

LOW-DOSE REPEATED CAFFEINE ADMINISTRATION FOR CIRCADIAN-PHASE-DEPENDENT PERFORMANCE DEGRADATION DURING EXTENDED WAKEFULNESS.

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OBJECTIVE: To investigate whether the effectiveness of a novel high-frequency low-dose caffeine regimen in counteracting the deterioration of performance during extended wakefulness is related to its interaction with homeostatic or circadian signals modulating performance and sleep propensity. **DESIGN:** Double-blind, placebo-controlled, parallel-group design in a 29-day forced desynchrony paradigm in which the period of the sleep-wake cycle was scheduled to be 42.85 hours, i.e., far removed from the circadian range. This design allowed for separate estimation of the sleep homeostatic, circadian, and caffeine contributions to performance deficits or improvements. **SETTING:** Private suite of a general clinical research center, in the absence of time of day information. **PARTICIPANTS:** Sixteen healthy normal-sleeping men (aged 18-30 years) **INTERVENTIONS:** Caffeine (0.3 mg per kg per hour) or placebo was administered hourly during the 28.57-hour wake episodes. **RESULTS:** Plasma caffeine concentrations rose in an exponential saturating manner during wakefulness. Rising caffeine levels markedly attenuated wake-dependent deterioration of a number of measures of cognitive performance, particularly at the circadian performance nadir. Moreover, caffeine enhanced the ability of subjects to remain consistently awake for extended periods, holding subjects back from completing the full transition to sleep, but at the expense of increasing subjective sleepiness. **CONCLUSIONS:** High-frequency low-dose caffeine administration is effective in countering the detrimental performance effects of extended wakefulness. These data are in accordance with the hypothesis that adenosine is a mediator of performance decrements associated with extended wakefulness and may lead to new strategies to use caffeine in situations in which neurobehavioral functioning is affected by sleep loss.