

# Publication

Caffeine-dependent changes of sleep-wake regulation: Evidence for adaptation after repeated intake

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Background: Circadian and sleep-homeostatic mechanisms regulate timing and quality of wakefulness. To enhance wakefulness, daily consumption of caffeine in the morning and afternoon is highly common. However, the effects of such a regular intake pattern on circadian sleep-wake regulation are unknown. Thus, we investigated if daily daytime caffeine intake and caffeine withdrawal affect circadian rhythms and wake-promotion in habitual consumers. Methods: Twenty male young volunteers participated in a randomised, double-blind, within-subject study with three conditions: i) caffeine (150 mg 3 x daily for 10 days), ii) placebo (3 x daily for 10 days) and iii) withdrawal (150 mg caffeine 3 x daily for eight days, followed by a switch to placebo for two days). Starting on day nine of treatment, salivary melatonin and cortisol, evening nap sleep as well as sleepiness and vigilance performance throughout day and night were quantified during 43 h in an in-laboratory, light and posture-controlled protocol. Results: Neither the time course of melatonin (i.e. onset, amplitude or area under the curve) nor the time course of cortisol was significantly affected by caffeine or withdrawal. During withdrawal, however, volunteers reported increased sleepiness, showed more attentional lapses as well as polysomnography-derived markers of elevated sleep propensity in the late evening compared to both placebo and caffeine conditions. Conclusions: The typical pattern of caffeine intake with consumption in both the morning and afternoon hours may not necessarily result in a circadian phase shift in the evening nor lead to clear-cut benefits in alertness. The time-of-day independent effects of caffeine withdrawal on evening nap sleep, sleepiness and performance suggest an adaptation to the substance, presumably in the homeostatic aspect of sleepwake regulation.

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