Caffeine at night delays human circadian clock, new study shows

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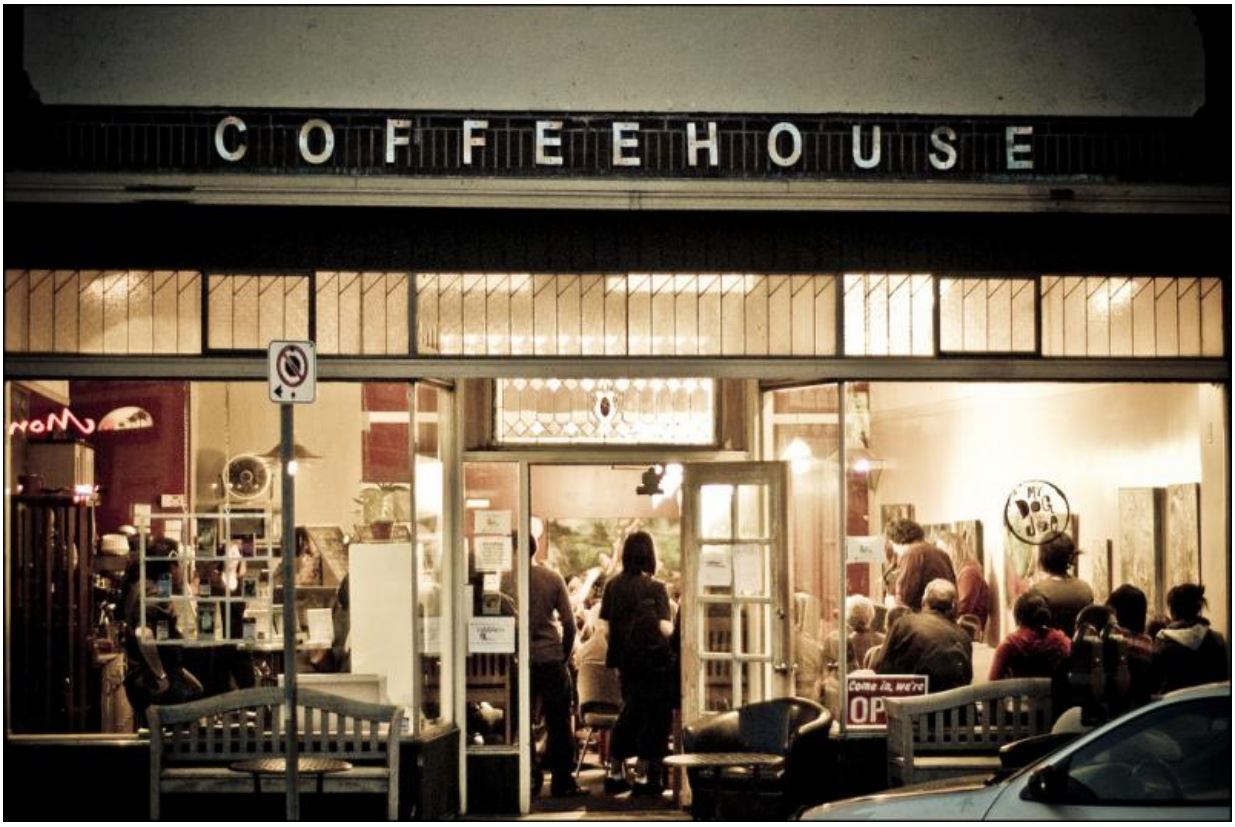

A new study led by CU-Boulder shows for the first time that caffeine in the evening can delay our our circadian clocks that tell us when ready for to sleep and for awakening. Credit: Kenneth Moyle

It's no secret that slugging down caffeinated drinks in the evening can disrupt sleep.

But a new study led by the University of Colorado Boulder and the Medical Research Council's Laboratory of Molecular Biology in Cambridge, England shows for the first time that evening caffeine delays the internal circadian clock that tells us when to get ready for sleep and when to prepare to wake up. The research team showed the amount of caffeine in a double espresso or its equivalent three hours before bedtime induced a 40-minute phase delay in the roughly 24-hour human biological clock.

The study also showed for the first time how caffeine affects "cellular timekeeping" in the human body, said CU-Boulder Professor Kenneth Wright, who co-led the study with John O'Neill of the Medical Research Council's Laboratory of Molecular Biology (LMB) in Cambridge. While it has been known that caffeine influences circadian clocks of even primitive creatures like algae and fruit flies, the new study shows that the internal clocks in human cells can be impacted by caffeine intake.

"This is the first study to show that caffeine, the mostly widely used psychoactive drug in the world, has an influence on the human circadian clock," said Wright, a professor in CU-Boulder's Department of Integrative Physiology. "It also provides new and exciting insights into the effects of caffeine on human physiology."

A paper on the subject led by Wright and O'Neill is being published online in the Sept 16 issue of *Science Translational Medicine*.

For the study the team recruited five human subjects, three females and two males, who went though a double-blind, placebo-controlled 49-day protocol through CU-Boulder's Sleep and Chronobiology Laboratory, which is directed by Wright. The subjects were tested under four conditions: low light and a placebo pill; low light and the equivalent of a 200-milligram caffeine pill dependent on the subject's weight; bright light and a placebo pill; and bright light and the caffeine pill.

Saliva samples of each participant were tested periodically during the study for levels of the hormone melatonin, which is produced naturally by the pineal gland when directed to do so by the brain's "master clock." The master clock is re-set by exposure to light and coordinates cellular clocks throughout the human body. Melatonin levels in the blood increase to signal the onset of biological nighttime during each 24-hour period and decrease at the start of biological daytime, said Wright.

Those who took the caffeine pill under low-light conditions were found to have a roughly 40-minute delay in their nightly circadian rhythm compared to those who took the placebo pill under low light conditions, said Wright. The magnitude of delay from the caffeine dose was about half that of the delay induced in test subjects by a three-hour exposure to bright, overhead light that began at each person's normal bedtime.

The study also showed that bright light alone and bright light combined with caffeine induced circadian phase delays in the test subjects of about 85 minutes and 105 minutes respectively. There were no significant differences between the dim light/caffeine combination and the bright light/placebo combination. Nor were there significant differences between the bright light/placebo and bright light/caffeine combinations. The results may indicate a "ceiling" was reached in the phase delay of the human circadian clock due to the external factors, Wright said.

In addition, researchers at O'Neill's lab at the LMB in Cambridge used "reporter" genes that made cells glow when the clock genes were expressed to measure changes caused by caffeine. O'Neill's group showed that caffeine can block cell receptors of the neurotransmitter adenosine, which normally promotes sleep and suppresses arousal.

The results may help to explain why caffeine-drinking "night owls" go to bed later and wake up later and may have implications for the treatment of some circadian sleep-wake disorders, said Wright.

The new results could benefit travelers. Properly timed caffeine use could help shift the circadian clocks of those flying west over multiple time zones, said Wright.

In a 2013 study, Wright and his research team showed one week of camping in the Rocky Mountains with no artificial light, not even flashlights, synchronized the circadian clocks of the eight study subjects with the timing of sunrise and sunset.

More information: Effects of caffeine on the human circadian clock in vivo and in vitro, *Science Translational Medicine*, stm.sciencemag.org/lookup/doi/ … scitranslmed.aac5125

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