Pharmacology, Biochemistry and Behavior 145 (2016) 27–32

Contents lists available at ScienceDirect

Pharmacology, Biochemistry and Behavior

journal homepage: www.elsevier.com/locate/pharmbiochembeh

Caffeine administration at night during extended wakefulness effectively mitigates performance impairment but not subjective assessments of fatigue and sleepiness

Gemma M. Paech [a,b,*], Siobhan Banks [a], Maja Pajcin [c], Crystal Grant [a], Kayla Johnson [d], Gary H. Kamimori [e], Chris B. Della Vedova [c]

[a] Centre for Sleep Research, University of South Australia, Adelaide, Australia
[b] Sleep and Performance Research Center and Elson S. Floyd College of Medicine, Washington State University Spokane, WA, United States
[c] School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, Australia
[d] Defence Science and Technology Group, Department of Defence, Edinburgh, Australia
[e] Behavioral Biology Branch, Walter Reed Army Institute for Research, Silver Spring, MD, United States

ARTICLE INFO

Article history:
Received 7 October 2015
Received in revised form 28 February 2016
Accepted 26 March 2016
Available online 7 April 2016

Keywords:
Sleep loss
Extended wakefulness
Stimulants
Caffeine
Karolinska Sleepiness Scale
Psychomotor vigilance task

ABSTRACT

The current study investigated the effects of repeated caffeine administration on performance and subjective reports of sleepiness and fatigue during 50 h extended wakefulness. Twenty-four, non-smokers aged 22.5 ± 2.9 y (mean ± SD) remained awake for two nights (50 h) in a controlled laboratory environment. During this period, 200 mg of caffeine or placebo gum was administered at 01:00, 03:00, 05:00 and 07:00 on both nights (total of 800 mg/night). Neurobehavioral performance and subjective reports were assessed throughout the wake period. Caffeine improved performance compared to placebo, but did not affect overall ratings of subjective sleepiness and fatigue. Performance and sleepiness worsened with increasing time awake for both conditions. However, caffeine slowed performance impairments such that after 50 h of wakefulness performance was better following caffeine administration compared to placebo. Caffeine also slowed the increase in subjective sleepiness and performance ratings, but only during the first night of wakefulness. After two nights of sleep deprivation, there was no difference in sleepiness ratings between the two conditions. These results demonstrate that strategic administration of caffeine effectively mitigates performance impairments associated with 50 h wakefulness but does not improve overall subjective assessments of sleepiness, fatigue and performance. Results indicate that while performance impairment is alleviated, individuals may continue to report feelings of sleepiness. Individuals who use caffeine as a countermeasure in sustained operations may feel as though caffeine is not effective despite impairments in objective performance being largely mitigated.

1. Introduction

Sustained operations—where hours of work extend past 24 h—are common within military, emergency and healthcare practices. Extended shifts involve sleep deprivation and working through the night at an adverse circadian phase, both of which are associated with various performance impairments such as decreased reaction time, vigilance and increased sleepiness (Dinges et al., 1997; Van Dongen et al., 2003; Zhou et al., 2011). These performance impairments can subsequently increase the risk of workplace incidents and accidents (Satterfield and Van Dongen, 2013). Indeed, sleep loss associated with extended shifts has been found to lead to increased risk of fatigue related incidents within the military (Lieberman et al., 2005; Tharion et al., 2003) and medical fields (Barger et al., 2006; Landrigan et al., 2004). To help mitigate performance impairments and the sleepiness and fatigue associated with working these extended shifts, countermeasures such as caffeine are frequently used.

Caffeine (1,3,7-trimethylxanthine) is a popular fatigue countermeasure partly because of its accessibility—being found in many food and beverages—and its relative safety (Fredholm et al., 1999; Nehlig, 1999). Caffeine (up to 600 mg) has been shown to effectively mitigate performance impairments during and following extended wakefulness (Lieberman et al., 2002; Wesensten et al., 2002, 2004, 2005). However, frequent use of caffeine may lead to tolerance, thereby reducing its efficacy (Evans and Griffiths, 1992). Strategic administration of caffeine during critical time points, such as the early morning hours when alertness is low (Wyatt et al., 1999; Zhou et al., 2011), may help to maximize the benefits of caffeine. Indeed, a repeated, moderate dose of caffeine (up to 200 mg) during the early morning hours may be more effective in mitigating performance impairments than a single high dose

* Corresponding author at: Sleep and Performance Research Center, PO Box 1495, Spokane, WA 99210, United States.
E-mail address: gemma.paech@wsu.edu (G.M. Paech).

http://dx.doi.org/10.1016/j.pbb.2016.03.011
0091-3057/

(e.g., 600 mg) during extended wakefulness (Kamimori et al., 2005; Killgore et al., 2007, 2011).

Although caffeine has been widely researched there is limited information regarding repeated caffeine administration and different cognitive measures, in particular its effects on subjective assessments of fatigue and sleepiness. In the workplace, subjective assessments of sleepiness and fatigue are frequently used to monitor impairment, with employers or managers often relying on an individual to report feelings of sleepiness and fatigue before they compromise safety. These subjective reports of sleepiness capture an individual's personal experience, which is what, perhaps more so than objective performance, may prompt them to complain of sleepiness and/or fatigue while working extended shifts and may led them to feel as though they are impaired (Oonk et al., 2008). Importantly, under conditions of sleep loss, individuals are often unable to accurately assess their performance capacity using subjective assessments of sleepiness and fatigue (Van Dongen et al., 2003; Zhou et al., 2012). As caffeine is such a ubiquitous countermeasure, it is important to know how it impacts the ability to self-monitor fatigue under conditions of extended sleep deprivation.

Therefore, the current study aimed to assess the effect of repeated caffeine administration on neurobehavioral performance and subjective assessments of sleepiness and fatigue. Investigating the effects of caffeine on both objective and subjective measures of sleepiness and fatigue may help better improve the self-monitoring of fatigue.

2. Methods and materials

2.1. Participants

A total of 24 non-smokers aged 22.5 ± 2.9 y (mean ± SD) participated in the study. Participants were physically and psychologically healthy as assessed by a general health questionnaire and normal blood chemistry (toxicology screen). All participants were low to moderate consumers of alcohol (<7 standard drinks/week) and caffeine (<250 mg caffeine/day; equivalent of <2 cups coffee/day). With the exception of three females who reported taking oral contraceptives, all participants were free from medications. Participants reported having regular sleep wake patterns with an average total sleep time (TST) of 7.3 ± 0.7 h, verified with sleep diaries and activity monitors (Actiwatch 2, Philips Respironics, Bend OR). In the three months prior to the study, participants had not undertaken any transmeridian travel or shiftwork. One week prior to the study, participants abstained from caffeine and alcohol, and maintained a regular sleep-wake schedule with a minimum of 8 h time in bed (TIB) which was confirmed with sleep diaries and activity monitors. One week of caffeine abstinence has been shown to be sufficient in reducing the effects of withdrawal (James, 2014).

The study had approval from the University of South Australia Human Ethics Research Committee, using guidelines established by the National Health and Medical Research Council of Australia. Participants were made aware that participation was completely voluntary and that they could withdraw at any time. All gave written consent to participate in the study. Upon completion of the study, participants were financially compensated for their time spent in the laboratory.

2.2. Study design

The study was a double-blind with participants randomly assigned to either a caffeine (n = 12 [4F]; age 22.5 ± 3.3 y; body mass index [BMI] 21.7 ± 1.5 kg/m^2) or placebo (n = 12 [5F]; age 22.5 ± 2.5 y; BMI 22.3 ± 2.1 kg/m^2) condition. Participants entered the laboratory at approximately 12:00 h on day one at which time they were familiarized with the laboratory and neurobehavioral tasks. Following a 10 h baseline sleep, participants underwent 50 h of continuous wakefulness. The 10 h sleep opportunity was included to ensure that participants had sufficient sleep (at least 8 h) such that they were not suffering from any prior sleep loss at the start of the sleep deprivation period. Caffeine or placebo gum was administered at 01:00 h, 03:00 h, 05:00 h and 07:00 h. Prior to leaving participants were given a 9 h daytime recovery sleep. The study design is demonstrated in Fig. 1. Results from sleep episodes are reported in Paech et al. (2015).

Neurobehavioral performance tests were administered at regular intervals throughout wake periods (Fig. 1) as described below. It should also be noted that while the current study involved a total of 50 h wakefulness, measures of performance and subjective sleepiness were only taken up until 46 h of wakefulness. This was primarily to allow for pre-sleep procedures, such as application of electrodes (for measuring sleep). Meals were provided for participants approximately every 6 h. During free time, participants could watch DVD's, play games (board/card), chat amongst themselves/with experimenters, read, or listen to music. Participants refrained from physical activity except if they were struggling to remain awake, when casual walking was allowed within the laboratory. Participants were continuously monitored (excluding toilet breaks) to ensure they did not sleep during scheduled wake periods. Participants were required to remain in the laboratory for the entire duration of the study.

Throughout the study light intensity at angle of gaze was <50 lx during wake periods and <0.03 lx (i.e., complete darkness) during scheduled sleep episodes, and ambient temperature was 23 ± 1 °C. Participants completed the protocol in groups of four, with each participant assigned an individual bedroom/testing suite. Participants ate all meals within a shared area. Participants were not exposed to clocks or social time cues (e.g., internet, mobile phones, real-time television) and were unaware of the time.

2.3. Caffeine administration

Caffeine or placebo was administered as two pieces of Military Energy Gum (MarketRight INC, Plano, IL) containing caffeine (100 mg/piece; a total of 200 mg, similar to the amount of caffeine found in a 16 oz drip coffee) or no caffeine (placebo). The caffeine and placebo gum were identical in appearance and flavour ('Artic Mint'). Participants were instructed to chew both pieces of gum simultaneously for a minimum of 5 min before disposing, allowing at least 85% of caffeine to be released (Kamimori et al., 2002).

2.4. Neurobehavioral performance

Participants completed two neurobehavioral test batteries; a full neurobehavioral test battery (fNTB) which lasted approximately 30 min, and a brief neurobehavioral test battery (bNTB), which lasted approximately 5 min. During day 1, participants became familiarized with the test batteries (Fig. 1), with data from these initial tests were used to establish baseline levels. The bNTB began 1 h after waking and was administered every 3 h, while the fNTB began 2 h after waking and was administered approximately every 5 h (Fig. 1). Details about the specific tests are included below.

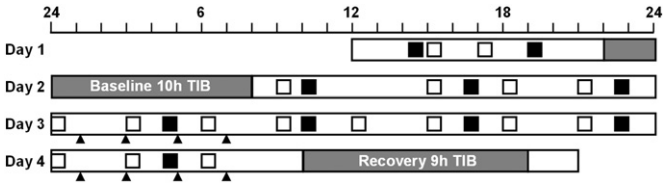

Fig. 1. Schematic of the four day protocol. Grey bars represent scheduled sleep episodes and open bars represent scheduled wake periods. Black squares represent the full neurobehavioral test battery (fNTB; 10 min PVT, DSST, subjective scales) and open squares represent the brief neurobehavioral test battery (bNTB; PVT-B, subjective scales). Black triangles show the timing of the caffeine or placebo administration.