Effects of Different Sources of Low-Dose Caffeine on Mood/Arousal and Cognitive Performance

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Abstract

In this study we investigated the effects of variously derived sources of low-dose caffeine on mood/arousal and cognitive performance. Twenty-two participants (15 men, 7 women; *M* age: 28.2, *SD* = 9.0 years) undertook five randomized, crossover trials in which they consumed either a water control (CON) or 80 mg of caffeine from one of four sources (coffee [COF], energy drink [END], capsule [CAP], and dissolvable mouth strip [STR]). We measured the participants' perceived efficacy of these varied caffeine sources pre-treatment; and we measured mood/arousal pre-treatment, and again at 15 and 45 minutes post-treatment. We also measured choice reaction-time at 15 and 45 minutes post-treatment, and participants completed the psychomotor vigilance task (PVT) 45 minutes post-treatment. Caffeine increased participant ratings of alertness and decreased their ratings of tiredness irrespective of source (*p*'s < .05), and all sources of caffeine decreased reaction time on the PVT (*p*'s < .05), with *ex*-Gaussian distributional analysis localizing this to the *tau*-parameter, indicating lower variability. However, only the COF source was associated with improved 'overall mood' (*p*'s < .05). Participants expected to perform better on the PVT with COF compared to CON, but there were no other significant associations between source expectancy and performance. In sum, a modest dose of caffeine, regardless of source, positively impacted mood/arousal and cognitive performance, and these effects did not appear to be influenced by expectations.

Keywords

Caffeinated, Cognitive Function, Vigilance, Expectancy

Introduction

Caffeine has a long history of use as a mild stimulant, and it is arguably the world's most commonly consumed psychoactive substance (Cappelletti et al., 2015). Its behavioral effects are well recognized, including positive changes to mood/affective state (e.g. reducing tiredness/fatigue, increasing physical arousal/alertness (Nehlig, 2010; Ruxton, 2008)) and enhanced performance on cognitive tasks requiring attention, vigilance and rapid responses (McLellan et al., 2016). In fact, many individuals consume caffeine precisely for these reasons, especially upon waking from sleep and prior to undertaking daily activities (Ágoston et al., 2018). The beneficial effects of caffeine have been demonstrated even at relatively low (e.g., 40 mg) doses (McLellan et al., 2016). These effects have seemed to be independent of gender, age, whether caffeine intake has been habitual (Smith, 2002), or whether participants have been well-rested (Irwin et al., 2020).

The main dietary sources of caffeine are coffee, tea, cocoa products (e.g., chocolate), and beverages such as cola products and energy drinks (Fulgoni et al., 2015). However, other 'non-conventional' caffeine sources include sports gels, chewing gums, nasal/oral aerosols and dissolvable mouth strips (Wickham & Spriet, 2018). These products have been manufactured for consumer convenience, especially in contexts where traditional sources of caffeine may not be practical (e.g., during exercise and military operations). Despite the wide array of available caffeinated products, most studies exploring caffeine effects on mood and cognitive performance have manipulated caffeine content of either a beverage (e.g., coffee vs decaffeinated coffee) or a capsule/tablet (Irwin et al., 2020; Ruxton, 2008). The efficacy of other 'non-conventional' sources has not been well researched (Wickham & Spriet, 2018).

Peak plasma caffeine concentrations (C_{max}) have typically been observed within 120 minutes following oral ingestion (Mumford et al., 1996). When consumed in foods/beverages or capsule form, caffeine is primarily absorbed via the gastrointestinal tract (Wickham &

Spriet, 2018). However, when suspended in the mouth (as is the case with gum and dissolvable mouth strips), caffeine has greater exposure to the highly vascularized oral mucosa (Zhang et al., 2002) and is absorbed more rapidly (Kamimori et al., 2002; Morris et al., 2019). Indeed, although gum and mouth strips expose consumers to similar total and maximum amounts of caffeine, these sources, with their greater oral bioavailability, more quickly elicit C_{max} (Kamimori et al., 2002). These products may therefore produce more rapid pharmacological effects and may be advantageous in situations where quick behavioral changes are desired.

Possible psychological moderations of caffeine effects relate to participants' beliefs regarding source efficacy (Shabir et al., 2018). Such beliefs may be formed through prior experience and/or exposure to advertising material and cultural tradition. Indeed, evidence from drug studies suggests that expectancies are an important determinant of the drug experience (Kirsch, 1999). However, research investigating the perceived efficacy of different caffeine sources and its influence on caffeine-related mood and cognitive performance is currently lacking. We expect data from this study to improve our understanding of caffeine's overall mechanism/s of action and to provide support for practical caffeine recommendations.

Therefore, we sought to investigate: (a) the effects of consuming the same amount of caffeine from different caffeine sources (i.e., coffee, energy drink, capsule, dissolvable mouth strip); and (b) participants' expectations of source efficacy on both mood/arousal and cognitive function (i.e., vigilance, reaction-time). We hypothesized that, irrespective of source, caffeine would improve participants' mood/arousal (e.g., increase alertness, reduce tiredness) and cognitive function, but the magnitude of improvement (relative to a 'no caffeine' control condition) would vary with participants' expectations of caffeine source efficacy.

Method

Study design

We employed a randomized, controlled, crossover study design in which participants completed five experimental trials (within-subjects design) involving the oral administration of either a water control (CON) or 80 mg caffeine from one of four sources: (a) coffee (COF); (b) energy drink (END); (c) capsule (CAP); and (d) dissolvable mouth strip (STR). While there is some evidence to suggest that lower doses of caffeine (e.g., ~30 mg) can elicit positive effects on mood and cognitive function (Guest et al., 2021; McLellan et al., 2016), we selected a dose of 80 mg on a pragmatic basis and to maximize ecological validity from a consumer perspective (e.g., 80 mg caffeine is present in a single can of Red Bull® energy drink (250 ml) and in one dissolvable Revvies™ mouth-strip, and 80 mg is the approximate dose provided in one cup of instant coffee (McLellan et al., 2016; Ruxton, 2008). Caffeine consumption trials were separated by a washout period of ≥4 days. Our research protocol was approved by the University's Human Research Ethics Committee (GU Ref No: 2019/619) and conducted in accordance with the Declaration of Helsinki (1983); and all participants provided their written informed consent.

Participants

We recruited participants using a mixture of convenience and snowball sampling, including general advertisement via a University broadcast email, presentations to university classes, posting of flyers on campus noticeboards, and posts on relevant social media (e.g. Facebook pages/Twitter). Twenty-two volunteer participants completed this study (15 men, 7 women; *M* age = 28.2, *SD* = 9.0 years; *M* weight = 75.6, *SD* = 10.7 kg; *M* body mass index [BMI] = 24.7, *SD* = 2.8). Potential volunteers completed an online screening form (which also

contained informed consent procedures) in the Research Electronic Data Capture (RedCap®) system. The form included items that elicited participants' demographic information and their estimated usual sleep duration. It also included a medical history and caffeine consumption questionnaire, and the Pittsburgh Sleep Quality Index (PSQI) which has been found to be a valid and reliable means of gathering self-perceived daytime sleepiness (Buysse et al., 1989). Inclusion criteria for this study were habitual low to moderate dose caffeine consumption (between 40 and 400 $mg \cdot day^{-1}$ from food and beverages), ≥18 years of age, and normal self-reported sleep patterns (i.e., ≥7 hours of $sleep \cdot night^{-1}$ and a PSQI score ≤5). We excluded from this study those individuals who self-reported a psychiatric disorder, head trauma or other central nervous system injury, and/or recent use of recreational drugs or psychoactive medications (e.g., benzodiazepines).

Pre-Experimental Procedures

Eligible participants attended an initial familiarization session in which they practiced each cognitive function task once, while seated comfortably in a quiet room. Participants also completed the 47-item caffeine expectancy questionnaire (CaffEQ) (Huntley & Juliano, 2012), with scores on the "Energy/work enhancement" and "Social/mood enhancement" subscales calculated to provide an indication of participants' general expectations regarding caffeine's capacity to elicit positive effects on these domains. A separate questionnaire was used to ascertain: (a) frequency of using the different caffeine sources employed in the study (5-point Likert scale: *"Never", "Daily", "Weekly", "Monthly", "Yearly"*); (b) whether participants had ever consumed caffeine to enhance cognitive performance (*"Yes/No"*); and (c) the source/s of caffeine previously used for this purpose. Upon their completion of these tasks, we used a pre-populated randomization schedule to assign participants to one of ten possible treatment (i.e., caffeine source consumption) orders. The ten orders constituted a balanced Latin square

and the schedule was generated using the website Randomization.com (http://www.randomization.com).

Experimental procedures

An overview of the experimental procedures is provided in Figure 1. Participants were instructed to arrive at the laboratory at ~7:00 AM following an overnight fast from all food and beverages (except water), abstaining from alcohol for ≥24 hours and from caffeine for ≥12 hours, having done no exercise that morning, and having spent at least eight hours in bed the previous night.

On arrival to the laboratory, participants verbally acknowledged compliance with these pre-trial standardization procedures; and they estimated the duration of their previous nights' sleep. We verified alcohol abstinence using a calibrated breathalyzer (Alcolizer LE5, Alcolizer Pty Ltd, Australia), and we collected a urine sample to determine hydration status (UG-α®, ATAGO Co. Ltd, Japan). If urine specific gravity (U_{SG}) was >1.024, indicating some degree of hypohydration (Armstrong et al., 2010), we gave the participant 500 mL of water to consume and took a subsequent urine sample (30 minutes later) to verify U_{SG} <1.020. Finally, we collected a venous blood sample for subsequent analysis of plasma caffeine concentration (i.e., baseline to confirm caffeine abstinence).

Participants then completed a series of baseline assessments including a subjective ratings questionnaire and an expectancy questionnaire requiring them to rate how they expected to perform on the cognitive tasks, based on the treatment they would receive for the trial. The assigned treatment was ingested on completion of the questionnaire. After a 15 minute rest, participants completed the same subjective ratings questionnaire (without the expectancy questions), followed by a computerized 'Choice Reaction Time' task (CRT (Borchert, 2017a); see description below). After a further 25 minutes rest (i.e., 40 minutes post-treatment), we

collected a second blood sample. Participants then repeated the subjective ratings questionnaire (i.e., 45 minutes post treatment), performed the same CRT task, and completed a computerized 'Psychomotor Vigilance Task' (PVT (Borchert, 2017b); see description below).

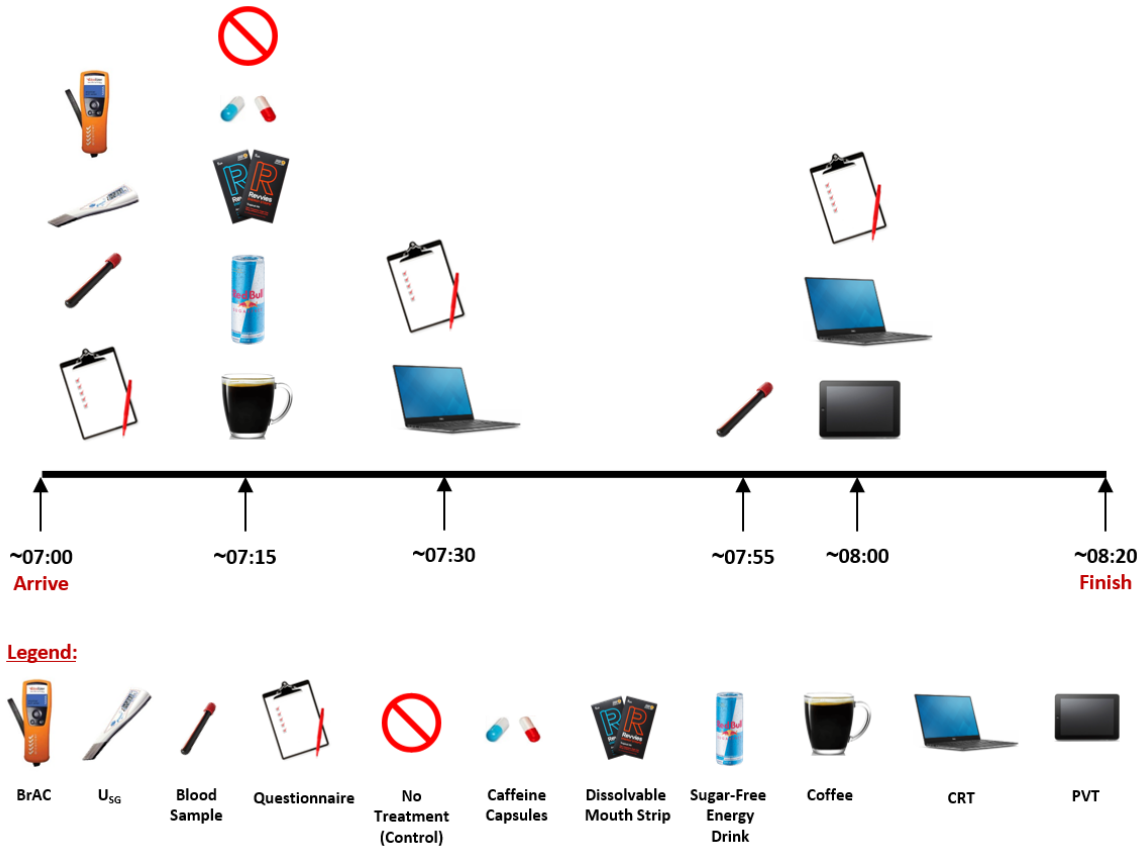

Figure 1. Experimental Trial Protocol.
Note: BrAC: Breath alcohol test; U_{SG}: Urine specific gravity test of hydration status; CRT: Choice Reaction Time task; PVT: Psychomotor Vigilance Task. Caffeine treatment conditions at ~07:15 h were randomized, with participants only receiving one treatment source on each trial. Individual trials were separated by ≥4 days.

Caffeine Treatments

The four different sources of caffeine (80 mg) were: (a) 'CAP': 80 mg anhydrous caffeine (PCCA, Australia) consumed with 250 mL of water; (b) 'COF': 3 g decaffeinated freeze-dried coffee (Woolworths Pty Ltd, Australia) and 80 mg anhydrous caffeine dissolved in 250 mL water; (c) 'STR': a caffeinated dissolvable mouth strip (Revvies™ Energy Strips, Caringbah, NSW, Australia) + 250 mL of water; and (d) 'END': 250 mL caffeinated, sugar-

free energy drink (Red Bull® Zero, Red Bull GmbH, Austria). In the Control (CON) condition, participants were provided with 250 mL of plain water only. In all conditions, participants were given five minutes to consume the allocated treatment and fluid.

Assessment Measures

Blood Sampling and Analysis

We placed 5 mL of blood drawn from a superficial mid-arm vein into a lithium heparin vacutainer and centrifuged it for 10 minutes at 3000 rpm and 10°C. We transferred the resultant plasma to individual Eppendorf tubes and stored it at -80°C until analysis. Plasma caffeine concentrations were determined using high performance liquid chromatography and previously published analytical methods (Bragg et al., 2017).

Subjective Ratings and Expectancy Questionnaires

We obtained the participants' subjective ratings of their mood/arousal (i.e., *Relaxed, Alert, Tired, Tense, Overall Mood)* using 100 mm visual analog scales (VAS), where zero represented "not at all" or "very bad" and 100 represented "extremely" or "very good." The expectancy questionnaire asked participants to rate how they expected to perform on the CRT and PVT, based on the treatment they were receiving for that trial. Ratings were obtained on a 100 mm VAS, where zero represented "very poorly" and 100 represented "very well".

Cognitive and Psychomotor Function (CRT and PVT)

The CRT and PVT tasks (Inquisit 4 Lab; Millisecond software, USA) were administered via a laptop computer (all tasks are available online at www.millisecond.com/download/library). The CRT task involved pressing one of four designated keys, each corresponding to one of four boxes on the laptop screen, whenever the

boxes changed from black to red (random intervals ranging between 400 and 2000 ms). Participants were instructed to press the key corresponding to the red box as quickly as possible and to avoid making mistakes. The task implemented is similar to that described by Armstrong et al. (2012). It took ~2 minutes to complete and involved a total of 52 trials, for which latency (i.e., response speed) and accuracy were recorded. Choice reaction time tasks have been shown to be sensitive to the effects of caffeine (Lieberman et al., 2002). The PVT (i.e., simple reaction time test) involved a red circle appearing on the laptop screen at random intervals (between 2 to 10 seconds). Participants were instructed to respond to the stimulus as quickly as possible by pressing the spacebar on the keyboard. The task is similar to that described by Thomann et al. (2014). It lasted for 5 minutes and involved up to 60 stimuli, for which latency and the number of lapses (defined as a reaction time >500 milliseconds) were recorded. The PVT is a widely used test of sustained attention with excellent reliability and validity (Lim & Dinges, 2008). While the PVT is typically a 10 minute test, a 5-minute PVT has provided a reasonable substitute (Roach et al., 2006). Caffeine has also been shown to alleviate performance impairments on the PVT associated with prolonged wakefulness (Paech et al., 2016).

Statistical Analysis

We performed statistical analyses using RStudio (Version 1.4). We determined an estimated target sample size *a priori* using the 'pwr' package (Champely, 2020). As Alford et al (2001) found that 80 mg caffeine (in an energy drink) decreased participants' (n = 14) choice reaction time (M = 528.6, SD = 64.7 ms) compared to a 'no drink' control (M = 558.7, SD = 60.9 ms), we used an equivalent effect size (Cohen's d_z = 0.6 at R = 0.7), an assumed power (1-ß) of 0.8 and a linear mixed effects repeated measures model with one sided planned comparisons and $\alpha = 0.05$ in this *a priori* calculation. This process derived an estimated need

for 19 participants in this research. Thus, we set a target sample size of 22 to account for attrition (typically 10-15% in repeated measures studies).

We analyzed the participants' cognitive performance, mood/arousal, and expectancy ratings data using linear mixed-effects models, utilizing the 'lme4' (Bates et al., 2015) and 'emmeans' (Lenth, 2022) packages. The models included 'Treatment', 'Trial Order' and Time (where appropriate) as fixed effects, and 'Participant' as a random effect. Models were generated using the restricted maximum likelihood (REML) criterion with no covariance structure specified (unstructured). Data were log-transformed and re-analyzed in case residuals were non-normally distributed (Shapiro-Wilk test, $p < .05$). The first model was retained if the log-transformation did not improve normality (Schielzeth et al., 2020). One-sided planned comparisons (pairwise) were used to compare each caffeine treatment (i.e., CAP, COF, STR, END) vs CON for cognitive performance outcomes. Two-sided pairwise comparisons (with *p*-values adjusted based on seven planned comparisons; $p < .007$) were conducted on mood/arousal and expectancy outcomes. We used Pearson's correlations to examine associations between the difference in *expectancy* and the cognitive performance difference for each caffeine treatment vs CON. Data are presented as means (and standard deviations, *SD*) when normally-distributed and medians (and inter-quartile range, *IQR*) when non-normally distributed. Statistical significance was accepted as $p < .05$ unless otherwise specified (i.e., where corrections were applied for multiple comparisons).

Prior to analzing CRT latency data, we removed all incorrect responses ($n = 284$), and correct responses with CRT <200 ms ($n = 19$) (Whelan, 2008). This resulted in removal of ~3% of the total data set. Central tendency values for PVT and CRT latency (i.e., global PVT and CRT) were then derived and analyzed. *Ex*-Gaussian parameters were also obtained for PVT and CRT latency using the quantile maximum likelihood estimation procedure in QMPE 2.18 (Heathcote et al., 2004). This procedure provides unbiased estimates for three parameters:

the mean (mu, μ) and standard deviation (sigma, σ) of the Gaussian (normal) component in the reaction time distributions, and the mean and standard deviation of the exponential component in the distributions (tau, τ) (Whelan, 2008). All fits successfully converged within 250 iterations.

Results

Participant characteristics

As noted above, 22 volunteer participants (15 men, 7 women; *M* age = 28.2, *SD* = 9.0 years; *M* body weight = 75.6, *SD* = 10.7 kg; *M* BMI = 24.7, *SD* = 2.8 $kg \cdot m^{-2}$) completed the study. Participants had an average habitual caffeine intake 247 mg/day^{-1} (*SD* =149 $mg \cdot day^{-1}$). Median (IQR) ratings for the two CaffEQ factors of relevance (i.e., "Energy/work enhancement" and "Social/mood enhancement") were 4.8 (0.8) and 3.8 (1.7) respectively when scored between 1-6, indicating that participants' generally expected caffeine to have a positive effect on these domains. Most participants (*n* = 13) based their responses to the CaffEQ on consumption of coffee, with fewer basing responses on tea (*n* = 3), caffeine generally (n = 5), or energy drinks (*n* = 1). Most participants had frequent day-to-day exposure to coffee (*n* = 16 daily, *n* = 3 weekly, *n* = 1 yearly, *n* = 2 never); energy drinks (*n* = 2 weekly, *n* = 3 monthly, *n* = 5 yearly, *n* = 12 never), capsules (*n* = 1 daily, *n* = 3 yearly, *n* = 18 never) and dissolvable mouth strips (*n* = 1 yearly, *n* = 21 never) were used less frequently. Overall, 19 participants reported intentional consumption of caffeine to enhance cognitive performance, with most having used coffee (*n* = 17) or energy drinks (*n* = 7) for this purpose; fewer used capsules (*n* = 2), and no participant reported using dissolvable mouth strips to improve cognition.

Baseline Measures

All participants verbally acknowledged compliance with pre-trial standardization procedures on arrival at the laboratory, and there were no positive breathalyzer tests. Participants' self-reported varied sleep duration prior to the caffeine administration trials such that group Medians (IQR) were: COF: 7.0 (1.0) hours; CAP: 7.3 (0.9) hours; END: 8.0 (1.0) hours; STR: 8.0 (1.0) hours, and no groups differed in this respect from CON: 7.5 (1.0) hours. Likewise, participants commenced all trials in a hydrated state (U_{SG} <1.024), with no differences in Median (IQR) U_{SG} values between caffeine sources: COF= 1.009 (0.010); CAP = 1.011 (0.008); END = 1.009 (0.012); STR= 1.013 (0.016) and CON = 1.010 (0.015); *p's* > .05. Participants also commenced each caffeine administration trial with similar ratings of mood/arousal to those reported on the CON trial (*p's* > .05).

Cognitive Performance (CRT and PVT)

CRT latency, accuracy (# errors) and *ex*-Gaussian distribution parameters are shown in Table 1. Neither global CRT latency nor accuracy differed significantly from CON on any of the trials involving caffeine administration (all *p's* > .05). Very few errors were made on any of the trials, with participants consistently demonstrating a high degree of accuracy (>90% correct). There were no significant differences between CON and any of the trials involving caffeine administration for the three *ex*-Gaussian parameters of CRT latency at 15 minutes post-treatment (all *p's* > .05) or for the μ- and σ-parameters 45 minutes post-treatment (all *p's* > .05). However, the τ-parameter was significantly lower at 45 minutes post-treatment on the COF trial compared to CON (p = .012).

Table 1. Participants' Cognitive Performance Means (and Standard Deviations) on CRT and PVT in Each Treatment Condition

	Treatment				
	CON	**COF**	**CAP**	**END**	**STR**
CRT (15 minutes)					
Global RT (ms)	427 (47)	422 (46)	424 (53)	420 (40)	439 (58)
Errors (#)	1.3 (1.2)	1.5 (1.1)	1.1 (1.1)	1.3 (1.3)	1.0 (1.0)
μ (ms)	377 (44)	368 (37)	376 (52)	373 (42)	387 (53)
σ (ms)	30 (15)	24 (10)	29 (20)	27 (12)	33 (18)
τ (ms)	50 (22)	54 (19)	48 (24)	47 (18)	52 (28)
CRT (45 minutes)					
Global RT (ms)	430 (49)	427 (54)	429 (52)	419 (43)	431 (54)
Errors (#)	1.5 (1.1)	1.1 (1.3)	1.1 (1.3)	1.4 (1.1)	1.3 ± 1.5
μ (ms)	373 (43)	385 (54)	371 (42)	364 (37)	380 (46)
σ (ms)	24 (11)	29 (19)	23 (13)	22 (10)	28 (15)
τ (ms)	57 (21)	42 (18) [a]	57 (29)	55 (23)	52 (30)
PVT (45 minutes)					
Global RT (ms)	374 (59)	355 (38) [a]	358 (48) [a]	354 (37) [a]	363 (47) [a]
Lapses (#)	4.0 (6.2)	2.0 (2.6) [a]	2.3 (3.0)	1.8 (2.1) [a]	2.8 (5.3)
μ (ms)	309 (36)	302 (29)	303 (31)	308 (31)	315 (34)
σ (ms)	21 (14)	21 (12)	17 (7)	21 (8)	22 (10)
τ (ms)	65 (39)	53 (21) [a]	54 (34) [a]	46 (20) [a]	48 (24) [a]

Note: CON: Control; COF: Coffee; CAP: Capsules; END: Sugar-free energy drink; STR: Dissolvable mouth strip; RT: Reaction Time; CRT: Choice Reaction Time; PVT: Psychomotor Vigilance Task; *μ: mu ex*-Gaussian parameter; *σ: sigma ex*-Gaussian parameter; *τ: tau ex*-Gaussian parameter; Values are Mean ± SD. [a] significantly different to CON Treatment at that Time ($p < .05$).

PVT latency, number of lapses and *ex*-Gaussian distribution parameters are shown in Table 1. Participants' PVT latency was significantly reduced following caffeine administration compared to CON, irrespective of treatment (*p's* < .05; Figure 2). Participants also had significantly fewer lapses on the COF ($p = .023$) and END ($p = .025$) trials compared to CON.

There were no significant differences between CON and any of the trials involving caffeine administration for the μ- or σ- *ex*-Gaussian parameters of PVT latency (*p's* > .05). However, the τ-parameter, which describes the Mean and *SD* of the exponential component of RT, was significantly lower for all caffeine trials compared to CON (*p's* < .05; Figure 2).

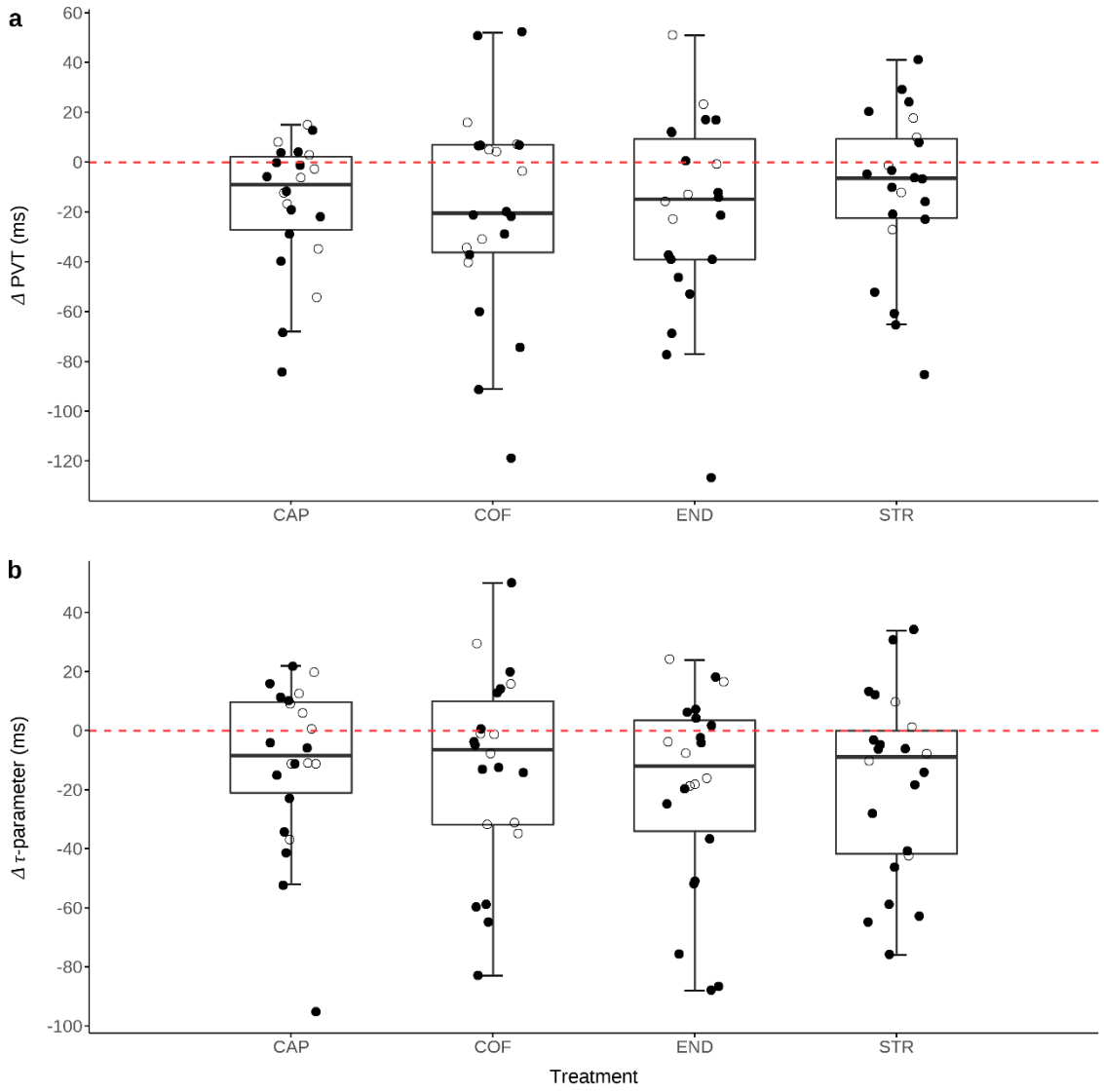

Figure 2. (a) Global PVT Latency Changes from CON for Each Treatment Condition; **(b)** PVT *Tau*-Parameter Changes from CON for Each Treatment Condition. Note: negative values represent improved performance (faster reaction times). PVT: Psychomotor Vigilance Task; CON: Control; COF: Coffee; CAP: Capsules; END: Sugar-free energy drink; STR: Dissolvable mouth strip. Black symbols indicate individuals who expected to perform better with the caffeine treatment compared to CON; Open symbols indicate individuals who did not expect to perform better with the caffeine treatment compared to CON.

Caffeine Source Expectancy Effects

Participants' expectancy ratings for the CRT and PVT tasks are summarized in Table 2. There were no differences in expected performance on the CRT task for any caffeine treatment compared to CON ($p > .05$). For the PVT, participants expected to perform better when consuming COF ($p = .039$) compared to CON, and there was a trend for better performance expected with STR compared to CON ($p = .072$); there were no other significant differences in comparisons to CON. Pearson's correlations between the differences in expectancies and differences in performance (for each caffeine treatment vs CON) on both the CRT and PVT were generally weak-moderate in strength, and all were non-significant.

Table 2. Expectancy of Caffeine Treatment on CRT and PVT Means (and Standard Deviations)

	Treatment				
	CON	**COF**	**CAP**	**END**	**STR**
CRT (0-100 mm VAS)	66.0 (15.7)	67.0 (13.0)	63.7 (16.1)	68.5 (17.5)	66.7 (13.4)
PVT (0-100 mm VAS)	67.4 (14.7)	71.6 (13.7) [a]	65.4 (13.9)	69.5 (14.9)	71.7 (14.3)

Note: CON: Control; COF: Coffee; CAP: Capsules; END: Sugar-free energy drink; STR: Dissolvable mouth strip; CRT: Choice Reaction Time; PVT: Psychomotor Vigilance Task; VAS: Visual Analog Scale. Values are Mean ± SD. [a] significantly different to CON Treatment ($p < .05$).

Participants' Subjective Self-Ratings

Participants' subjective ratings of mood/arousal are summarized in Table 3. Participants' ratings of '*Alert*' were significantly higher for measurements at both 15 and 45 minutes after caffeine administration (irrespective of treatment) compared to CON (*p's* < .05). Ratings for '*Alert*' were also significantly higher 15 minutes post-treatment, compared to baseline, when COF ($p = .006$) and END ($p < .001$) were administered, and at 45 minutes, compared to baseline, when COF ($p = .005$), CAP ($p = .005$) and END ($p < .001$) were administered. Participants' ratings of '*Tired*' were significantly lower 15 and 45 minutes after administration of caffeine compared to CON on all source trials ($p < .05$) except CAP. Ratings

for '*Tired*' were also significantly lower at 15 minutes post-treatment compared to baseline, when COF ($p < .001$) and END ($p < .001$) were administered, and at 45 minutes after COF ($p < .001$) and END ($p < .001$). '*Overall Mood*' ratings were significantly higher at 15 minutes ($p = .005$) and 45 minutes ($p < .001$) post-treatment on the COF trial, compared to baseline; and significantly higher at 45 minutes post-treatment on the END trial, compared to CON ($p = .005$). There were no other significant differences in mood/arousal (compared to CON or baseline).

Table 3. Participants' Subjective Mood/Arousal Means (Standard Deviations) Across Treatment Conditions

	Treatment				
	CON	**COF**	**CAP**	**END**	**STR**
Baseline (0 minutes)					
Relaxed	70.6 (15.1)	72.0 (12.8)	72.5 (14.8)	65.4 (19.9)	76.3 (14.4)
Alert	54.0 (19.0)	60.2 (18.9)	56.9 (18.7)	60.8 (16.0)	63.9 (17.7)
Tired	44.1 (23.1)	47.7 (20.4)	41.6 (20.2)	40.0 (20.2)	34.8 (21.5)
Tense	21.9 (15.2)	14.6 (21.1)	16.3 (17.9)	17.2 (16.2)	13.5 (14.3)
Overall Mood	72.7 (12.5)	70.6 (11.7)	72.6 (13.1)	75.1 (12.3)	77.6 (13.5)
15 minutes					
Relaxed	70.4 (13.6)	66.1 (16.1)	70.0 (14.6)	63.9 (16.2)	68.2 (15.8)
Alert	55.0 (20.3)	73.1 (12.3) [a,b]	67.2 (13.5) [a]	76.7 (12.3) [a,b]	67.9 (18.1) [a]
Tired	43.4 (20.5)	27.5 (20.3) [a,b]	35.5 (22.5)	20.7 (17.9) [a,b]	29.3 (19.9) [a]
Tense	15.3 (15.0)	22.0 (23.1)	22.2 (20.1)	16.9 (14.2)	16.8 (18.8)
Overall Mood	73.6 (12.8)	77.4 (12.7) [b]	73.5 (10.9)	75.8 (19.8)	75.9 (12.7)
45 minutes					
Relaxed	67.4 (19.7)	67.1 (15.1)	63.0 (22.6)	64.7 (14.5)	66.1 (19.0)
Alert	55.0 (19.5)	73.3 (13.9) [a,b]	71.2 (16.3) [a,b]	76.0 (14.4) [a,b]	70.5 (18.5) [a]
Tired	42.2 (24.2)	29.1 (23.0) [a,b]	31.8 (20.5)	21.5 (19.6) [a,b]	25.5 (22.1) [a]
Tense	16.3 (19.2)	23.1 (23.0)	20.2 (18.1)	16.7 (14.7)	16.7 (19.0)
Overall Mood	73.9 (10.8)	80.2 (9.0) [b]	74.7 (12.1)	81.9 (11.6) [a]	75.9 (12.9)

Note: CON: Control; COF: Coffee; CAP: Capsules; END: Sugar-free energy drink; STR: Dissolvable mouth strip; Values are Mean ± SD. [a] significantly different to CON Treatment at that Time ($p < .05$); [b] significantly different to Baseline for that Treatment ($p < .05$). Ratings are based on VAS (0-100 mm) where 0 = 'not at all' or 'very bad' and 100 = 'extremely' or 'very good'.

Plasma Caffeine Analysis

Despite their acknowledged compliance to the pre-trial standardization procedures (i.e., 12 hours of abstinence from caffeinated foods/beverages), baseline blood samples from some participants contained residual caffeine (*M* CON: 3.6 (5.3) $\mu g \cdot mL^{-1}$ (n = 12); *M* COF: 2.9 (4.2) $\mu g \cdot mL^{-1}$ (n = 11); *M* CAP: 1.5 (3.0) $\mu g \cdot mL^{-1}$ (n = 8); *M* END: 2.1 (4.0) $\mu g \cdot mL^{-1}$ (n = 10); *M* STR: 3.5 (5.1) $\mu g \cdot mL^{-1}$ (n = 12)). These data have therefore been analyzed and interpreted in terms of the change (Δ) in plasma caffeine concentration. Plasma caffeine concentration increased in all trials involving caffeine administration, irrespective of caffeine source; with the Δ plasma caffeine levels recorded as: *M* COF: 10.0 (5.0) $\mu g \cdot mL^{-1}$; *M* CAP: 7.4 (4.5) $\mu g \cdot mL^{-1}$; *M* END: 8.8 (2.4) $\mu g \cdot mL^{-1}$; and *M* STR: 6.3 (6.9) $\mu g \cdot mL^{-1}$.

Discussion

We investigated the effects of participants' consumption of different sources of caffeine and their expectations of source efficacy on mood/arousal and cognitive performance. Overall, caffeine ingestion improved participants' self-report ratings of their alertness and tiredness, irrespective of source; ratings of 'overall mood' also increased, but only when COF or END were consumed. Caffeine ingestion had a positive effect on psychomotor vigilance (via improved latency) irrespective of source. While participants expected to perform better on the PVT following COF compared to CON, associations between expectancy and actual performance were not significant. Other aspects of cognitive performance (i.e., # lapses on PVT and CRT latency distribution) were caffeine source dependent, with positive effects isolated to trials involving ingestion of either COF or END.

In agreement with our hypothesis, caffeine ingestion generally increased alertness, decreased tiredness, and improved 'overall mood' compared to CON. These findings are consistent with reports that acute ingestion of caffeine induces positive changes in

mood/arousal; particularly an increase in alertness, ability to concentrate, wakefulness and vitality, even with relatively modest doses and in well-rested individuals (Irwin et al., 2020; McLellan et al., 2016; Ruxton, 2008). While we observed differences in participant's ratings of alertness (and for the most part tiredness as well) at both 15 and 45 minutes post-ingestion with all caffeine sources (relative to CON), changes within a trial (compared to baseline) were only observed with administration of COF, END (both at 15 and 45 minutes) and CAP (only at 45 minutes). Although similar directional changes were observed after the consumption of STR, the non-significant time effect may reflect the subtly higher ratings of alertness and lower ratings of tiredness reported at baseline. Furthermore, while similar directional changes in alertness and tiredness were observed at 15 minutes compared to baseline for CAP, the non-significant result could be related to the lack of stimulating oro-sensory properties received when ingesting capsules with plain water. Indeed, a small number of studies suggest that sensory effects associated with consuming coffee/tea and energy drinks, particularly in those conditioned to the stimulus, may contribute in part to the positive effects these caffeinated products have on mood (Hindmarch et al., 1998; Quinlan et al., 2000; Smit et al., 2004). For example, Smit et al. (2004) found that consuming placebo energy drink compared to a water control resulted in higher (albeit transient) ratings for the mood constructs 'energetic arousal' (including the mood components "awake" and "revitalized") and 'hedonic tone' (i.e. euphoric vs dysphoric mood). Thus, while caffeine is clearly capable of eliciting a positive effect on mood/arousal, the magnitude and time-course of this effect appears to depend on other factors such as the source of caffeine and its associated sensory properties, as well as individuals' baseline mood/arousal state.

Ingestion of caffeine in the present study positively impacted PVT performance, with faster global reaction times observed on all caffeine trials relative to CON. *Ex*-Gaussian analysis localized this improvement to the τ (skewed)-component of the reaction time

distribution, suggesting participants were less variable in their speed of responding to stimuli after consuming caffeine, irrespective of source. In contrast, the influence of caffeine on PVT lapses was less consistent, with significantly fewer lapses only observed on COF and END trials compared to CON. Overall, these findings align with the general scientific consensus that caffeine improves "lower-order" cognitive functions such as simple reaction time, especially on tasks that require attention and/or vigilance, and with relatively modest doses (<50 mg) (McLellan et al., 2016). Previous work has also demonstrated that acute caffeine consumption can reduce both mean reaction time and response time variability, but not necessarily influence number of PVT lapses (Lanini et al., 2016). The beneficial effects of caffeine on PVT performance in the present study were observed even though participants were not necessarily devoid of caffeine in their blood at baseline. Although we employed standardization protocols, including a 12-hour caffeine abstinence period prior to trials (with compliance verified verbally), some participants (36-55% depending on the trial) had residual caffeine in their system at baseline. Previous work has implied that the beneficial effect of caffeine on performance can be attributed to a reversal of adverse withdrawal effects associated with short periods of abstinence (James & Rogers, 2005), although this has been debated in more recent investigations (Einother & Giesbrecht, 2013). Overall, we found that acute caffeine consumption had a consistent beneficial effect on vigilance, particularly response speed on tasks requiring sustained attention, irrespective of the source of caffeine administration and whether complete caffeine abstinence had been achieved.

We found a significant difference in participants expectation to perform on the PVT only with COF compared to CON. Yet, more than half our participants expected all the caffeine sources to improve PVT performance compared to CON (see Figure 2); possibly due to a general belief that caffeine has 'energy/work enhancement' as demonstrated in the CaffEQ.

Previous reports suggested that caffeine's effects could differ, depending on one's expectancies, and that these are typically formed by prior experiences (Oei & Hartley, 2005).

Limitations and Directions for Further Research

While our study's small sample size was sufficiently large to generate needed statistical power, generalizability to other populations is limited until there has been replicative cross-validation, ideally with larger and more age and ethnically diverse participants. Regarding the expectancy issue, most studies that investigated caffeine expectancies employed placebo-controlled designs (as opposed to a no treatment control), where treatment expectancy was manipulated through information provided to participants (i.e., receive placebo and told caffeine paradigm). Since individuals knowingly consume caffeine, we compared groups to a water control condition. Unfortunately, in this design it was not possible to determine whether the positive effects observed were driven by participants' satisfaction with consuming caffeine on various caffeine trials or their dissatisfaction with not receiving caffeine on the CON trial. It is also possible that other underlying biological factors (e.g., sex, genetic polymorphisms) influencing individuals' rate of caffeine metabolism and sensitivity to its effects played an important role in their cognitive performance outcomes (Carswell et al., 2020; Temple & Ziegler, 2011), irrespective of an individuals' belief in a source's efficacy. Thus, further research is required to explore how these factors may work in either a complimentary or opposing fashion with regards to mood and cognitive performance outcomes.

In contrast to our hypothesis, caffeine administration had no impact on CRT performance, with participants having performed equally well (both response speed and accuracy) on the CON trial compared to all caffeine trials. Results were consistent irrespective of the analytical technique employed (i.e., central tendency vs *ex*-Gaussian), except that COF resulted in a lower τ-parameter at 45 minutes compared to CON (i.e., less skew in the reaction time distribution).

It is possible that the CRT task we employed was not sensitive to the effects of modest doses of caffeine, or that the task was of insufficient duration (i.e., 2 minutes) to observe a reliable effect. Indeed, findings from a previous review indicate that higher doses of caffeine (i.e., ≥200 mg) may be required to generate an effect on CRT tasks, and that tasks lower in complexity (i.e., do not require focused attention) and short in duration (i.e., ~3 minutes) are less likely to demonstrate consistent caffeine-mediated effects (Einother & Giesbrecht, 2013).

Conclusion

In summary, we found that ingestion of 80 mg of caffeine from various sources had a consistently positive effect on alertness and tiredness, and improved adult participants' response speeds to stimuli on a psychomotor vigilance task. Overall, findings from this study suggest that a modest dose of caffeine, regardless of source, can positively impact mood/arousal and cognitive performance; and these effects are unlikely to be greatly mediated by individuals' expectancies regarding caffeine source efficacy.

Disclosure of interest

The authors report no conflict of interest.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

Ágoston, C., Urbán, R., Király, O., Griffiths, M. D., Rogers, P. J., & Demetrovics, Z. (2018). Why do you drink caffeine? the development of the motives for caffeine consumption questionnaire (MCCQ) and Its relationship with gender, age and the types of

caffeinated beverages. *International Journal of Mental Health and Addiction*, *16*(4), 981-999. https://doi.org/10.1007/s11469-017-9822-3

Alford, C., Cox, H., & Wescott, R. (2001). The effects of red bull energy drink on human performance and mood. *Amino Acids*, *21*(2), 139-150. https://doi.org/10.1007/s007260170021

Armstrong, L. E., Ganio, M. S., Casa, D. J., Lee, E. C., McDermott, B. P., Klau, J. F., Jimenez, L., Le Bellego, L., Chevillotte, E., & Lieberman, H. R. (2012). Mild dehydration affects mood in healthy young women. *J Nutr*, *142*(2), 382-388. https://doi.org/10.3945/jn.111.142000

Armstrong, L. E., Pumerantz, A. C., Fiala, K. A., Roti, M. W., Kavouras, S. A., Casa, D. J., & Maresh, C. M. (2010). Human hydration indices: acute and longitudinal reference values. *International Journal of Sports Nutrition and Exercise Metabolism*, *20*(2), 145-153. https://doi.org/10.1123/ijsnem.20.2.145

Bates, D., Maechler, M., Bolker, B., & Walker, S. (2015). Fitting linear mixed-effects models using lme4 *Journal of Statistical Software*, *67*(1), 1-48. https://doi.org/doi:10.18637/jss.v067.i01

Borchert, K. (2017a, November). *Inquisit Four Choice Reaction Time Task*. Millisecond Software. https://www.millisecond.com/download/library/v6/fourchoicereactiontimetask/fourchoicereactiontimetask/fourchoicereactiontimetask.manual

Borchert, K. (2017b, July). *Inquisit Psychomotor Vigilance Test*. https://www.millisecond.com/download/library/v6/psychomotorvigilancetest/psychomotorvigilance/psychomotorvigilancetest.manual

Bragg, C., Desbrow, B., Hall, S., & Irwin, C. (2017). Effect of meal glycemic load and caffeine consumption on prolonged monotonous driving performance. *Physiology & Behavior*, *181*, 110-116. https://doi.org/10.1016/j.physbeh.2017.09.013

Buysse, D. J., Reynolds, C. F., 3rd, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The pittsburgh sleep quality index: a new instrument for psychiatric practice and research. *Psychiatry Research*, *28*(2), 193-213. https://doi.org/10.1016/0165-1781(89)90047-4

Cappelletti, S., Piacentino, D., Sani, G., & Aromatario, M. (2015). Caffeine: cognitive and physical performance enhancer or psychoactive drug? *Current Neuropharmacology*, *13*(1), 71-88. https://doi.org/10.2174/1570159X13666141210215655

Carswell, A. T., Howland, K., Martinez-Gonzalez, B., Baron, P., & Davison, G. (2020). The effect of caffeine on cognitive performance is influenced by CYP1A2 but not ADORA2A genotype, yet neither genotype affects exercise performance in healthy adults. *European Journal of Applied Physiology*, *120*(7), 1495-1508. https://doi.org/10.1007/s00421-020-04384-8

Champely, S. (2020, 2021 Nov 5). *R package pwr: Basic Functions for Power Analysis. Version 1.3-0 [software]*. https://CRAN.R-project.org/package=pwr

Einother, S. J. L., & Giesbrecht, T. (2013). Caffeine as an attention enhancer: reviewing existing assumptions. *Psychopharmacology*, *225*(2), 251-274. https://doi.org/10.1007/s00213-012-2917-4

Fulgoni, V. L., 3rd, Keast, D. R., & Lieberman, H. R. (2015). Trends in intake and sources of caffeine in the diets of US adults: 2001-2010. *American Journal of Clinical Nutrition*, *101*(5), 1081-1087. https://doi.org/10.3945/ajcn.113.080077

Guest, N. S., VanDusseldorp, T. A., Nelson, M. T., Grgic, J., Schoenfeld, B. J., Jenkins, N. D. M., Arent, S. M., Antonio, J., Stout, J. R., Trexler, E. T., Smith-Ryan, A. E., Goldstein, E. R., Kalman, D. S., & Campbell, B. I. (2021). International society of sports nutrition position stand: caffeine and exercise performance. *Journal of the*

International Society of Sports Nutrition, *18*(1), 1. https://doi.org/10.1186/s12970-020-00383-4

Heathcote, A., Brown, S., & Cousineau, D. (2004). QMPE: Estimating lognormal, wald, and weibull RT distributions with a parameter-dependent lower bound. *Behavior Research Methods, Instruments & Computers*, *36*(2), 277-290. https://doi.org/10.3758/BF03195574

Hindmarch, I., Quinlan, P. T., Moore, K. L., & Parkin, C. (1998). The effects of black tea and other beverages on aspects of cognition and psychomotor performance. *Psychopharmacology*, *139*(3), 230-238. https://doi.org/10.1007/s002130050709

Huntley, E. D., & Juliano, L. M. (2012). Caffeine expectancy questionnaire (CaffEQ): construction, psychometric properties, and associations with caffeine use, caffeine dependence, and other related variables. *Psychological Assessment*, *24*(3), 592-607. https://doi.org/10.1037/a0026417

Irwin, C., Khalesi, S., Desbrow, B., & McCartney, D. (2020). Effects of acute caffeine consumption following sleep loss on cognitive, physical, occupational and driving performance: a systematic review and meta-analysis. *Neuroscience and Biobehavioral Reviews*, *108*, 877-888. https://doi.org/10.1016/j.neubiorev.2019.12.008

James, J. E., & Rogers, P. J. (2005). Effects of caffeine on performance and mood: withdrawal reversal is the most plausible explanation. *Psychopharmacology*, *182*(1), 1-8. https://doi.org/10.1007/s00213-005-0084-6

Kamimori, G. H., Karyekar, C. S., Otterstetter, R., Cox, D. S., Balkin, T. J., Belenky, G. L., & Eddington, N. D. (2002). The rate of absorption and relative bioavailability of caffeine administered in chewing gum versus capsules to normal healthy volunteers. *International Journal of Pharmaceutics*, *234*(1-2), 159-167. https://doi.org/10.1016/s0378-5173(01)00958-9

Kirsch, I. (1999). *How expectancies shape experience* [doi:10.1037/10332-000]. American Psychological Association. https://doi.org/10.1037/10332-000

Lanini, J., Galduroz, J. C. F., & Pompeia, S. (2016). Acute personalized habitual caffeine doses improve attention and have selective effects when considering the fractionation of executive functions. *Human Psychopharmacology-Clinical and Experimental*, *31*(1), 29-43. https://doi.org/10.1002/hup.2511

Lenth, R. V. (2022, 2022 Jan 16). *R package emmeans: Estimated Marginal Means, aka Least-Squares Means. Version 1.7.0 [software]*. https://CRAN.R-project.org/package=emmeans

Lieberman, H. R., Tharion, W. J., Shukitt-Hale, B., Speckman, K. L., & Tulley, R. (2002). Effects of caffeine, sleep loss, and stress on cognitive performance and mood during U.S. Navy SEAL training. Sea-Air-Land. *Psychopharmacology (Berl)*, *164*(3), 250-261. https://doi.org/10.1007/s00213-002-1217-9

Lim, J., & Dinges, D. F. (2008). Sleep Deprivation and Vigilant Attention. *Annals of the New York Academy of Sciences*, *1129*(1), 305-322. https://doi.org/https://doi.org/10.1196/annals.1417.002

McLellan, T. M., Caldwell, J. A., & Lieberman, H. R. (2016). A review of caffeine's effects on cognitive, physical and occupational performance. *Neuroscience and Biobehavioral Reviews*, *71*, 294-312. https://doi.org/10.1016/j.neubiorev.2016.09.001

Morris, C., Viriot, S. M., Farooq Mirza, Q. U. A., Morris, G. A., & Lynn, A. (2019). Caffeine release and absorption from caffeinated gums. *Food & Function*, *10*(4), 1792-1796. https://doi.org/10.1039/c9fo00431a

Mumford, G. K., Benowitz, N. L., Evans, S. M., Kaminski, B. J., Preston, K. L., Sannerud, C. A., Silverman, K., & Griffiths, R. R. (1996). Absorption rate of methylxanthines

following capsules, cola and chocolate. *European Journal of Clinical Pharmacology*, *51*(3-4), 319-325. https://doi.org/10.1007/s002280050205
Nehlig, A. (2010). Is caffeine a cognitive enhancer? *J Alzheimers Dis*, *20 Suppl 1*, S85-94. https://doi.org/10.3233/JAD-2010-091315
Oei, A., & Hartley, L. R. (2005). The effects of caffeine and expectancy on attention and memory. *Human Psychopharmacology*, *20*(3), 193-202. https://doi.org/10.1002/hup.681
Paech, G. M., Banks, S., Pajcin, M., Grant, C., Johnson, K., Kamimori, G. H., & Vedova, C. B. D. (2016). Caffeine administration at night during extended wakefulness effectively mitigates performance impairment but not subjective assessments of fatigue and sleepiness. *Pharmacology Biochemistry and Behavior*, *145*, 27-32. https://doi.org/https://doi.org/10.1016/j.pbb.2016.03.011
Quinlan, P. T., Lane, J., Moore, K. L., Aspen, J., Rycroft, J. A., & O'Brien, D. C. (2000). The acute physiological and mood effects of tea and coffee. *Pharmacology Biochemistry and Behavior*, *66*(1), 19-28. https://doi.org/10.1016/s0091-3057(00)00192-1
Roach, G. D., Dawson, D., & Lamond, N. (2006). Can a shorter psychomotor vigilance task be used as a reasonable substitute for the ten-minute psychomotor vigilance task? *Chronobiology International*, *23*(6), 1379-1387. https://doi.org/10.1080/07420520601067931
Ruxton, C. (2008). The impact of caffeine on mood, cognitive function, performance and hydration: a review of benefits and risks. *Nutrition Bulletin*, *33*, 15-25. https://doi.org/10.1111/j.1467-3010.2007.00665.x
Schielzeth, H., Dingemanse, N. J., Nakagawa, S., Westneat, D. F., Allegue, H., Teplitsky, C., Réale, D., Dochtermann, N. A., Garamszegi, L. Z., & Araya-Ajoy, Y. G. (2020). Robustness of linear mixed-effects models to violations of distributional assumptions. *Methods in Ecology and Evolution*, *11*(9), 1141-1152. https://doi.org/https://doi.org/10.1111/2041-210X.13434
Shabir, A., Hooton, A., Tallis, J., & M, F. H. (2018). The influence of caffeine expectancies on sport, exercise, and cognitive performance. *Nutrients*, *10*(1528), nu10101528. https://doi.org/10.3390/nu10101528
Smit, H. J., Cotton, J. R., Hughes, S. C., & Rogers, P. J. (2004). Mood and cognitive performance effects of "energy" drink constituents: caffeine, glucose and carbonation. *Nutritional Neuroscience*, *7*(3), 127-139. https://doi.org/10.1080/10284150400003041
Smith, A. (2002). Effects of caffeine on human behavior. *Food and Chemical Toxicology*, *40*(9), 1243-1255. https://doi.org/https://doi.org/10.1016/S0278-6915(02)00096-0
Temple, J., & Ziegler, A. (2011). Gender Differences in Subjective and Physiological Responses to Caffeine and the Role of Steroid Hormones. *Journal of Caffeine Research*, *1*(1), 41-48. https://doi.org/10.1089/jcr.2011.0005
Thomann, J., Baumann, C. R., Landolt, H.-P., & Werth, E. (2014). Psychomotor vigilance task demonstrates impaired vigilance in disorders with excessive daytime sleepiness. *Journal of Clinical Sleep Medicine*, *10*(9), 1019-1024. https://doi.org/10.5664/jcsm.4042
Whelan, R. (2008). Effective analysis of reaction time data. *The Psychological Record*, *58*(3), 475-482. https://doi.org/10.1007/BF03395630
Wickham, K. A., & Spriet, L. L. (2018). Administration of caffeine in alternate forms. *Sports Medicine*, *48*(1), 79-91. https://doi.org/10.1007/s40279-017-0848-2
Zhang, H., Zhang, J., & Streisand, J. B. (2002). Oral mucosal drug delivery: clinical pharmacokinetics and therapeutic applications. *Clinical Pharmacokinetics*, *41*(9), 661-680. https://doi.org/10.2165/00003088-200241090-00003