

Small, Frequent Doses Of Caffeine Best Strategy For Staying Awake, According To New Study

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Summary: Caffeine is the world's most widely-used stimulant yet, scientists still do not know exactly how it staves off sleep.

FULL STORY

Boston, MA - May 11, 2004 - Caffeine is the world's most widely-used stimulant yet, scientists still do not know exactly how it staves off sleep. Researchers at Brigham and Women's Hospital, Harvard Medical School and other institutions have now discovered that caffeine works by thwarting one of two interacting physiological systems that govern the human sleep-wake cycle. The researchers, who report their findings in the May issue of the journal *Sleep*, propose a novel regimen, consisting of frequent low doses of caffeine, to help shift workers, medical residents, truck drivers, and others who need to stay awake get a bigger boost from their tea or coffee.

"Most people take a huge jolt of coffee in the morning to jumpstart their day-they get the super grande latte from Starbucks," said Charles Czeisler, who was recently appointed the Frank Baldino Jr. PhD professor of sleep medicine at Harvard Medical School. "Their caffeine levels soar only to fall as the day progresses in the face of rising sleepiness. They might be better off taking much smaller more frequent doses of caffeine, equivalent to a quarter of a cup of coffee, as the day wears on."

Though many studies have measured caffeine's sleep-averting effects, most do not take into account that sleep is governed by two opposing but interacting processes. The circadian system promotes sleep rhythmically-an internal clock releases melatonin and other hormones in a cyclical fashion. In contrast, the homeostatic system drives sleep appetitively-it builds the longer one is awake. If the two drives worked together, the drive for sleep would be overwhelming. As it turns out, they oppose one another.

Czeisler, who also leads the Division of Sleep Medicine at HMS, and his colleagues had reason to suspect that caffeine might be working to blunt the homeostatic system. For one thing, caffeine is thought to block the receptor for adenosine, a critical chemical messenger involved in the homeostatic drive for sleep. If that were true, then caffeine would be most effective if it were administered in parallel with growing pressure from the sleep homeostatic system, and also with accumulating adenosine.

To test their hypothesis, the scientists sequestered 16 male subjects in private suites, free of time cues, for 29 days. Instead of keeping to a 24 hour day researchers scheduled the subjects to live on a 42.85 hour day (28.57-hour wake episodes), simulating the duration of extended wakefulness commonly encountered by doctors, and

military and emergency services personnel. The extended day was also designed to disrupt the subjects' circadian system while maximizing the effects of the homeostatic push for sleep.

Following a randomized, double-blind protocol, subjects received either one caffeine pill, containing 0.3 mg per kilogram of body weight, roughly the equivalent of two ounces of coffee, or an identical-looking placebo. They took the pills upon waking and then once every hour. The goal of the steady dosing was to progressively build up caffeine levels in a way that would coincide with-and ultimately, counteract-the progressive push of the homeostatic system, which grows stronger the longer a subject stays awake.

The strategy worked. Subjects who took the low-dose caffeine performed better on cognitive tests. They also exhibited fewer accidental sleep onsets, or microsleeps. EEG tests showed that placebo subjects were unintentionally asleep 1.57 percent of the time during the scheduled wake episodes, compared with 0.32 percent for those receiving caffeine. Despite their enhanced wakefulness, the caffeine-taking subjects reported feeling sleepier than their placebo counterparts, suggesting that the wake-promoting effects of caffeine do not replace the restorative effects gained through sleep.

"Our results highlight the impairments in cognition that accompany all work schedules that lie outside the usual 9 to 5 workday. In addition, they reveal an entirely new way to use caffeine to maintain alertness and performance in the face of sleep loss," said lead author of the study, James Wyatt.

As the researchers hypothesized, the behavioral differences between the groups appear to be due to caffeine's effects on the homeostatic rather than circadian system.

Czeisler and his colleagues suggest that shift workers, medical residents, truck drivers, and others who need to stay alert consider taking frequent low doses of caffeine. "While caffeine is no substitute for sleep, those who must stay awake for extended periods would benefit from this kind of dosing regimen to help maintain their performance and reduce the risk of lapses of attention," said Czeisler.

All authors on the paper were in the Division of Sleep Medicine at Harvard Medical School when the study was conducted. First author James Wyatt is now at Rush University Medical Center in Chicago, Illinois. Derk-Jan Dijk is at the University of Surrey, England, and Christian Cajochen is at the Psychiatric University Clinic in Basel, Switzerland. Angela Ritz-DeCecco, PhD is a research assistant in medicine at Harvard.

KEY FACTS ABOUT SLEEP DISORDERS

The National Commission on Sleep Disorders Research reported that approximately 40 million Americans suffer from chronic disorders of sleep and wakefulness. Of these, it is estimated that more than 6 million Americans have a moderate to severe sleep-related breathing disorder (sleep apnea), resulting in increased daytime sleepiness, reduced productivity, increased likelihood of accidents and a higher frequency of hypertension, myocardial infarction and stroke.

Chronic insomnia afflicts more than 10 percent of adult Americans, who regularly experience difficulty falling or staying asleep at night.

Another 250,000 Americans have narcolepsy, a genetically heritable neurological sleep-wake disorder characterized by uncontrolled sleep attacks. Due to limited awareness of sleep disorders among practicing physicians, even at top schools, who receive on average between one and two hours of education in sleep in their four-year medical school curriculum - the majority of these patient groups still remain undiagnosed and untreated.

Eight million people in the U.S. regularly work at night and attempt to sleep by day, resulting in circadian misalignment and sleep disruption, with attendant reductions in industrial productivity and increased risk of accident or even catastrophe, such as the infamous grounding of the Exxon Valdez for which the National Transportation Safety Board cited crew sleep deprivation as the probable cause.

Due to the high-paced demands of modern society, relatively few Americans obtain the 8-9 hours of sleep that they need each night. This can result in chronic sleep debt, which not only interferes with glucose metabolism by increasing insulin resistance akin to what occurs in diabetes, but also degrades neurobehavioral performance and increases the risk of error and accident. It is also seen that night shift workers suffer from increased prevalence of cardiovascular and gastrointestinal illness.

Sleepiness is cited as a principal cause of more than 56,000 motor vehicle crashes annually in the United States. More than 70,000 people are injured and more than 1,500 die in those crashes. Young people in their teens and twenties, who are particularly susceptible to the effects of chronic sleep loss, are involved in more than half of the fall-asleep crashes on the nation's highways each year.

Sleep loss also interferes with the learning of young people in our nation's schools, with 60 percent of grade school and high school children reporting that they are tired during the daytime and 15 percent of them admitting to falling asleep in class.

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