sleep fragmentation was not quantified in any of these studies it is difficult to determine if the decrease in stage 3–4 sleep and slow wave activity is a direct pharmacological effect as seen with drugs like the benzodiazepines, or is secondary to the sleep disruptive effects of caffeine as seen in conditions like sleep apnea.

In summary, the sleep disruptive effects of caffeine, even at doses equivalent to a single cup of coffee, have been well documented. Both sleep onset (i.e., when taken early enough before sleep to allow adequate absorption) and sleep time are adversely affected. The sleep stage effects are unique, when compared to other stimulants, and are consistent with its mechanism of action, adenosine blockade. Stage 3–4 sleep is decreased and EEG slow wave activity is suppressed by caffeine. In contrast, the psychomotor stimulants are more likely to suppress REM sleep.

Caffeine effects on daytime alertness and performance

Laboratory studies of the effects of caffeine on performance and mood have a long history dating to the late nineteenth century. The acknowledged first placebo controlled study was published in 1907.[15] The investigators reported that 500 mg caffeine improved finger muscle strength. The classic review article of Weis and Laties summarized the pre-1960s literature and concluded that the evidence clearly indicates that caffeine enhances a wide range of performance with the exception of "intellectual" tasks.[16] Weis and Laties then raised the critical question whether caffeine is actually producing superior performance or merely restoring performance "degraded by fatigue, boredom and so on" (p. 30, 16).

The post-1960s literature provides additional information regarding the two issues raised by Weis and Laties: does caffeine affect "intellectual" performance and does caffeine restore or improve performance. First, as to whether "intellectual" performance is improved, Weis and Laties were probably referring to what is currently described as cognitive performance, which includes various types of memory and problem solving performance. A recent review of the effects of caffeine on human behavior included a review of the effects of caffeine on cognitive performance.[17] The literature supporting a positive effect of caffeine on complex cognitive processes is not as strong as that for attention and psychomotor performance. Methodological issues, discussed in more detail below, may explain some of the negative results. Without completely reviewing this literature, several illustrative studies can be cited.

A recent study in non-consumers and habitual consumers, reporting 218 mg per day on average, administered 0, 75, and 150 mg caffeine.[18] In addition to improving attention and reaction time performance, the caffeine also improved numeric working memory and sentence verification accuracy performance. The magnitude of caffeine-associated improvements did not differ between consumers and non-consumers. Another study administered a larger caffeine dose (4 mg/kg–280 mg for a 70 kg participant) to young adults with

an unspecified caffeine drinking history.[19] Caffeine improved performance on semantic memory, logical reasoning, free recall and recognition recall performance. In summary, while there are a number of negative studies, studies with positive effects of caffeine on complex cognitive function are available. Negative studies have to be cautiously interpreted because of the various methodological issues discussed below.

The second issue raised by Weis and Laties is whether caffeine is restoring or improving performance. There is no question that caffeine acutely restores performance and mood under explicit conditions of sleep restriction, sleep deprivation, and sleep phase reversals as seen in shift work, where prior performance impairment is clear. The literature assessing the use of stimulants, including caffeine, to improve performance during periods of extended wakefulness was recently reviewed by a Task Force of the American Academy of Sleep Medicine.[20] Similarly, a large number of laboratory and field studies have documented performance impairment associated with night work and have shown that caffeine can minimize the performance impairment that is associated with night work.[21]

But, what of performance under conditions of habitual sleep without explicit sleep loss or circadian disruption? Is there evidence that there is fatigue and degraded performance in the typical caffeine study of normal healthy volunteers? And if so, what is the cause of the sleepiness and degraded performance? Identification of the probable causal factor(s) is necessary to determine whether or not performance is degraded. The factors that might be considered and discussed are: (1) a high rate of basal sleepiness in the typical study participants (i.e., young adults specifically and the general population more broadly), (2) a rebound sleepiness following acute discontinuation of caffeine as required in most studies, and/or (3) a withdrawal syndrome associated with caffeine dependence in study participants.

A high rate of basal sleepiness, and potentially degraded performance, in the typical study participants is an important consideration. An early study assessed the level of sleepiness in a large sample ($n = 129$) of young adult volunteers for studies of the effects of caffeine, alcohol, and benzodiazepines.[22] These volunteers reported an average 7.2 h of nightly sleep, no daytime sleepiness, and habitual daily caffeine intake of 200 mg or less. Yet 20% of these young adults had a daily average sleep latency on the Multiple Sleep Latency Test (MSLT) of 6 min or less, which is considered a pathological level of sleepiness. In a population-based study ($n = 259$) of adults aged 21–65 yr, 15% of the sample had a daily average sleep latency of 6 min or less and 20% had an Epworth Sleepiness Scale score of 11 or greater, a score generally considered pathological.[23,24] A complete caffeine intake history was not done in this study and a daily caffeine intake is not available for these participants. A study compared the psychomotor performance of sleepy young adults, defined as a MSLT of 6 min or less, with their alert counterparts, defined as a MSLT of 16 min or greater, who did not differ in daily caffeine intake (i.e., $\leqslant$200 mg).[25] The sleepy individuals showed degraded performance relative to the alert individuals. Finally, an extended bedtime of 10 h nightly for 6 consecutive nights improved the performance of the sleepy individuals.[26] In fact, even 8 h in bed across several nights produced an increase in alertness in healthy volunteers, who had no prior self-reported sleepiness.[24,27,28] Thus, the evidence suggests that in the typical caffeine study there could be increased sleepiness (i.e. reduced alertness) and degraded performance among "normal volunteer" study participants. The increased sleepiness and degraded performance in such individuals is likely due to a chronic sleep insufficiency relative to that individual's sleep need.

Other important considerations are the time-of-day and the homeostatic sleep load (i.e., the level of sleepiness) at which the caffeine is administered and its effect assessed. Under conditions of habitual sleep, a circadian rhythm of sleepiness has been described with increased sleepiness over the midday as the homeostatic sleep drive has increased as a function of the accumulated time awake. Studies have found that the sedative effects of alcohol differ as a function of time-of-day and under differing basal levels of sleepiness at the same time-of-day; the effects are greater with greater sleepiness and over the midday than in the evening. The same may be the case with the alerting effects of caffeine (i.e. they are clearly present over the midday, but less so in the evening).

It is unlikely that basal sleepiness alone explains degraded performance in studies of caffeine's performance enhancing effects. In the large sample studies cited above approximately 20% of the sample had excessive sleepiness. The latter two factors mentioned above, rebound sleepiness and/or a withdrawal syndrome, appearing as a result of the caffeine discontinuation required in almost all caffeine studies, must be discussed. These two factors suggest the possibility of caffeine dependence.

Caffeine dependence

Caffeine dependence is evident by the signs of behavioral and physiological dependence.[29] These two dependences often co-exist, but can be differentiated. Physiological dependence is a state induced by repeated drug use that results in a withdrawal syndrome when the drug is discontinued or an antagonist is administered. Among discontinuation effects, withdrawal should be differentiated from rebound phenomenon. Withdrawal is a collection of signs and symptoms that differs from rebound phenomenon in that there are multiple signs and symptoms and the signs and symptoms are new, not present prior to drug administration. Rebound is the expression of a single sign or symptom that is the reverse of the drug effect (i.e., for caffeine, rebound sleepiness) and with intensity beyond the basal state. Rebound can occur after single administrations of high drug doses, while withdrawal typically requires repeated drug administration and can occur with moderate or low drug doses.[29] Behavioral dependence is a pattern of behavior characterized by repetitive and compulsive drug seeking and consumption. The drug acts as a reinforcer either by reversing an ''aversive'' state or producing a ''positive'' state. Behavioral dependence can be studied by assessing the likelihood of self-administering the drug and concurrently measuring its subjective and mood effects.

What then is the evidence for rebound sleepiness and withdrawal during caffeine discontinuation, for sleepiness/withdrawal associated degraded performance, and then for continued caffeine self-administration to reverse the sleepiness and performance impairment? A critical review of the literature regarding caffeine withdrawal was recently conducted.[30] A total of 57 experimental and 9 survey studies could be identified. The experimental studies were conducted as double-blind placebo controlled studies. To assess the presence and nature of the various withdrawal symptoms, the studies employed several common methodologies and comparisons including: (1) acute abstinence versus preceding caffeine baseline, (2) acute abstinence versus caffeine, (3) acute abstinence in caffeine consumers versus non-consumers, or (4) acute abstinence versus chronic abstinence. The symptoms and signs that were reported in the comparisons (i.e., acute abstinence versus preceding caffeine baseline) of the 57 studies were then classified and a given class was considered as valid if it appeared in six or more studies. The symptom classes considered valid were headache, fatigue, decreased energy, decreased alertness, drowsiness-sleepiness, decreased contentedness, depressed mood, difficulty concentrating, irritability, and fogginess. In addition, flu-like symptoms, nausea and vomiting, and painful joints and stiffness were also considered as probable valid symptom classes. While this review did not differentiate rebound sleepiness (i.e., an isolated symptom) from a withdrawal syndrome, drowsiness-sleepiness was found in 78% of studies, second only to headache. The symptoms appeared after 12–24 h of abstinence and after as little as 100 mg of caffeine for 3–7 days.

As to whether degraded performance is associated with the caffeine discontinuation, the standard practice in most placebo controlled caffeine studies is to require discontinuation of caffeine use the evening prior to entrance to the laboratory and the next-day caffeine or placebo administration. Given the half-life of caffeine (i.e., 3–7 h) and the previously cited time-course for the appearance of withdrawal symptoms (12–24 h), in most studies that employ an over-night abstinence placebo or caffeine is being administered in the midst of a potential withdrawal or at the very least a rebound sleepiness. It has been argued by James and Rogers that caffeine's effects on performance and mood are withdrawal reversal.[31]

James and Rogers argue that the most definitive method to assess caffeine effects is to require a prior long-term abstinence before assessment.[28] To make their point, they compared placebo controlled caffeine effects after a long-term abstinence (i.e., 3 weeks) versus an overnight abstinence.[32] The young adult study participants reported 400 mg daily caffeine intake on average. Relative to the long-term abstinence, the overnight abstinence was associated with degraded performance including cognitive performance. Caffeine in a 1.2 mg/kg dose improved performance relative to placebo in the overnight abstinence condition only. After the chronic abstinence no performance enhancement was found. Therefore, the Weiss and Laties hypothesis that performance is impaired during caffeine discontinuation due to withdrawal related sleepiness and that caffeine restores the performance impairment is directly supported by this study.

The final question raised is whether reversal of caffeine withdrawal or rebound sleepiness enhances the likelihood of self-administering caffeine. Early caffeine self-administration studies reported that 25–50% of participants reliably self-administered caffeine.[33,34] These studies suggested that caffeine functioned as a reinforcer for some individuals, but not others. The variable suggested to explain these individual differences was caffeine

withdrawal. A study examined caffeine's withdrawal effects in moderate caffeine consumers (379 mg/day on average) and assessed choice between money and capsules that contained caffeine or placebo.[35] The participants chose caffeine rather than $0.38 on caffeine days, but forfeited $2.51 to avoid the capsule on placebo days, suggesting that avoidance of withdrawal promotes caffeine choices. The implication of this study is that the primary reinforcing function of caffeine is reversal of a negative state rather than the production of a positive state. A final study in this series of studies directly manipulated caffeine dependence.[36] The participants received caffeine (300 mg/70 kg per day) and placebo in counterbalanced study phases of 9–12 days. After the caffeine phase they chose caffeine two times as frequently as after the placebo phase. These studies suggest that caffeine functions as a negative reinforcer by reversing caffeine withdrawal. It should be noted that these effects were seen in moderate caffeine consumers with a daily caffeine intake similar to the mean intake seen in population-based studies as reviewed below.

The major problem with all of the laboratory studies of caffeine and caffeine discontinuation is that the study participants are volunteers. Caffeine study volunteers may represent a highly select sample of individuals who have various biases and expectancies regarding caffeine effects relative to their own level of daily caffeine intake. The critical question is whether in the general population daily dietary caffeine intake is associated with nocturnal sleep and/or daytime sleepiness problems.

Dietary caffeine in the population: sleep and daytime alertness

Accurate survey data on caffeine consumption in the general population are difficult to collect due to the variety of caffeine sources and the variability of caffeine content in various beverages. A survey of the caffeine content reported by various authors found a range of 64–124 mg reported in a 150 ml (5 oz) cup of brewed coffee.[37] This variability is a problem in attempting to associate caffeine consumption with indices of sleep and daytime alertness and requires that investigators assign a caffeine content value to a reported cup of coffee. The value suggested by Barone and Roberts is 85 mg per 150 ml for brewed coffee and they also provided values for other beverages.[37] On this basis they estimated that adults in the US daily consumed 4 mg/kg (i.e., 280 mg for a 70 kg person) caffeine per day from all sources.

Using the values of 85 mg/5 oz cup of coffee, 40 mg/5 oz cup of tea, and 40 mg/12 oz cup of soda, a survey of caffeine intake in Vermont reported that 83% of respondents currently used one or more caffeinated beverages weekly and the average daily intake was 186 mg.[38] Forty-one percent of respondents had stopped use of at least one type of beverage and 14% stopped all caffeine use. Insomnia was among the health concerns leading to cessation or reduction of use. A survey of a Southern California community found that among lifetime coffee-drinkers, women were more likely to curtail caffeine use than men and did so because of sleep problems.[39] A recent survey of seven European countries evaluated factors contributing to reports of nonrestorative sleep.[40] Daily caffeine intake contributed to nonrestorative sleep as a bivariate, but not an independent predictor. However, the assessment of caffeine intake in this survey merely consisted of a yes/no response to a question regarding daily use of caffeine. Yet, these limited data suggest that in the general population sleep problems are associated with caffeine use. However it is important to remember that the relation can be bi-directional. Disturbed sleep leads to sleepiness and hence increased caffeine consumption. Similarly, as previously discussed caffeine consumption can, as well, lead to disturbed sleep. Thus, it is not difficult to imagine that in some individuals this can be a vicious circle leading to elevated caffeine consumption.

Several population-based studies have also suggested that high caffeine use is associated with daytime sleepiness. A representative sample of the British population assessed daytime sleepiness and associated factors.[41] Those with the most severe sleepiness, meaning daily sleepiness for a month or greater, reported high daily caffeine consumption defined as 7 or more cups of tea or coffee per day. The prevalence of severe sleepiness was 5.9% in moderate caffeine users, while it was 10.6% in the high caffeine consumers. A questionnaire and diary-based study assessed sleep habits and caffeine use of workers in the French National Gas and Electricity Company.[42] Time-in-bed was associated with caffeine use such that, as caffeine use increased time-in-bed decreased. The association suggests caffeine is shortening sleep and/or is being used to counter the sleepiness associated with short time-in-bed. The latter explanation is the more likely since caffeine use was not associated with total sleep time.

Sleep problems and sleepiness associated with caffeine use is also found in children and adolescents

as reported in multiple studies. Several surveys from the 1980s reported children and adolescents, aged 5–18 yr, consumed 37 mg or 0.9 mg/kg caffeine daily.[43] The majority of the caffeine intake was derived from soda, chocolate, and tea and between 75% and 98% of respondents consumed caffeine. Caffeine intake in children and adolescents was estimated to be about 1.0 mg/kg daily in 1998.[43] Some smaller sample studies of teenagers have reported much higher daily caffeine intakes and have found caffeine dependence, defined as the observation of withdrawal signs and symptoms during the caffeine discontinuation.[44,45] In the 26–40% of participants showing dependence, daily caffeine intake was 2.4–3.2 mg/kg. Among the more common withdrawal signs in these teenagers was daytime sleepiness.

The US National Institute of Child Health and Human Development conducted a US survey in 1998 of children in grades 6–10.[46] Sixty-eight percent drank one or more soda or coffee drinks per day. After adjusting for socio-demographic factors those reporting high caffeine intake were 1.9 times more likely to report difficulty sleeping and 1.8 times more likely to be tired in the morning. Two-week sleep diaries were collected in a large sample of 7–9 grade students from Columbus, Ohio.[47] On average 52.7 mg of caffeine was consumed daily and 20% of the sample averaged more than 100 mg daily. Unfortunately, this study did not correct for body weight and thus these data cannot be compared to the earlier studies. The data clearly show high caffeine intake was associated with increased wakefulness during the sleep period and with a shortened bedtime. The authors speculate that the caffeine is being used to counter sleepiness associated with the shortened sleep and bedtime. A survey of Italian high school students specifically assessed daytime sleepiness and found high use of caffeine was associated with increased daytime sleepiness.[48] However, the association was only found in evening types, as defined by the Morningness–Eveningness scale adapted for children.[48] In other studies it has been shown that evening types sleep less than morning types.

To summarize, population and large sample studies find an association between daily dietary caffeine intake and sleep problems and daytime sleepiness. The levels of daily caffeine intake in adult population studies are comparable to the caffeine doses administered in laboratory studies showing caffeine is disruptive of sleep. In children and adolescents the levels of caffeine intake, corrected for body weight, are lower than that of adults, but caffeine dependence can be found among some children. Even at the lower caffeine daily intake levels, and without clear indications of dependence, an association of sleep disturbance and daytime sleepiness with caffeine use is found.

Practice points

1. Assessment of patients' caffeine intake must be comprehensive including a wide variety of dietary sources (see Table 1) and it should be recognized that low dose caffeine use has risks.
2. Regular use of even low caffeine doses can be disruptive of sleep and contribute to patients' insomnia complaints.
3. Sleepiness is a common discontinuation effect of caffeine and could be a factor in patients' morning sleepiness following over-night abstinence.
4. Caffeine use should be considered in assessing sleep disturbance or daytime sleepiness in children and adolescents.
5. Persistent caffeine use and inability to discontinue may reflect caffeine dependence which requires a clinician guided gradual reduction of caffeine intake.
6. Discontinuation of caffeine within a day or across time can be a potential cause or contributing factor in patients complaining of excessive sleepiness.

Research agenda

1. Further study of the disruptive effects of dietary caffeine on sleep and daytime alertness in the population is important.
2. Further study of the extent of sleep and daytime alertness problems associated with caffeine use in children and adolescents is necessary.
3. Studies determining the degree to which sleep restriction or restriction of time in bed leads to caffeine consumption.
4. Further studies are needed to determine what aspects of human performance are aided, which are not, and which are worsened by caffeine.
5. Studies investigating the alerting-performance enhancing effects of caffeine at differing basal levels of sleepiness–alertness, ranging from a sleep satiated state to a totally sleep deprived state.

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