

Effects of caffeine on alcohol-related changes in behavioural control and perceived intoxication in light caffeine consumers

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Abstract

Rationale Caffeinated alcoholic beverages have been associated with increased risk of alcohol-related harms. However, few studies have examined these combined effects on behavioural control, which is believed to underlie many of the negative effects of alcohol consumption. In addition, studies have often omitted subjective measures, and none have directly assessed the role of caffeine consumer history.

Objectives To examine the combined effects of alcohol and caffeine on measures of behavioural control and perceived intoxication in abstinent, light caffeine consumers.

Methods Participants ($n=28$; 50% male) attended four sessions at which they consumed one of the following beverages in a randomised order: placebo, alcohol alone (0.6 g/kg), caffeine alone (2.0 mg/kg), and alcohol/caffeine. They completed measures of mood, intoxication, anxiety and alcohol craving before and after a task battery comprising measures of behavioural control and reaction time performance.

Results Caffeine attenuated alcohol-related performance deficits on stop-signal accuracy, had no effect on go–no-go performance deficits, and worsened accuracy on the Stroop task. Caffeine did not influence absolute changes in perceived intoxication but there was suggestion that caffeine may have changed the nature of intoxication with increases in stimulation.

Conclusions Caffeine appears to have mixed effects on alcohol intoxication that are task-dependent. We found increased stimulation in the alcohol/caffeine condition, supporting the contention that caffeinated alcoholic beverages enable an

individual to drink for longer. Future research should model real world drinking behaviour by examining how these effects change across multiple drink administrations.

Keywords Caffeine · Alcohol · Intoxication · Behavioural control · Stroop task · Reaction time · Caffeinated alcoholic beverages · Abstinence

Introduction

There is growing concern regarding the popularity of caffeinated alcoholic beverages (Benac 2010; Howland et al. 2011), due to reports of increased risk of alcohol-related harms and alcohol poisoning (Howland et al. 2011; O'Brien et al. 2008; Thombs et al. 2010). Caffeine is often seen as a means to “sober-up” when intoxicated, and drinkers may functionally use caffeine to attenuate alcohol intoxication. However, this may be a dangerous misconception. It has been proposed that caffeine decreases *perceived* intoxication with little or no change to the cognitive and motor impairing effects of alcohol (Weldy 2010) and decreases the sedative effects of alcohol, thereby enabling the individual to consume more drinks over a longer period of time (Howland et al. 2011). As a consequence, restrictions have been set on the marketing and development of pre-mixed caffeinated alcoholic beverages, yet caffeinated energy drinks are widely available and significant percentages of consumers report mixing their own energy drink–alcohol cocktails (Malinauskas et al. 2007; O'Brien et al. 2008; Oteri et al. 2007).

Laboratory studies examining the combined effect of caffeinated energy drinks and alcohol have shown no effect of energy drinks on alcohol-related impairment of physical activity (ergometer test) (Ferreira et al. 2004), but some attenuation of other negative effects including headache,

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dry mouth, weakness and motor coordination (Ferreira et al. 2006). However, the mechanisms underlying these effects are difficult to elucidate given that energy drinks contain numerous constituents including carbohydrates, vitamins taurine, and glucuronolactone, all of which conceivably exert relevant effects alone or in combination.

As caffeine is considered the primary psychoactive ingredient of these drinks, many studies have directly manipulated caffeine in alcoholic drinks using anhydrous caffeine powder. Caffeine has been shown to compensate for alcohol-related impairment on dual-task interference (Marczinski and Fillmore 2006), digit symbol substitution (Mackay et al. 2002), memory recall (Drake et al. 2003), simple reaction time (SRT) (Azcona et al. 1995), intentional control (Grattan-Miscio and Vogel-Sprott 2005), sleep latency (Drake et al. 2003) and brake latency in simulated driving (Liguori and Robinson 2001), but to have limited or no effect on speed deviation/variation or crash risk in simulated driving (Howland et al. 2010), sustained attention (reaction time) (Howland et al. 2010), and mixed findings have been reported on choice reaction time (Drake et al. 2003; Liguori and Robinson 2001; Mackay et al. 2002). It should be noted that in some of the positive cases noted above, comparisons between alcohol and alcohol/caffeine conditions did not reach significance; instead, compensation was inferred on the basis that only the alcohol-alone condition significantly differed from placebo.

Surprisingly, given that one of the main assertions regarding the alcohol/caffeine relationship is that caffeine may decrease perceived intoxication whilst leaving the cognitive and motor impairment unaffected, few studies have included subjective measures of mood or intoxication. The subjective data that are available show that caffeine failed to offset alcohol-related increases in confusion (Liguori and Robinson 2001), high (Liguori and Robinson 2001), dizziness (Drake et al. 2003; Liguori and Robinson 2001) and “drunkenness” (Azcona et al. 1995), but did compensate for increased fatigue and sleepiness (Drake et al. 2003). These data partially support the anecdotal evidence as, although participants did not seem to perceive themselves as less intoxicated per se, caffeine did reduce sedative aspects of intoxication.

There is substantial variation in findings across studies that makes interpretation somewhat difficult; however, even without this ambiguity, it remains unclear how the above-mentioned cognitive outcomes relate to real-world alcohol-related behaviours. Alcohol-induced deficits in behaviour control (e.g., increased impulsivity and decreased inhibition of pre-potent responses) are believed to underlie many of the risky behaviours associated with alcohol consumption, and therefore, it is particularly important to examine the effect of caffeine on these behaviours. Only a few studies have

incorporated such measures and the data are somewhat contradictory, possibly due to differences in the tasks used. Fillmore and Vogel-Sprott (1999) employed a computerised stop-signal task in which responding to stimuli had to be withheld on presentation of a tone. Alcohol (0.65 g/kg) consumption significantly reduced the number of inhibitions from baseline, and this detrimental effect was compensated for by a fairly high dose of caffeine (4.4 mg/kg). Subjective effects of mood and intoxication were not assessed. More recently, Marzinski and Fillmore (2003) used a cued go–no-go task in which participants were instructed to respond (“go”) to one stimulus and withhold a response (“no-go”) to another. Alcohol (0.65 g/kg) had detrimental effects on response inhibition and reaction time on error trials. Caffeine failed to offset performance detriment on response inhibition but did compensate for the slowing of reaction times, but only at a higher dose (4.0 mg/kg). This study also included a measure of subjective intoxication. Alcohol significantly increased sedation and stimulation compared to vehicle. Although these effects were not significantly changed by co-administration of caffeine, the pattern of effect suggested that caffeine reduced sedation and increased stimulation compared to alcohol alone. Insufficient power due to a small sample size ($n=12$) may explain the lack of significance.

Thus, in one study caffeine attenuated alcohol deficits of response inhibition, yet in the other study, caffeine appeared to decrease alcohol deficits of response execution. The differences in tasks used may limit the comparability of these effects and suggest that it is important to utilise different measures of behavioural control. In the current study, we examined the effects of alcohol alone (0.6 g/kg) and in combination with caffeine (2.0 mg/kg) on three of the most commonly employed cognitive measures of response inhibition (stop-signal, go–no-go and classic Stroop tasks). In order to assess how selective the effects may be to behavioural control we added a comparison SRT task, which is known to be particularly sensitive to the effects of caffeine (Brice and Smith 2002; Lieberman et al. 1987; Smit and Rogers 2000; Smith et al. 1994a,b). We also compared the cognitive outcomes with subjective ratings of mood and intoxication.

It is noteworthy that most studies do not consider the role of caffeine consumption histories and pre-study caffeine restrictions (if any) are not reported. Consequently, it is impossible to elucidate whether observed effects are net benefits of caffeine or are due to reversal of caffeine withdrawal. In the current study, we restricted inclusion to light caffeine consumers who were caffeine-abstinent throughout the study, to limit interference from caffeine withdrawal effects.

There is also substantial ambiguity in the caffeine literature regarding its effects of performance. This is likely to be,

at least in part, due to substantial between-subject variation in responsiveness to caffeine. For reasons not well understood, but probably related to their recent history of caffeine consumption, some individuals do not show performance enhancement on tasks that are widely considered sensitive to the effects of caffeine (e.g., simple reaction time) (Attwood et al. 2007; Rogers et al. 2003). It is, therefore, plausible that individuals who show no effect of caffeine on basic performance may also show no changes in alcohol-related performance after caffeine. In order to assess whether individual differences in responsiveness to caffeine moderated the primary outcomes, we undertook exploratory analysis investigating whether caffeine responsiveness as measured by SRT performance (Attwood et al. 2007) predicted effects of caffeine on alcohol-related response inhibition.

Methods

Participants

Twenty-eight (50% male) non-smoking, social alcohol drinkers (between 5 and 35 U/week for females and between 10 and 50 U/week for males) and light caffeine consumers (at least one caffeinated beverage per week but no more than two per day) were recruited from staff and students of the University of Bristol and from the general population by means of poster and flyer advertisements and word of mouth. Participants were required to abstain from alcohol consumption 12 h prior to each test session and to abstain from caffeinated beverages for the duration of the study beginning 5 days prior to the first test session. Participants were required to be aged between 18 and 40, in good physical and psychological health and not taking psychiatric medication or have a familial history of alcoholism as verified by self report. Participants were reimbursed £40 or awarded equivalent course credits at the end of the study. The study was approved by the Faculty of Science Research Ethics Committee at the University of Bristol.

Materials

Computer task battery

Stroop task Stimuli for the colour-naming Stroop comprised four words (red, blue, green, and yellow) presented on a grey background. For congruent trials, words were displayed in the same colour text as the word meaning (e.g., the word blue presented in blue text). For incongruent trials, words were presented in a different coloured text from the word meaning (e.g., the word blue displayed in red text). All stimulus words were 1.5 cm high, presented in Arial font.

Participants manually responded to the presentation of a word using four colour-coded buttons on the keyboard (yellow, red, green and blue). Participants were instructed to respond as quickly and accurately as possible. Each trial began with a fixation cross presented for 500 ms, followed by the stimulus word, which was presented until a response was made or 2,500 ms had elapsed. The task comprised 96 trials, with 48 congruent and 48 incongruent trials presented in a pseudorandom sequence. The task was divided into two blocks with a short break between blocks. The duration of the task was approximately 5 min. Dependent variables were the number of congruent and incongruent errors, and reaction time to correct responses.

Go/no-go task This task was adapted from Rose and Duka (2007). Stimuli consisted of black arrows (5.2 cm×3 cm) presented in the centre of a white screen. Go stimuli were vertically-presented arrows, whilst no-go stimuli were the same arrows rotated 45° clockwise. Participants were instructed to respond to the vertical arrows (go trials) by pressing the spacebar on the keyboard, and to not respond to rotated arrows (no-go trials). Each trial began with a central fixation cross presented for 500 ms, followed by an arrow stimulus presented for 2,000 ms, with an inter-stimulus interval (ISI) of 1,500 ms. The task comprised five blocks, presented in a sequential order as follows; Block 1=go and no-go (g/ng), Block 2=go only, Block 3=g/ng, Block 4=go only, and Block 5=g/ng. Each block consisted of 24 trials, with g/ng blocks including 12 go trials and 12 no-go trials. Go-only blocks were included to encourage habitual response to go stimuli. The duration of the task was approximately 5 min. Dependent variables were errors of commission and omission, and reaction time to go-trials.

Stop-signal task This task was adapted from Mulvihill et al. (1997). Go stimuli were four 1.5-cm high black letters in Arial font (A, B, C, and D) presented in the centre of a white screen. The stop-signal consisted of a 900-Hz auditory tone, presented for 500 ms. Each trial began with a central fixation cross presented for 500 ms, followed by one of the target letters (A, B, C, and D) for 500 ms. Participants were instructed to place their fingers on adjacent keys on the keyboard and told to respond using the left key if the “A” or “B” letter appeared in the centre of the screen and the right key if the “C” or “D” letter appeared. Additionally, participants were instructed to withhold their response every time a stop-signal tone was sounded during the presentation of a letter. Stop-signals were infrequent and presented at 50-ms, 150-ms or 250-ms delays from the presentation of the letter. Each letter presented constituted a single trial, and each trial was separated by an ISI of 2,500 ms. The task included 132 trials divided into two blocks of 66 trials. An auditory stop-signal occurred at random on 36 trials, with 12

trials at each of the three stop-signal delay times (50 ms, 150 ms, and 250 ms). The duration of the task was approximately 8 min. Dependent variables were errors of commission and omission, and reaction time to go trials.

Simple reaction time For each trial, a white asterisk appeared centrally of a black screen (Heatherley et al. 2005). Participants were required to press the space bar as soon as possible after the asterisk appeared. The asterisk stayed on screen until a response was made. Inter-trial intervals were varied to reduce anticipatory responses based on a predictable presentation interval. Six inter-trial intervals were used on eight trials each (1, 2, 3, 7, 9 and 12 s) and trial order was randomised. The task lasted approximately 6 min.

Questionnaires

The questionnaire measures comprised intake questionnaires of general caffeine and alcohol consumption, the Eysenck Personality Questionnaire—Revised (EPQ-R) (Eysenck and Eysenck 1991), the Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al. 1993), the Spielberger State Trait Anxiety Inventory state sub-scale (STAI-State) (Spielberger et al. 1983), the Alcohol Urges Questionnaire (AUQ) (Bohn et al. 1995) and visual analogue scales measuring ratings of “happy”, “drowsy”, “depressed”, “anxious”, “energetic”, “irritable” and “intoxicated” on a 100-mm scale ranging from “Not at all” to “Extremely”. The Biphasic Alcohol Effects Scale (BAES) (Martin et al. 1993) was also completed to assess perceived alcohol intoxication. The scale was adapted to a visual analogue scale as detailed above in order to increase sensitivity to small changes in perceived intoxication.

Drinks

In advance of the study sessions, the experimenter made four drinks for each participant: placebo, alcohol, caffeine, alcohol and caffeine. The drinks were labelled by an experimental collaborator in the order pre-specified by the study randomisation. Alcoholic drinks comprised 0.6 g/kg of alcohol, using vodka at 37.5% alcohol, with one part vodka to 2.5 parts tonic water. Non-alcoholic drinks consisted of an equal total volume of tonic water. Drinks were caffeinated by addition of 2.0 mg/kg anhydrous caffeine powder. All drinks were flavoured with lime cordial and chilled prior to serving.

Procedure

Participants attended five afternoon sessions (start time between 12 and 5 pm with individual participants attending

their sessions at approximately the same time of day). Participants were asked to eat similarly on each study session by consuming meals of a size standard to them at times usual for them. The first was a pre-study screening/baseline session at which informed consent was obtained and eligibility confirmed. Participants were weighed and then completed baseline assessments of the computer tasks (task order was randomised across participants). Experimental sessions were scheduled approximately 1 week apart with no sessions being scheduled within 7 days of each other.

The remaining four sessions (1–4) followed the same procedure with the exception of drink content. Drink administration was double-blind and drink order was randomised across participants. On arrival, breath alcohol (Alcoholhawk Breathalyser, UK Breathalysers) and carbon monoxide (PICO Smokerlyzer, Bedford Scientific Ltd.) readings were taken and a saliva swab was taken to simulate verification of caffeine abstinence (i.e., not analysed). Participants then complete the questionnaire measures of alcohol craving, state anxiety, alcohol intoxication and mood. Following this, a drink was presented to participants who were given 10 min to consume all of the drink, followed by a further 10 min to sit quietly. This was to allow drink absorption and during this time participants completed the AUDIT, caffeine consumption questionnaire and EPQ-R (session 1 only). Following the absorption interval, the state questionnaire measures were completed again, after which participants completed the computer task battery (task order was randomised across participants). Prior to leaving, participants completed the state questionnaire measures and were asked whether they thought that their drink had contained alcohol and/or caffeine. At the end of the final test session, participants were debriefed and unblinded as to which drinks they received during which session, and reimbursed as appropriate.

Statistical analysis

All statistical analyses were performed using SPSS Version 18 (SPSS, Inc., Chicago, Illinois). Square root transformations were applied to data sets where variables were not normally distributed and Greenhouse–Geisser statistics are reported where Mauchly’s Test of Sphericity was significant ($p < 0.05$). For SRT data, outliers were assumed and removed if reaction times fell below 100 or above 2,000 ms (0.3% of data set). As all other tasks had a limited response window (see “Materials”), only lower exclusions of 100 ms were considered reaction time outliers and were removed (<1% of data in all cases). In addition, participants were removed from the analysis if their mean reaction time fell three or more standard deviations above the group mean on any test session.

Task data were analysed using a series of one-way ANOVAs with drink (placebo, alcohol, and alcohol/caffeine)

as the within-subjects factor. Additional within-subjects of congruence (congruent and incongruent) and stop signal (50, 150 and 250 ms) were included for Stroop and stop-signal commission errors, respectively. Where appropriate, post-hoc paired *t*-tests were used for pairwise comparisons.

For subjective ratings of anxiety, mood and craving, a series of 3×3 repeated measures ANOVAs were used with drink (placebo, alcohol, and alcohol/caffeine) and time (baseline, pre-drink, and post-drink) as within-subjects factors.

In order to explore the relationship between caffeine “responsiveness” and caffeine-related compensation for alcohol impairment, a responsiveness score was calculated by subtracting mean SRT on the caffeine-only session from the same score at baseline. We used SRT as it is particularly sensitive to the effects of caffeine and has been used previously to identify caffeine “responders” (Attwood et al. 2007). Simple linear regressions were performed on each cognitive outcome obtained during the alcohol/caffeine session (GNG commission errors, stop-signal commission and omission errors and Stroop reaction time and errors for incongruent and congruent trials) with responsiveness score as the predictor variable.

Results

Participants

Participants were aged between 18 and 33 years ($M=23$, $SD=5$) and had AUDIT scores between 4 and 28 ($M=13$, $SD=6$). All were low consumers of caffeine drinking with reported intake of between 14 and 233 mg per day ($M=101$, $SD=47$). Two participants failed to complete all of the experimental sessions, and therefore, the final data set comprised 26 participants. Data were missing for one participant

for the stop-signal task due to computer malfunction. Drink condition means for all task data are presented in Table 1.

Simple reaction time

A main effect of drink was observed [$F(2,48)=3.33$, $p=0.044$], with the slowest times occurring after alcohol and the fastest times after placebo. Post-hoc paired *t*-tests revealed that participants were significantly faster after placebo compared to alcohol [$t(24)=2.24$, $p=0.034$]. There was a trend towards faster reaction times after placebo compared to alcohol/caffeine [$t(24)=1.90$, $p=0.070$] drinks. There was no significant difference in SRT between alcohol/caffeine compared to the alcohol alone condition [$t(24)=0.97$, $p=0.34$].

Go–no-go errors

There was a trend towards a main effect of drink for commission errors [$F(2.0,36.3)=3.31$, $p=0.062$], with fewer errors occurring after placebo compared to alcohol [$t(25)=1.78$, $p=0.09$] and alcohol/caffeine [$t(25)=2.73$, $p=0.01$]. Alcohol and alcohol/caffeine conditions did not significantly differ [$t(25)=0.06$, $p=0.95$]. Omission errors were not analysed due to too few data points (total count of 10 omission errors across all sessions and participants).

For reaction time, there was a trend main effect of drink [$F(2,50)=2.92$, $p=0.063$] with faster reaction times occurring after placebo compared to alcohol [$t(25)=2.13$, $p=0.043$] and alcohol/caffeine [$t(25)=2.01$, $p=0.055$]. Alcohol and alcohol/caffeine conditions did not significantly differ [$t(25)=0.43$, $p=0.67$].

Stroop

There was a main effect of drink for number of errors [$F(2,50)=3.31$, $p=0.045$], with significantly more errors occurring in the alcohol/caffeine condition compared to

Table 1 Task outcome means for placebo, alcohol and alcohol/caffeine drink conditions

	Placebo	Alcohol/caffeine	Alcohol	Significance (<i>p</i> -value)	Effect size (η^2)
SRT (ms)	395.5 (43.2)	411.9 (49.4)	422.0 (48.1)	0.044	0.12
GNG commission errors ^a	1.30 (0.9)	1.69 (0.9)	1.71 (1.1)	0.062	0.12
GNG reaction time	338.7 (52.3)	357.9 (60.6)	362.4 (63.6)	0.063	0.11
Stroop errors ^a	1.10 (0.68)	1.44 (0.70)	1.24 (0.76)	0.045	0.12
Stroop RT (ms)	618.4 (64.4)	625.5 (76.9)	637.7 (74.1)	0.16	0.07
Stop signal omission errors ^a	1.30 (1.00)	1.23 (1.24)	1.84 (1.71)	0.037	0.14
Stop signal commission errors ^a	0.54 (0.44)	0.63 (0.37)	0.74 (0.46)	0.021	0.15
Stop signal reaction time (go trials)	518.6 (48.3)	524.8 (59.3)	518.6 (48.3)	0.12	0.08

Standard deviations given in parenthesis

^aTransformed data

placebo [$t(25)=2.51, p=0.019$]. No other comparisons were significant ($ps>0.17$). There was no main effect of congruence [$F(1,25)=1.61, p=0.22$] or congruence by drink interaction [$F(2,50)=0.19, p=0.83$].

For Stroop reaction time, there was a main effect of congruence [$F(1,25)=60.8, p<0.001$] with faster times occurring on congruent ($M=602.4, SD=63.9$) versus incongruent ($M=652.0, SD=71.3$) trials. There was no main effect of drink ($p=0.16$) or congruence by drink interaction ($p=0.59$).

Stop-signal

There was a significant main effect of drink for overall omission errors [$F(1.5, 35.3)=4.05, p=0.037$]. More errors were made in the alcohol only condition compared to placebo [$t(24)=-1.87, p=0.074$] and alcohol/caffeine [$t(24)=2.59, p=0.016$]. Placebo and alcohol/caffeine conditions did not significantly differ ($p=0.67$). There was no main effect of drink for reaction time on correct go trials [$F(2,48)=2.21, p=0.12$].

There was a main effect of drink for commission errors [$F(2,48)=4.18, p=0.021$] with significantly more errors occurring after alcohol compared to placebo [$t(24)=-2.65, p=0.014$] and alcohol/caffeine [$t(24)=-2.17, p=0.040$]. There was also a main effect of stop signal [$F(1.3,31.5)=86.5, p<0.001$] with a linear increase in number of errors as stop signal (i.e., difficulty increased). The drink by stop signal interaction was not significant [$F(2.9,69.1)=1.23, p=0.30$].

BAES

There was a significant drink by time interaction for the stimulation sub-scale [$F(4,100)=5.59, p<0.001$]. Ratings of stimulation decreased over time in the placebo and alcohol conditions and increased over time in the alcohol/caffeine condition, although these main effects of time were not statistically significant ($ps>0.1$). However, there were significant linear decreases in stimulation across all time points following in the placebo condition [$F(2,50)=6.36, p=0.003$] (see Fig. 1a).

For the sedation subscale, there was a main effect of time [$F(2,50)=10.47, p<0.001$], with linear increases in sedation over time. In addition, there was a trend towards a time by drink interaction [$F(4,100)=2.16, p=0.079$]. Further analyses revealed main effects of time for alcohol [$F(2,50)=14.05, p<0.001$] and placebo [$F(2,50)=5.33, p=0.008$], and a trend effect of time for alcohol/caffeine [$F(2,50)=2.89, p=0.065$]. There was an increase in sedation across all drink conditions which was greatest in the alcohol only condition (see Fig. 1b).

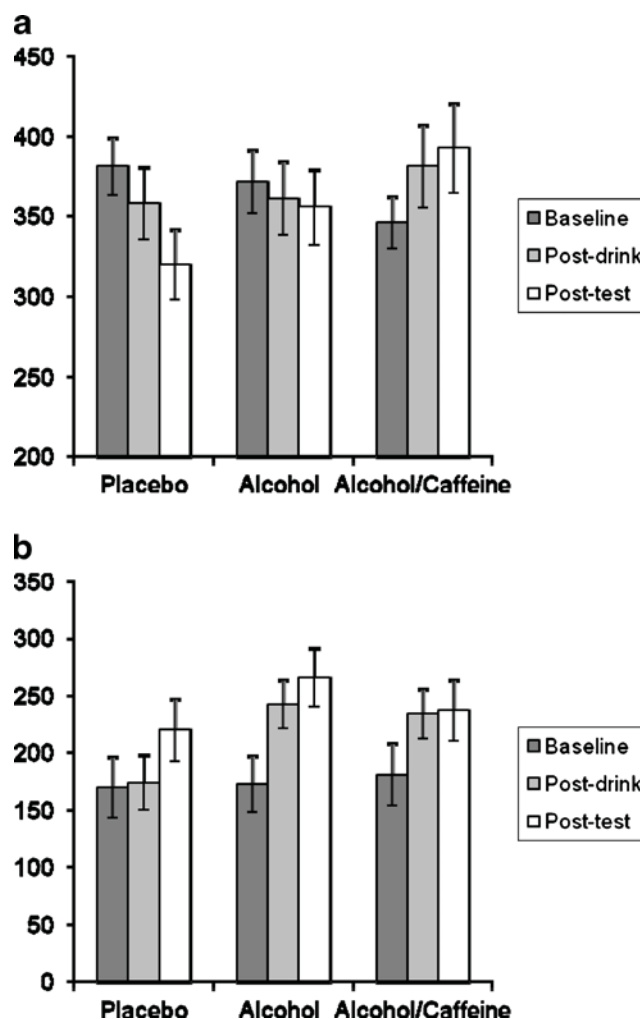


Fig. 1 **a** Total mean (\pm SE) score for BAES stimulation across placebo, alcohol only and alcohol/caffeine sessions. **b** Total mean (\pm SE) score for BAES sedation across placebo, alcohol only and alcohol/caffeine sessions

STAI

There was a main effect of time [$F(2,50)=20.62, p<0.001$] with decreases in state anxiety across time. There was no main effect of drink [$F(2,50)=0.77, p=0.47$] or drink by time interaction [$F(4,100)=0.67, p=0.62$].

AUQ

There were no main effects of time [$F(2,50)=0.30, p=0.74$] or drink [$F(2,50)=2.08, p=0.14$]. There was a significant time by drink interaction [$F(4,100)=5.14, p=0.001$] with significant decreases in alcohol craving in the placebo condition [$F(1.6,40.2)=6.19, p=0.004$] but no significant change occurring in the alcohol [$F(1.3,31.6)=2.17, p=0.15$] or alcohol/caffeine [$F(1.2,30.5)=0.21, p=0.81$] conditions.

Visual analogue scales

Main effects of time were observed on ratings of anxiety [$F(1.3,32.6)=4.82$, $p=0.027$] and drowsiness [$F(2,50)=4.46$, $p=0.017$], with decreases in anxiety and increases in drowsiness occurring over time.

In addition, there was a main effect of time [$F(2,50)=92.0$, $p<0.001$] and drink [$F(2,50)=38.1$, $p<0.001$] for ratings of intoxication, but these were qualified by a drink by time interaction [$F(3.1,78.3)=29.5$, $p<0.001$]. There were significant increases in intoxication over time in all conditions ($ps<0.002$), but these increases were significantly greater in the alcohol-containing drink conditions. Ratings of intoxication were significantly higher for alcohol and alcohol/caffeine compared to placebo at both post-drink timepoints ($ps<0.001$). In contrast, alcohol and alcohol/caffeine conditions did not differ significantly at any timepoint ($ps>0.05$) (see Fig. 2).

There was also a significant time by drink interaction for ratings of anxiety [$F(2.2,54.5)=5.08$, $p=0.001$]. There were linear decreases in anxiety over time in alcohol and alcohol/caffeine conditions, and a linear increase in anxiety in the placebo condition. Post-hoc tests revealed that this effect of time was only significant for the alcohol condition [$F(1.5,37.7)=9.0$, $p<0.001$].

Effects of caffeine and exploratory analysis of caffeine responsiveness

One participant was removed from the analysis due to being an extreme outlier on SRT. When this participant was removed, the data did not significantly differ from normality. The linear regressions revealed that the responsiveness score did not significantly predict outcome in the alcohol/caffeine session on any of the other behavioural measures (go–no-go commission errors, go trial reaction time, stop-signal

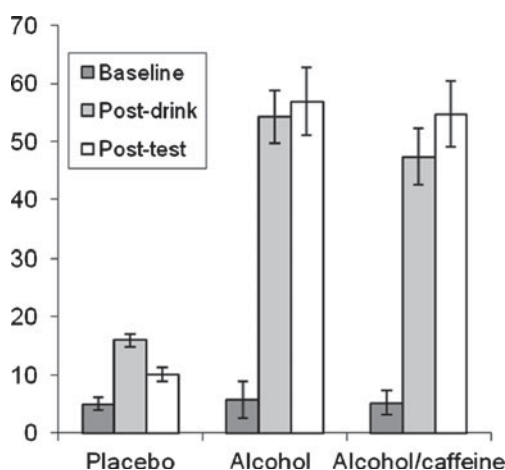


Fig. 2 Mean (\pm SE) VAS intoxication score across placebo, alcohol only and alcohol/caffeine sessions

commission errors, omission errors and go trial reaction time, and Stroop reaction time and errors) ($ps>0.22$).

Discussion

The aim of this study was to explore the cognitive and subjective effects of caffeine in combination with alcohol in order to assess the hypothesis that caffeine compensates for perceived intoxication but not alcohol-related detriments in behavioural control. Effects of drink were observed on SRT, Stroop errors, go–no-go commission errors and go trial reaction times, and stop-signal commission and omission errors. For all but Stroop errors, worst performance was observed after alcohol with scores differing from placebo. There was evidence that caffeine offset alcohol-related detriment of stop-signal performance, but not performance on the other tasks. For Stroop accuracy, worst performance was observed in the alcohol/caffeine condition. In sum, there was mixed support for compensation for alcohol-induced performance deficits on inhibitory control tasks, with attenuation, no effect and worsened performance being found across the three behavioural control tasks.

There was some support for subjective differences across drink conditions. Based on the BAES questionnaire, stimulation decreased over time in the alcohol and placebo conditions, but increased in the alcohol/caffeine condition. Sedation increased across all conditions but the magnitude of this effect was greatest after alcohol, suggesting that caffeine may have offset some of the sedative effects of alcohol. In contrast, caffeine did not affect absolute levels of perceived intoxication (VAS), implying that caffeine may change perceived intoxication qualitatively, rather than quantitatively. That is, the addition of caffeine may change the nature of intoxication rather than the degree of intoxication per se.

These findings are consistent with anecdotal reports stating that caffeinated alcoholic beverages may increase arousal (compared to alcohol alone), thereby enabling the individual to drink for a longer period of time. Alongside this, there was limited evidence that caffeine offsets some aspects of alcohol-induced performance deficit, although this was task-dependent. Stop-signal accuracy was better after alcohol/caffeine compared to alcohol alone, although this was accompanied by slower reaction times (non-significant) in the alcohol/caffeine condition, and therefore, a speed–accuracy trade off cannot be ruled out. However, it is also noteworthy that when considering many task outcomes, performance was “better” in the alcohol/caffeine condition compared to alcohol, although these effects were not statistically significant. Given the small effect sizes, a greater sample size may be required in future studies to elucidate whether this pattern of effect constitutes a real benefit of caffeine.

Caffeine is a psychostimulant drug that acts as an adenosine receptor antagonist. When administered alone, caffeine's performance-enhancing effects are believed to be related largely to its ability to increase arousal. Therefore, it has been argued that benefits of caffeine depend on the relative benefit of arousal on any given task. As such, acute doses of caffeine (versus placebo) are usually associated with enhanced performance on relatively non-demanding tasks such as SRT and sustained attention, particularly when baseline arousal is low (e.g., caffeine withdrawal, post-lunch dip, etc.), with no (or even detrimental) effects on more cognitively demanding tasks. This may explain why the addition of caffeine had negative consequences on the Stroop task, which involves cognitive interference of distracting information that engages automatic processes. In contrast, although the stop-signal is relatively demanding, the monitoring of the presence of the tone requires sustained attention, which fits with the known profile of caffeine performance benefit.

The current study replicated the findings of Fillmore and Vogel-Sprott (1999), with caffeine compensating for alcohol-induced deficits in stop-signal performance. Furthermore, we demonstrated this at a lower dose (2.0 mg/kg) than was previously administered. Similarly, we replicated the findings of Marczinski and Fillmore (2003) in which caffeine failed to compensate for alcohol-induced impairment of response inhibition on the go–no-go task. These authors did report facilitation of “response execution” after caffeine and alcohol (compared to alcohol alone), but as this was based on reaction time to no-go trials (i.e., errors in responding); it is debatable whether this is truly a benefit of response execution and should be interpreted with caution. In addition, we must remain careful when comparing findings directly across studies that utilise different methodologies. For example, Marczinski and Fillmore (2003) used pure ethanol compared to this study which administered vodka that has additional constituents that may affect responding.

Despite some support of anecdotal reports of the effects of caffeinated alcoholic beverages (i.e., limited/weak behavioural changes and increased stimulation), it is clear that there is a discrepancy between the rather weak findings of laboratory studies and the reports of substantial negative consequences in the real world. It is plausible that the risks associated with these drinks have been exaggerated, but there are also important differences between laboratory studies and real-world drinking behaviour. Firstly, laboratory studies generally administer only one drink and the caffeine-to-alcohol ratio is often higher than in real life situations. Although the drinks may contain a relatively high dose of alcohol for a single beverage, this paradigm is not readily comparable to an evening of sustained drinking. The effects of and risks associated with caffeinated alcoholic beverages are likely to increase as more drinks are consumed. In addition, laboratory studies are blinded in order

to assess pharmacological effects by limiting the influence of expectancy. In the real world, however, the expectancy of heightened stimulation is likely to be an important factor in the effects caffeinated drinks elicit when paired with alcohol, and warrants further investigation.

A secondary aim of this study was to control caffeine consumer history and assess the importance of caffeine responsiveness on any combined effects with alcohol. The effects of caffeine appear to be dependent on caffeine consumer history and abstinence status, and in order to reduce noise associated with individual differences, we controlled history and abstinence in this study by only recruiting light consumers who were a week abstinent prior to the study, and remained caffeine abstinent throughout the study. The purpose of this was twofold: i) to reduce the noise associated with caffeine withdrawal and determine whether any effects of caffeine on alcohol would be observed in a non-withdrawn sample and ii) to better model the real world drinking in which alcohol/caffeine drinkers may not routinely drink caffeine otherwise and, if they do, are not likely to be in an acutely withdrawn state. In order to assess caffeine responsiveness, we included a caffeine-only session, in which we could assess the participant's response when given caffeine alone. Using a responsiveness estimate reported previously (Attwood et al. 2007), we assessed whether basic responsiveness to caffeine predicted caffeine's effects when paired with alcohol. We did not find any significant effects from this analysis, implying caffeine responsiveness does not mediate the effects of caffeine on alcohol. However, these findings are extremely preliminary and future research should examine individual factors that moderate the caffeine–alcohol relationship including previous exposure and tolerance to both alcohol and caffeine.

There are some limitations of the study that should be acknowledged. We balanced effects of sex by recruiting equal numbers of male and female participants, but the study was not sufficiently powered to make gender comparisons, which may be important and informative. It should be noted that we did not modify alcohol dose for female participants, which is an increasingly common practice in alcohol challenge studies due to differences in alcohol pharmacokinetics between males and females. We do not expect this to have affected the outcome of the study as this was a within-subjects design and, therefore, noise associated with differences in BAC would be systematic across alcohol groups. However, this is a limitation of the current study that may have resulted in higher blood alcohol concentrations in females relative to males. In addition, participants were all regular consumers of alcohol drinking between 5 and 35 U/week if female and between 10 and 50 U/week if male, and had a mean AUDIT score of 13. These figures are relatively higher than that recommended for the general population and are indicative of hazardous drinking. However,

our sample was predominantly undergraduate students and this level of alcohol consumption is relatively normal in this group and equivalent to our previous studies using undergraduate samples. Nevertheless, this potential limitation should be kept in mind when interpreting results and when generalising these findings to the general population. Finally, we asked participants to provide saliva samples to promote compliance with the requirement to abstain from consuming caffeine for the duration of the study but, as we did not analyse these samples, compliance cannot be objectively verified. However, it is worth noting that the participants were light caffeine consumers, so it might be expected that they would find it relatively unproblematic to abstain. Furthermore, in another recent study from our laboratory, analysis of mid-morning salivary caffeine concentration indicated that only five out of 222 (2%) caffeine consumers (mean daily caffeine intake=240 mg) failed to comply with the instruction to abstain from caffeine overnight (Rogers et al. 2010). The current study used a relatively low dose of caffeine (2.0 mg/kg) that is closer to the amount of caffeine usually contained in real-world caffeinated alcoholic drinks. This was chosen to assess whether a lower dose than previously reported, and one more consistent to a normal energy drink serving, could elicit relevant changes in alcohol-related performance. We found consistent outcomes with previous studies using a higher dose (4.4 mg/kg) and a study which used two doses of caffeine did not find dose effects on performance (Marczinski and Fillmore 2003). However, the dose-response curve should be investigated in future studies as it has been proposed that caffeine may decrease alcohol-related physical and cognitive impairment when alcohol blood levels are low but have little or no effect when blood levels are high (Liguori and Robinson 2001; Weldy 2010). This will have further implications for generalising the laboratory-based findings to real world situations, as performance benefits of caffeine may only occur after one or two drinks.

In sum, these data suggest that caffeine may alter the qualitative nature of intoxication without altering perceived degree of intoxication. The subsequent effect on cognition may also be more complicated than initially believed, with the addition of caffeine improving some facets of behavioural control after alcohol but inducing further deficits on others. When interpreting data from laboratory studies, we need to stay mindful that the effects and risks associated with caffeinated alcoholic beverages are likely to increase with the number of drinks consumed. Therefore, laboratory studies only provide a snapshot of potential real world effects, which may be diluted due to limited influence of other important factors such as expectancy. Future studies should begin to assess effects of multiple drinks and investigate the role of individual differences and expectancy.

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