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

Running title: Caffeine, sleep loss and performance

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Abstract

The current study investigated the effects of repeated caffeine administration on performance and subjective reports of sleepiness and fatigue during 50h extended wakefulness. Twenty-four, non-smokers aged 22.5 ± 2.9 y (mean $\pm$ SD) remained awake for two nights (50h) in a controlled laboratory environment. During this period, 200mg of caffeine or placebo gum was administered at 01:00, 03:00, 05:00 and 07:00 on both nights (total of 800mg/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 50h 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 50h 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.

Keywords: sleep loss, extended wakefulness, stimulants, caffeine, Karolinska Sleepiness Scale, Psychomotor vigilance task

1. Introduction

Sustained operations—where hours of work extend past 24h—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 600mg) has been shown to effectively mitigate performance impairments during and following extended wakefulness (Lieberman et al., 2002; Wesensten et al., 2002; Wesensten et al., 2004; Wesensten et al., 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 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 200mg) during the early morning hours may be more effective in mitigating performance impairments than a single high dose (e.g., 600mg) during extended wakefulness (Kamimori et al., 2005; Killgore et al., 2007; Killgore et al., 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 $\pm$ 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 8h 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/m²) or placebo ($n=12$ [5F]; age 22.5 ± 2.5 y; BMI 22.3 ± 2.1 kg/m²) condition. Participants entered the laboratory at approximately 12:00h on day one at which time they were familiarised with the laboratory and neurobehavioral tasks. Following a 10h baseline sleep, participants underwent 50h of continuous wakefulness. The 10h sleep opportunity was included to ensure that participants had sufficient sleep (at least 8h) 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 01:00h, 03:00h, 05:00h and 07:00h. Prior to leaving participants were given a 9h daytime recovery sleep. The study design is demonstrated in Figure 1. Results from sleep episodes are reported in Paech et al. (In Press).

Neurobehavioral performance tests were administered at regular intervals throughout wake periods (Figure 1) as described below. It should also be noted that while the current study involved a total of 50h wakefulness, measures of performance and subjective sleepiness were only taken up until 46h 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 6h. 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 lux during wake periods and <0.03 lux (i.e., complete darkness) during scheduled sleep episodes, and ambient temperature was $23 \pm 1^{\circ}\text{C}$. 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.

Insert Figure 1

2.3. Caffeine administration

Caffeine or placebo was administered as two pieces of Military Energy Gum (MarketRight INC, Plano, IL) containing caffeine (100mg/piece; a total of 200mg, similar to the amount of caffeine found in a 16oz 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 5min 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 30min, and a brief neurobehavioral test battery (bNTB), which lasted approximately 5 min. During day 1, participants became familiarized with the test batteries (Figure 1), with data from these initial tests were used to establish baseline levels. The bNTB began 1h after waking and was administered every 3h, while the fNTB began 2h after waking and was administered approximately every 5h (Figure 1). Details about the specific tests are included below.

2.4.1. Full neurobehavioral test battery

The fNTB consisted of a 10min psychomotor vigilance task (PVT) (Dinges and Powell, 1985; Doran et al., 2001), standard digit symbol substitution test (DSST) (Wechsler, 1981), Karolinska Sleepiness Scale (KSS) (Åkerstedt and Gillberg, 1990), a 9-point Likert scale assessing subjective sleepiness and a 7-point Likert scale assessing subjective performance.

The PVT is a simple reaction time (RT) task which is sensitive to the effects of sleep deprivation and is considered a standard measure of the effects of sleep deprivation (Dorrian et al., 2005). Participants were required to respond by pressing a button with their dominant thumb as quickly as possible to a visual stimulus (millisecond counter) displayed on a computer screen. The stimulus was presented at random intervals of 2-10secs (i.e., inter-stimulus interval). Participants were required to respond as quickly as possible to the stimulus whilst avoiding anticipating when the stimulus would appear (false

starts). Outcome measures included the number of PVT lapses (RT >500ms) and the fastest 10% PVT RT (i.e., top 10% of RT).

The DSST was a 3min computerised version of the cognitive performance test in the Wechsler Adult Intelligence Scale of the same name (Wechsler, 1981). In this task, participants are required to match numbers (1-9) with a series of randomly presented symbols based on a code displayed at the top of the screen. Participants were instructed to respond accurately, but as quickly as possible. The outcome measure was the number of correct responses.

The KSS is a standard measure of subjective sleepiness (Åkerstedt and Gillberg, 1990). This is a 9 point Likert-type scale on which participants were required to rate their sleepiness ranging from 1 (“extremely alert”) to 9 (“very sleepy, great effort to stay awake”). Participants rated their exhaustion on a 9-point Likert scale ranging from 1 (“physically exhausted”) to 9 (“energetic”). At the end of the fNTB participants rated their performance on a 7-point Likert scale ranging from 1 (“extremely good”) to 7 (“extremely poor”).

2.4.2. Brief neurobehavioral test battery

The bNTB consisted of a brief 3min PVT (PVT-B) (Basner et al., 2011) and a 10 point sleepiness Likert-type scale. The PVT-B is a validated (Basner et al., 2011) shorter version of the PVT (explained above), which is performed on a hand-held device (PVT-192; Ambulatory Monitoring Inc., Ardsley, NY, USA). As above, participants were required to respond as quickly as possible to a visual stimulus, whilst avoiding false starts, by pressing a button on the hand-held device. The inter-stimulus interval was 1-4secs. The outcome measures for the PVT-B were the number of PVT-B lapses (RT >355ms) and the PVT-B fastest 10% RT. The sleepiness scale was performed on the same PVT-B device. Participants were required to rate if they felt sleepy (1=“no”) or not (10=“yes”).

In operational settings, a 10min task to test performance may not always be feasible, and so in these situations, a shorter version such as the PVT-B can be used to test performance while minimising the time required for the task. It should be noted that the definition for lapses for the PVT-B are different for that of the PVT. This is due to an overall shorter time on task (Basner et al., 2011).

2.5. Statistical Analyses

All data were analysed using SPSS v.21 for Windows. Separate mixed model analyses were performed to assess the main and interaction effects of hours of wakefulness (“wakefulness”) and “condition” (caffeine or placebo) on neurobehavioral tests and subjective assessments of sleepiness and fatigue, as mentioned above. Where a significant interaction effect between “wakefulness” and “condition” was found, separate mixed models were performed on each condition to assess the main effect of “wakefulness”. Where appropriate, pairwise comparisons were used to compare caffeine to

1 placebo for each time point. Significance was assumed at $p \leq 0.05$. All data are reported as mean $\pm$ SD
2 unless indicated otherwise.

3. Results

3.1. Cognitive performance

3.1.1. PVT

7 There was a main effect of wakefulness ($F_{(8,176)}=20.8$, $p < 0.001$) and condition ($F_{(1,22)}=15.9$, $p < 0.001$)
8 on PVT lapses. On average, PVT lapses increased with increasing wakefulness (Figure 2) and there
9 were more PVT lapses in the placebo condition (12.1 ± 13.8) compared to the caffeine condition
10 (3.23 ± 5.4). There was an interaction effect between wakefulness and condition ($F_{(8,176)}=10.5$,
11 $p < 0.001$) on PVT lapses. Separate analyses of the two conditions revealed a main effect of
12 wakefulness for both the placebo ($F_{(8,88)}=18.8$, $p < 0.001$) and caffeine ($F_{(8,88)}=4.6$, $p < 0.001$) conditions
13 on PVT lapses. Figure 2 demonstrates significant differences observed between the two conditions as
14 determined by pairwise comparisons. In the placebo condition, PVT lapses increased with increasing
15 wakefulness, with the exception of a decline during the afternoon and evening (32.5h and 38.5h
16 wakefulness) while PVT lapses were fairly stable across all hours of wakefulness in the caffeine
17 condition (Figure 2).

18 There was a main effect of wakefulness ($F_{(8,176)}=26.1$, $p < 0.001$) and condition ($F_{(1,22)}=9.93$, $p < 0.01$) on
19 fastest 10% RT. On average, participants performed worse with increasing wakefulness (Figure 2) and
20 on average, performed poorer in the placebo condition (233.5 ± 31.6) compared to caffeine condition
21 (213.2 ± 20.2). There was a main interaction effect between wakefulness and condition ($F_{(8,176)}=7.1$,
22 $p < 0.01$) on fastest 10% RT. Separate analyses of the two conditions showed a main effect of
23 wakefulness for both the placebo ($F_{(8,88)}=20.6$, $p < 0.001$) and caffeine ($F_{(8,88)}=6.5$, $p < 0.001$) conditions
24 on fastest 10% RT. Figure 2 demonstrates significant differences observed between the two
25 conditions as determined by pairwise comparisons. In the placebo condition, fastest 10% RT
26 gradually increased after approximately 20.5h of wakefulness, while fastest 10% RT remained
27 relatively stable in the caffeine condition (Figure 2).

3.1.2. DSST

29 On average, the number of correct responses on the DSST decreased with increasing wakefulness
30 (Figure 2), with a main effect of wakefulness ($F_{(8,176)}=7.0$, $p < 0.001$). Overall, the number of correct
31 responses did not significantly differ between the placebo (97.4 ± 15.8) and caffeine (104.1 ± 11.6)
32 conditions, with no main effect of condition ($F_{(1,22)}=2.1$, $p=0.2$). There was an interaction effect
33 between wakefulness and condition ($F_{(8,176)}=3.7$, $p < 0.01$) on DSST correct responses. Separate
34 analyses of the two conditions showed a main effect of wakefulness for the placebo ($F_{(8,88)}=20.6$,

$p<0.001$) condition but not for the caffeine ($F_{(8,88)}=6.5$, $p<0.001$) condition. Figure 2 demonstrates significant differences observed between the two conditions as determined by pairwise comparisons.

Insert Figure 2

3.1.3. PVT-B

There was a main effect of wakefulness on the PVT-B lapses ($F_{(15,330)}=5.5$, $p<0.001$) and PVT-B fastest 10% RT ($F_{(15,330)}=5.3$, $p<0.001$). On average, the number of lapses and the PVT-B fastest 10% RT increased with hours of wakefulness (Figure 3). There was a main effect of condition on PVT-B lapses ($F_{(1,22)}=6.5$, $p<0.05$) but not for PVT-B fastest 10% RT ($F_{(1,22)}=3.7$, $p=0.07$). On average, there were fewer PVT-B lapses in the caffeine condition (3.0 ± 3.6) compared to the placebo condition (6.9 ± 8.0). On average, the PVT-B fastest 10% RT was similar between the placebo (183.6 ± 19.1) and caffeine conditions (173.7 ± 17.0). There was an interaction effect between wakefulness and condition for PVT-B lapses ($F_{(15,330)}=3.7$, $p=0.07$). Separate analyses of the two conditions revealed a main effect of wakefulness for both the placebo ($F_{(15,165)}=9.3$, $p<0.001$) and caffeine ($F_{(15,165)}=2.7$, $p<0.001$) conditions. There was an interaction effect between wakefulness and condition for PVT-B fastest 10% RT ($F_{(1,22)}=3.7$, $p=0.07$). Separate analyses of the two conditions revealed a main effect of wakefulness for both the placebo ($F_{(15,165)}=9.3$, $p<0.001$) and caffeine ($F_{(15,165)}=2.7$, $p<0.001$) conditions. Figure 3 demonstrates significant differences observed between the two conditions as determined by pairwise comparisons.

Insert Figure 3

3.2. Subjective assessments

For all subjective measures of sleepiness and fatigue there was a main effect of wakefulness (KSS, $F_{(8,176)}=40.2$, $p<0.001$; performance, $F_{(8,176)}=9.3$, $p<0.001$; exhaustion, $F_{(8,176)}=26.5$, $p<0.001$; sleepiness, $F_{(15,330)}=17.0$, $p<0.001$) but not of condition (KSS, $F_{(1,22)}=0.7$, $p=0.4$; performance, $F_{(1,22)}=0.3$, $p=0.6$; exhaustion, $F_{(1,22)}=0.2$, $p=0.6$; sleepiness, $F_{(1,22)}=0.3$, $p=0.6$). On average, all subjective measures worsened with increasing wakefulness (Figure 2 and Figure 3), and there was no significant difference in mean scores between placebo (KSS, 5.5 ± 2.4 ; performance, 4.1 ± 1.3 ; exhaustion, 4.4 ± 2.4 ; sleepiness, 5.8 ± 2.8) and caffeine (KSS, 5.2 ± 2.1 ; performance, 3.9 ± 1.3 ; exhaustion, 4.6 ± 2.0 ; sleepiness, 5.4 ± 2.6) conditions.

There was an interaction effect between wakefulness and condition on KSS ($F_{(8,176)}=4.2$, $p<0.001$) and performance ($F_{(8,176)}=3.1$, $p<0.01$) scores. Separate analyses of the two conditions revealed a main effect of wakefulness for both the placebo (KSS, $F_{(8,88)}=21.8$, $p<0.001$; performance, ($F_{(8,88)}=2.4$,

$p < 0.05$) and control (KSS, $F_{(8,88)} = 22.8$, $p < 0.001$; performance, ($F_{(8,88)} = 10.5$, $p < 0.001$)) conditions. Figure 2 demonstrates significant differences observed between the two conditions as determined by pairwise comparisons. For both KSS and performance, scores were lower during the first night for the caffeine condition (Figure 2). There was no interaction effect between wakefulness and condition on exhaustion ($F_{(8,176)} = 1.8$, $p = 0.07$) and sleepiness ($F_{(15,330)} = 1.4$, $p = 0.1$) scores.

4. Discussion

The current study assessed the effect of repeated caffeine administration on neurobehavioral performance and subjective assessments of sleepiness and fatigue. In concordance with previous work (Kamimori et al., 2005; Killgore et al., 2007; Killgore et al., 2011), findings demonstrate that strategic use of caffeine during the early morning hours effectively mitigates performance impairments during 50h of wakefulness. While caffeine reduced subjective sleepiness and performance on the first night, caffeine administration on the second night of sleep deprivation did not improve subjective ratings. These results demonstrate that while caffeine may be protective against performance impairment, it is less protective in regards to feelings of sleepiness and fatigue.

The early morning hours can be a particularly risky time for individuals working sustained operations (Åkerstedt, 2003; Satterfield and Van Dongen, 2013) with this time of day associated with poor performance and increased errors (Zhou et al., 2011), as also demonstrated in the placebo condition in the current study (Fig. 2). Results show that repeated administration of caffeine was effectively able to mitigate performance impairments on both the PVT (10min) and PVT-B during the early morning hours, supporting earlier findings (Kamimori et al., 2005; Killgore et al., 2007; Killgore et al., 2011). Although caffeine was not administered during the daytime, performance remained relatively stable in the caffeine condition and showed some improvement in the placebo condition (Fig 2). This is most likely due to a strong circadian drive for wakefulness which has been shown to maintain performance even under conditions of sleep loss (Zhou et al., 2011).

Important to note, after approximately 38h wakefulness, performance worsened slightly in the caffeine condition (Fig 2). While the increase in performance impairments was only small, compared to the placebo condition, this demonstrates that although caffeine is an effective fatigue countermeasure, it has its limits. This study confirms that strategic caffeine administration during the early morning hours is not only an effective fatigue countermeasure for this critical time frame, but can help in mitigating impairments throughout an extended shift period, common to sustained operations.

Although caffeine was able to reduce performance impairments associated with extended wakefulness, it was less effective at alleviating feelings of sleepiness and fatigue. During the first night of sleep loss caffeine was able to reduce feelings of sleepiness and fatigue. Similarly, caffeine

maintained subjective performance assessments at near baseline levels, but only during the first night. This effect diminished around 26h of wakefulness after which there were no differences between the placebo and caffeine groups. Some studies have shown that subjective sleepiness is sensitive to caffeine (Lieberman et al., 1987; Lieberman et al., 2002; Patat et al., 2000) however our results are similar to those by Kamimori et al., (2005) and suggest the effects of caffeine on subjective sleepiness and performance are short-lived.

Even though caffeine was able to alleviate performance impairments on the PVT, caffeine did not appear to improve overall performance on the DSST. The DSST is known to display a practice effect across repeated test bouts (Tucker et al., 2010; Van Dongen et al., 2003) and although participants did practise the task, this continued learning (for both conditions) may explain why there was less of an effect of caffeine on overall DSST performance. However, this finding could also be explained by the sensitivity of the tasks to sleep loss. Simple tasks such as the PVT have been shown to be highly sensitive to sleep loss, while other more complex tasks such as those involving decision making seem to be less affected (Lim and Dinges, 2010). Studies by Killgore et al., (2007; 2012) found that caffeine did not improve participants' ability to make decisions during sustained wakefulness. As such, while caffeine may be a beneficial countermeasure for some tasks, it may not reliably alleviate the effects of sleep loss on more complex cognitive functions. In industries where it may be necessary to perform complex cognitive tasks while sleep deprived (e.g., the military, medical and emergency services), individuals need to be aware that caffeine may be less effective in minimising the effects of sleep loss on these more complex cognitive processes.

It is important to note that the current study was conducted in controlled laboratory environment with healthy individuals. Shift workers were excluded because their shift schedules vary greatly, which differentially impacts their sleep (Åkerstedt, 2003; Paech et al., 2014). Many shift workers are older and some habitually consume more caffeine than the participants in the current study. This might affect tolerance and sensitivity to caffeine (Evans and Griffiths, 1992; James, 2014). Shift workers may also be more sleepy and fatigued as they are regularly exposed to sleep loss and may not always be able to recover (Banks et al., 2010; Lamond et al., 2007). Future studies should examine the effects of caffeine in shift workers, those who work in sustained operations and those who habitually consume caffeine to validate the effects of caffeine in real world environments. Finally, while the aims of the current study were to investigate how multiple administrations of a single dose of caffeine during critical time points affected performance and subjective ratings, it is important to note that as only a single dose of caffeine compared to placebo was evaluated the current study does not provide multiple dose-related effects.

4.1. Conclusions

In conclusion, this study demonstrates that strategic use of caffeine during the early morning hours effectively mitigates performance impairments during 50h of wakefulness. However while

1 performance was improved, caffeine did not reduce subjective ratings of sleepiness, fatigue, or
2 perceived performance during the entire period of wakefulness. Results indicate that while
3 performance impairment is alleviated, individuals may continue to report feelings of sleepiness and
4 fatigue. Individuals who use caffeine as a countermeasure in sustained operations may feel as though
5 caffeine is not ‘working’ despite objective performance impairments being largely mitigated.

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Figure captions

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; 10min 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.

Fig. 2. Effect of caffeine (●) or placebo (○) gum on fNTB neurobehavioral performance and subjective sleepiness, performance and fatigue ratings as a function of hours of wakefulness. Objective assessments are shown on the left panel and subjective assessments on the right panel. Data represent mean±SE. Grey shading represents the timing of caffeine or placebo administration (01:00h, 03:00h, 05:00h and 07:00h on both nights). Zero hours of wakefulness represents baseline data from tests performed on Day 1. A) shows 10min psychomotor vigilance task (PVT) lapses (reaction times >500ms), B) shows 10min PVT fastest 10%, C) shows digit symbol substitution (DSST) correct responses, D) shows Karolinska sleepiness scale (KSS) ratings where 1= “very alert” and 9= “very sleepy, great effort to stay awake, fighting sleep”, E) shows ratings from a 7-point Likert scale where 1= “extremely good” and 7= “extremely poor”, and F) shows ratings from a 9-point Likert scale where 1= “physically exhausted” and 9= “energetic”. Note that for A, B, D and E higher scores represent worse performance and subjective assessments, whereas for C and F lower scores represent impaired performance/subjective assessments. Asterisks denote significant ($p<0.05$) difference between caffeine and placebo conditions.

Fig. 3. Effect of caffeine (●) or placebo (○) gum on bNTB neurobehavioral performance and subjective sleepiness as a function of hours of wakefulness and time of day. Data represent mean±SE. Grey shading represents the timing of caffeine or placebo administration (01:00h, 03:00h, 05:00h and 07:00h on both nights). Zero hours of wakefulness represents baseline data from tests performed on Day 1. The top panel shows brief psychomotor vigilance task (PVT-B) lapses (reaction times >355ms), the middle panel shows PVT-B fastest 10% and the bottom panel shows subjective feelings of sleepiness where 1=“no” (I do not feel sleepy) and 10=“yes” (I feel sleepy). Asterisks denote significant ($p<0.05$) difference between caffeine and placebo conditions.

Figure 1

Figure 2

Figure 3