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A novel bedtime pulsatile-release caffeine formula ameliorates sleep inertia symptoms immediately upon awakening

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Abstract

Sleep inertia is a disabling state of grogginess and impaired vigilance immediately upon awakening. The adenosine receptor antagonist, caffeine, is widely used to reduce sleep inertia symptoms, yet the initial, most severe impairments are hardly alleviated by post-awakening caffeine intake. To ameliorate this disabling state more potently, we developed an innovative, delayed, pulsatile-release caffeine formulation targeting an efficacious dose briefly before planned awakening. We comprehensively tested this formulation in two separate studies. First, we established the in vivo caffeine release profile in 10 young men. Subsequently, we investigated in placebo-controlled, double-blind, cross-over fashion the formulation's ability to improve sleep inertia in 22 sleep-restricted volunteers. Following oral administration of 160 mg caffeine at 22:30, we kept volunteers awake until 03:00, to increase sleep inertia symptoms upon scheduled awakening at 07:00. Immediately upon awakening, we quantified subjective state, psychomotor vigilance, cognitive performance, and followed the evolution of the cortisol awakening response. We also recorded standard polysomnography during nocturnal sleep and a 1-h nap opportunity at 08:00. Compared to placebo, the engineered caffeine formula accelerated the reaction time on the psychomotor vigilance task, increased positive and reduced negative affect scores, improved sleep inertia ratings, prolonged the cortisol awakening response, and delayed nap sleep latency one hour after scheduled awakening. Based on these findings, we conclude that this novel, pulsatile-release caffeine formulation facilitates the sleep-to-wake transition in sleep-restricted healthy adults. We propose that individuals suffering from disabling sleep inertia may benefit from this innovative approach.Trials registration: NCT04975360.

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Figures

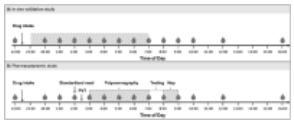

Figure 1 Illustration of the study procedures...

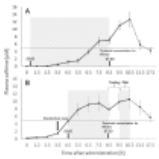

Figure 2 Evolution of the caffeine plasma...

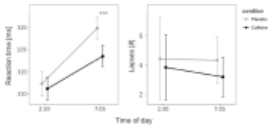

Figure 3 Median PVT reaction time (left)...

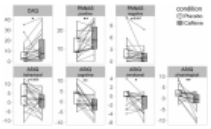

Figure 4 Post-awakening (7:15–8:00) assessments of

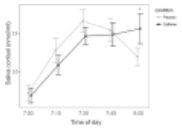

Figure 5 Salivary cortisol awakening response (CAR)....

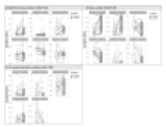

Figure 6 Visually-sored sleep variables in (...

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