Pharmacology, Biochemistry and Behavior 102 (2012) 569–577

Contents lists available at SciVerse ScienceDirect

Pharmacology, Biochemistry and Behavior

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

Differential cognitive effects of energy drink ingredients: Caffeine, taurine, and glucose

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ARTICLE INFO

Article history:
Received 31 May 2012
Received in revised form 4 July 2012
Accepted 11 July 2012
Available online 20 July 2012

Keywords:
Caffeine
Taurine
Glucose
Cognition
Mood
Cortisol
Heart rate

ABSTRACT

Energy drinks containing caffeine, taurine, and glucose may improve mood and cognitive performance. However, there are no studies assessing the individual and interactive effects of these ingredients. We evaluated the effects of caffeine, taurine, and glucose alone and in combination on cognitive performance and mood in 24-hour caffeine-abstained habitual caffeine consumers. Using a randomized, double-blind, mixed design, 48 habitual caffeine consumers (18 male, 30 female) who were 24-hour caffeine deprived received one of four treatments (200 mg caffeine/0 mg taurine, 0 mg caffeine/2000 mg taurine, 200 mg caffeine/2000 mg taurine, 0 mg caffeine/0 mg taurine), on each of four separate days, separated by a 3-day wash-out period. Between-participants treatment was a glucose drink (50 g glucose, placebo). Salivary cortisol, mood and heart rate were measured. An attention task was administered 30-minutes post-treatment, followed by a working memory and reaction time task 60-minutes post-treatment. Caffeine enhanced executive control and working memory, and reduced simple and choice reaction time. Taurine increased choice reaction time but reduced reaction time in the working memory tasks. Glucose alone slowed choice reaction time. Glucose in combination with caffeine, enhanced object working memory and in combination with taurine, enhanced orienting attention. Limited glucose effects may reflect low task difficulty relative to subjects' cognitive ability. Caffeine reduced feelings of fatigue and increased tension and vigor. Taurine reversed the effects of caffeine on vigor and caffeine-withdrawal symptoms. No effects were found for salivary cortisol or heart rate. Caffeine, not taurine or glucose, is likely responsible for reported changes in cognitive performance following consumption of energy drinks, especially in caffeine-withdrawn habitual caffeine consumers.

1. Introduction

Energy drinks have become a popular beverage. Over half of college students surveyed reported drinking at least one energy drink per month (Malinauskas et al., 2007). The most common reasons for energy drink consumption include counteracting sleepiness and increasing energy, maintaining alertness while studying and driving, and reducing symptoms of a hangover (Attila and Cakir, 2011; Malinauskas et al., 2007). Laboratory studies have confirmed that energy drinks can reduce fatigue and improve psychomotor speed and behavioral control (Alford et al., 2001; Horne and Reyner, 2001; Howard and Marczinski, 2010; Kennedy and Scholey, 2004; Smit et al., 2004). Researchers who have examined the cognitive effects of energy drinks typically attribute changes in cognitive performance and mood to the combination of caffeine, taurine, and glucose in the drinks. Similarly, studies assessing energy drink ingredients have found that the combination of caffeine and taurine decreased reaction time relative to placebo (Seidl et al., 2000), and attenuated fatigue-induced reaction time increases (Childs and de Wit, 2008), but had no effect on short-term memory (Bichler et al., 2006). To our knowledge the only previous study to examine the effects of energy drink ingredients, alone and together, showed that a whole energy drink containing caffeine, glucose, ginseng and ginkgo biloba improved memory and attention, but each ingredient alone had no effect on mood or cognition (Scholey and Kennedy, 2004). However, because the ingredients of interest were not assessed using a cross-over design, it is impossible to determine whether the effects were due to an interaction between two or more ingredients.

Caffeine (1,3,7-trimethylxanthine) is the most commonly used behaviorally-active substance in the world. Daily caffeine intake averages 170 to 210 mg/day in the United States, United Kingdom, and Canada (Koppelstaetter et al., 2010; Smith, 2011). Common energy drinks contain approximately 80 mg caffeine per 8 oz serving, but commercially available energy drinks are often sold in 16-oz containers, and can contain up to 505 mg of caffeine.

Caffeine reliably enhances vigilance and psychomotor performance (Smith, 2011). It has been suggested that the beneficial effects of

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doi:10.1016/j.pbb.2012.07.004

caffeine on cognitive performance are actually due to the reversal of caffeine withdrawal (James and Rogers, 2005) or the reversal of environmental-induced cognitive impairments, such as sleep deprivation, physical fatigue and psychological stress (Koppelstaetter et al., 2010; Lieberman, 2003; Lorist and Tops, 2003). Whether caffeine enhances cognition or rather reverses withdrawal-induced cognitive impairment remains controversial. Caffeine improved vigilance in both habitual and non-habitual caffeine consumers (Hewlett and Smith, 2007) and reaction time in habitual consumers after consuming caffeine ad lib as well as after abstaining from caffeine (Lane, 1997; Phillips-Bute and Lane, 1998). However others found that caffeine enhanced reaction time in the abstained state only (Addicott and Laurienti, 2009), and in high relative to moderate habitual caffeine consumers (Attwood et al., 2007).

There is less evidence to support an effect of caffeine on non-motor cognitive domains. Most studies have failed to find effects of caffeine on episodic memory, though some have described beneficial effects of caffeine on working memory and semantic memory retrieval (for review, see Smith, 2011). Caffeine improved N-Back working memory performance in habitual caffeine consumers following both caffeine abstinence and normal caffeine intake (Addicott and Laurienti, 2009) but had no effect in another study, which used a lower caffeine dose (Koppelstaetter et al., 2008). Caffeine has been found to enhance attention regardless of habitual caffeine consumption (Brunyé et al., 2010a,b; Yeomans et al., 2002), but caffeine may have greater effects on some aspects of attention (i.e. response time, lapses in attention) in non-habitual than habitual caffeine consumers (Smith et al., 2006). Given that energy drinks influence similar cognitive domains, i.e. psychomotor performance, memory and attention (Alford et al., 2001; Childs and de Wit, 2008; Horne and Reyner, 2001; Howard and Marczinski, 2010; Kennedy and Scholey, 2004; Smit et al., 2004), it is of interest whether other ingredients in energy drinks have any effects beyond those of caffeine.

Taurine (2-aminoethanesulfonic acid) is a sulfonated β-amino acid, derived from diet or synthesized from cysteine, mainly in the liver (Junyent et al., 2011; Kimura et al., 2009; Stapleton et al., 1997). Taurine is highly concentrated in the heart and liver as well as the central nervous system including the brain stem and hippocampus (Ito et al., 2009; Vohra and Hui, 2000), where it plays a role in osmoregulation, membrane stabilization, neuroprotection, neuromodulation, and regulation of cellular calcium level (Junyent et al., 2009, 2011). Dietary sources include meat and some dairy products (Stapleton et al., 1997) and more recently energy drinks such as Red Bull®, Monster®, and Rockstar®, which generally contain 1000 mg taurine per 8 oz serving. The majority of research investigating the cognitive effects of taurine has been done in animals. This work suggests that taurine may prevent or reverse neurotoxin-induced deficits in learning, memory, and long-term potentiation, but does not enhance cognitive performance in healthy, intact animals (Chepkova et al., 2006; Ito et al., 2009; Vohra and Hui, 2000; Zhu et al., 2005). Despite the increasing consumption of taurine-containing energy drinks and the wealth of research into the cognitive effects of caffeine, to our knowledge no study to date has assessed whether taurine influences caffeine-induced changes in cognitive performance.

Glucose is thought to improve some aspects of cognitive performance, notably spatial, logical, short- and long-term memory, however, the results are inconsistent (for review, see Gorby et al., 2010). This inconsistency may be due to differences in study participants and design. Glucose has greater enhancing effect in older adults than younger adults (Meikle et al., 2004) and in tasks with high levels of difficulty or that require divided attention (Kennedy and Scholey, 2000; Scholey et al., 2001; Sunram-Lea et al., 2002). Energy drinks contain approximately 27 g glucose per 8-oz serving (roughly the amount in 8-oz of Coca Cola Classic®). While the glucose content of these drinks is purported to contribute to their energizing effects, only three studies have assessed the differential contributions of glucose and caffeine to cognitive performance and results are somewhat equivocal (Adan and Serra-Grabulosa, 2010). Adan and Serra-Grabulosa (2010) showed that caffeine and glucose, alone and together, reduced reaction time and together improved sustained attention and verbal memory. However Serra-Grabulosa et al., 2010 found no effect of caffeine and glucose, taken together, on sustained attention. Scholey and Kennedy (2004) assessed the influence of energy drink ingredients including caffeine, glucose, ginseng and ginkgo biloba as well as a whole energy drink on multiple measures of cognition and mood. They found that whole energy drink intake improved attention and "secondary memory," including immediate and delayed recall. Caffeine intake showed trends towards improved attention, choice reaction time and memory, particularly delayed word recognition, but caffeine, glucose, ginseng and ginkgo biloba evidenced no significant effects, possibly due to low sample size (Scholey and Kennedy, 2004).

1.1. Present study

The primary objective of the present study was to examine the relative effects of caffeine, taurine, and their combination on measures of attention, working memory and reaction time. We chose the Attention Network Task (Fan et al., 2002, 2005) because it simultaneously tests individual performance of the three neuroanatomically-defined visual attention networks: *alerting, orienting, executive control* (Posner, 1990). The alerting and executive control networks are particularly sensitive to the effects of caffeine in both habitual and non-habitual caffeine consumers (Brunyé et al., 2010a,b). These networks rely on frontal and pre-frontal areas (Fan et al., 2005), regions in which caffeine is known to influence dopaminergic activation. We assessed working memory using the N-Back Task (Nystrom et al., 2000) because it allowed us to assess three working memory systems (verbal, spatial, and object), and because the task activates areas associated with both working memory performance and caffeine intake (e.g. anterior cingulate, parietal and frontal regions), as caffeine's affinity for A_1 receptors in the basal forebrain and A_{2A} receptors in the hypothalamus are thought to mediate the cholinergic, noradrenergic, histaminergic, orexinergic pathways, which are involved in its arousing properties (Ferre, 2010). We chose simple and 2-choice reaction time tasks to measure psychomotor performance based on previous studies on energy drinks and caffeine that used these tasks (Adan and Serra-Grabulosa, 2010; Addicott and Laurienti, 2009; Attwood et al., 2007; Childs and de Wit, 2008; Smit et al., 2004).

We hypothesized that caffeine would enhance cognitive performance. Although taurine alone has not been studied in humans, the limited literature to date suggests that taurine does not enhance cognitive performance in healthy, intact animals. We expected that taurine would have little effect on mood and cognitive performance. Energy drinks contain both sugar and caffeine, which may have interactive effects on cognitive performance that cannot be explained by either substance alone (Adan and Serra-Grabulosa, 2010). Therefore, a secondary objective was to assess the impact of glucose, alone and in combination with caffeine and taurine, on cognitive performance. We expected that glucose would enhance cognitive performance relative to placebo. The present study also sought to determine the effects of each ingredient alone and in combination on cortisol and heart rate. Previous research found that whole energy drinks increased heart rate (Alford et al., 2001) whereas caffeine and taurine reduced heart rate (Bichler et al., 2006). In studies looking at only habitual caffeine consumers, caffeine alone had no effect on heart rate (Koppelstaetter et al., 2008; Lane, 1997) and mixed effects on cortisol (Lovallo et al., 1996, 2005).

2. Materials and methods

2.1. Participants

Forty eight undergraduate students (18 male, 30 female; mean age 20.08 ± 1.85 years; mean BMI 21.85 ± 4.29) participated for monetary

compensation ($10 USD/h). All participants were moderate to high habitual caffeine consumers (at least 200 mg/day, M = 527.59 ± 277.13 mg/day), non-nicotine users, in good health, and did not use prescription medication other than oral contraceptives. Written informed consent was obtained, and all procedures were approved by the Tufts University Institutional Review Board.

2.2. Design

We used a double-blind, mixed factor, repeated measures design with caffeine and taurine treatment as within participants factors and glucose treatment as a between participants factor. All participants completed the four caffeine and taurine treatments: 1) 0 mg caffeine, 0 mg taurine; 2) 0 mg caffeine, 2000 mg taurine; 3) 200 mg caffeine, 0 mg taurine and 4) 200 mg caffeine and 2000 mg taurine. These treatments were crossed with glucose, such that half of the participants were administered glucose, 50 g (9 male, 15 female), and half were administered placebo, 50 g Stevia (8 male, 16 female). The values chosen for glucose, caffeine and taurine approximate those found in the commonly consumed energy drink Monster® (160 mg caffeine, 2000 mg taurine, 52 g sugar) and are no more than could be purchased from a variety of commercially available products. Caffeine and taurine were administered in identical capsule form with water. Treatment order was counterbalanced across participants using a Latin square. Glucose or placebo was administered as a 500-ml drink (250 ml glucose + 250 ml sparkling water; 250 ml placebo + 250 ml sparkling water). The placebo contained artificial sweeteners so that it was matched for appearance and taste with the experimental beverage.

2.3. Questionnaires and cognitive tasks

Participants were evaluated using multiple measures of caffeine withdrawal symptoms, mood, and cognitive performance. Questionnaires were administered on desktop computers, with the exception of the Typical Consumption Questionnaire which was administered by paper and pencil.

2.3.1. Typical consumption

The Typical Consumption Questionnaire (TCQ) asks for typical consumption of a variety of caffeinated products, including coffee, tea, soft drinks, and energy drinks. The TCQ was completed during the consent/screening session.

2.3.2. Withdrawal questionnaire

The Withdrawal Questionnaire (WQ) determines the degree of caffeine withdrawal participants are experiencing (Evans and Griffiths, 1999). Participants were asked to rate each of the 26 items on a 4-point scale from "not at all" (0) to "very much" (3), based on how they felt at that moment. The WQ was analyzed using the 5 subscales corresponding to headache/poor mood (e.g. depressed, headache), activity/alertness (e.g. alert, content), physical symptoms (e.g. lightheaded, jittery), tiredness (e.g. drowsy, sluggish), and flu-like symptoms (e.g. muscle pain, runny nose).

2.3.3. Profile of mood states questionnaire

The Profile of Mood States (POMS) is an inventory of subjective mood and arousal states (McNair et al., 1971). Participants were asked to rate a series of 65 mood related adjectives on a five point scale, using the response set of "how are you feeling right now?" The adjectives factor into six mood subscales (tension, depression, anger, vigor, fatigue, and confusion; Lieberman et al., 1996). The POMS is sensitive to a wide range of environmental factors, including sleep loss, nutritional manipulations, and sub-clinical doses of various drugs (Banderet and Lieberman, 1989; Fine et al., 1994; Lieberman et al., 1996, 2002).

2.3.4. Attention network test (ANT)

The ANT simultaneously tests individual performance of the three neuroanatomically-defined visual attention networks (*alerting, orienting, executive control*; Posner, 1990). An ANT trial involves viewing a visual cue and then responding to the direction of a central arrow within an array of horizontally-aligned arrows that can appear either above or below central fixation (Fan et al., 2002). A cue can alert an individual that a trial is about to be presented only ("center"), or it can also orient the individual to where the trial will be presented (above or below fixation: "spatial"; both above and below fixation: "double"). A central target arrow is then presented within an array of horizontally-aligned congruent arrows (same facing direction), incongruent arrows (opposite facing direction), or neutral lines (without arrow heads). Change scores were calculated for each of the three attention networks: alerting, orienting, and executive function, which allowed for the independent assessment of each (Fan et al., 2002, 2005; Redick and Engle, 2006). The alerting change score was calculated by subtracting average double-cue RTs from the no-cue RTs. The orienting change score was calculated by subtracting average spatial cue RTs from center cue RTs. Higher alerting and orienting change scores indicate more efficient functioning of the alerting and orienting systems. A conflict change score was calculated by subtracting average congruent flanker RTs (across all cue types) from incongruent flanker RTs; lower change scores thus indicate more efficient executive control functioning with conflicting information.

Participants completed three blocks of 96 trials (total of 288 trials) presented in random order. Each block presents two trials for each of the four cue conditions (none, center, double, spatial), two target locations (top, bottom), two target directions (left, right), and three flanker conditions (neutral, congruent, incongruent). Each trial consisted of a fixation period (400–1600 ms), cue (100 ms), fixation period (400 ms), target arrow (maximum 1700 ms), and variable intertrial interval (calculated as 3500 ms minus first fixation duration minus reaction time). Reaction time and accuracy were measured when the participant responded to the central arrow's direction (left or right).

2.3.5. N-back task (NB)

The NB task challenges working memory by asking participants to monitor a series of briefly presented stimuli and decide on each trial if the currently presented stimulus is the same as the one presented one, two or three trials before. The main emphasis of this task is thus on monitoring and constant updating of working memory. The current design utilizes verbal, spatial, and object N-Back tasks, each at three levels of task load (1-back, 2-back, and 3-back; (Nystrom et al., 2000). Participants completed 3 separate blocks, 1 for each stimulus type, which contained 57 trials within each of the 3 loads (171 trials per stimulus). Each stimulus was presented for 500 ms followed by a blank screen (2500 ms). Participants could respond either during the stimulus presentation or the blank screen. The verbal task involves monitoring the identity of centrally-presented letters, the spatial task involves monitoring the location of objects presented in varied screen regions, and the object task involves monitoring the shape of centrally-presented objects. The order in which the verbal, spatial, and object conditions were presented was counterbalanced among participants. Dependent measures include reaction time, hit rate and sensitivity (d'). Sensitivity is a composite index of hit rate and false alarm rate, which was calculated by subtracting the z-score of the false alarm rate from the z-score of the hit rate.

2.3.6. Reaction time task (RTT)

In the RTT participants were asked to perform a series of simple and choice reaction time trials in response to colored targets displayed on the computer monitor. Participants completed 5 blocks each of simple and 2-choice reaction time. Simple reaction time included 24 trials per block and choice reaction time included 12 trials per block. Each trial was presented for a maximum of 3000 ms

followed by a 500 ms intertrial interval. Dependent measures include reaction time and accuracy.

2.4. Measures of arousal

2.4.1. Salivary cortisol

Saliva was collected for analyses of salivary cortisol (a biomarker for arousal/stress). Participants were instructed to spit through a straw into a 15 ml saliva collection tube. They were asked to fill the tube half-way and to avoid touching the mouth of the tube with their hands. Samples were aliquoted into 2–1.8 ml plastic vials. The samples were stored at −20 °C until they were assayed. Samples were analyzed in duplicate in an independent laboratory (Salimetrics LLC, State College, Pennsylvania).

2.4.2. Heart rate

Heart rate data was collected continuously throughout each test session using Equivital® heart rate monitors.

2.5. Procedure

During an initial screening/practice session, participants were fully screened, signed the informed consent, and completed the TCQ. The four test sessions took place in the afternoon, beginning between 1300 and 1430 h. Participants abstained from caffeine, over-the-counter medications, and herbal supplements for 24 hr prior to each test session. A 24-hr abstinence period is thought to be a sufficient wash-out period to attenuate the effects of earlier caffeine and taurine consumption, given that the mean plasma and elimination half-life of caffeine ranges from 3 to 10 h (Blanchard and Sawers, 1983; Nehlig et al., 1992; Scott et al., 1989) and for taurine from 0.7 to 1.4 h (Ghandforoush-Sattari et al., 2010). Adherence to the caffeine abstinence period was assessed using a caffeine withdrawal questionnaire, which confirmed that participants were in a state of caffeine withdrawal (e.g. caffeine reduced feelings of headache: caffeine = −.535 ± .537; no caffeine = .078 ± .042; for complete results, see Section 3.1).

Before each test session, participants consumed their normal breakfast and were asked to not eat or drink anything except water as of 0900 the morning of their test session. To control for macronutrient intake, participants came to the lab between 1100 and 1230 h to eat lunch, which consisted of a peanut butter and jelly sandwich, two Oreo® cookies, and a banana (722 kcal, 23.7 g fat, 116.7 g carbohydrate, 16.7 g protein). Participants returned to the lab 2 h later to begin the test session. For a schematic presentation of the study schedule, see Fig. 1.

To allow for absorption while still conducting the cognitive battery while treatment constituents remained at near-maximal plasma levels, participants completed the ANT 30 min after consuming the constituents, and completed the NB and RTT 60 min after consuming the constituents. The ANT and NB/RTT tasks were divided by a 10-minute break to reduce the influence of cognitive fatigue on performance. Results from our lab suggest that the ANT is sensitive to the effects of caffeine within 20-minutes post-intake (Brunyé et al., 2010a,b). Previous research has shown that caffeine peak plasma concentrations vary between individuals and occur between 30 and 120 min after consumption (Arnaud, 1987; Blanchard and Sawers, 1983; Smith, 2002), taurine peak plasma concentrations occur between 60 and 150 min after intake (Ghandforoush-Sattari et al., 2010) and glucose peak plasma levels occur within 30 min after intake (Kennedy and Scholey, 2000).

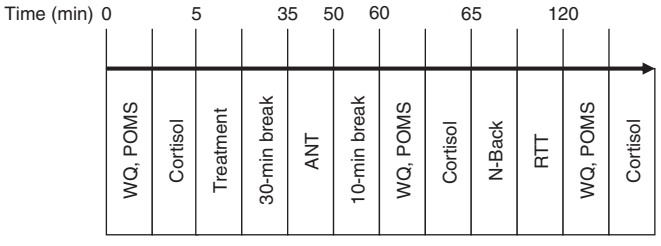

Fig. 1. Schematic representation of the study schedule. During the study sessions, participants first completed baseline measures of the WQ and POMS and provided 6 mL saliva samples. They consumed their assigned treatment capsule and drink. They then took a 30-minute break, completed the ANT, and then took a 10-minute break. Participants then provided a second saliva sample and completed WQ and POMS. They then completed the NB Task and RTT. Finally, they provided a third saliva sample, WQ and POMS. Practice sessions were identical to test sessions with the exceptions that during practice session, participants did not consume a treatment capsule and drink and did not take the breaks.

2.6. Statistics

Analyses of the questionnaires, heart rate and saliva data were conducted using an Analyses of Variance (ANOVA) with Caffeine (present, absent), Taurine (present, absent) and Time (change scores; 60 min-baseline, 120 min-baseline) as within-participant variables and Glucose (present, absent) as a between-participant variable. Analyses of the ANT task consisted of repeated measures ANOVA with Caffeine (present, absent) and Taurine (present, absent) as within-participant variables and Glucose (present, absent) as a between-participant variable for each attention network: orienting, alerting, and executive control. Analyses of the NB task consisted of repeated measures ANOVA with Caffeine (present, absent), Taurine (present, absent), Load (1, 2, and 3-Back) as within-participant variables and Glucose (present, absent) as a between-participant variable, on each stimulus type: verbal, spatial, and object. Analyses of the RTT task consisted of repeated measures ANOVA with Caffeine (present, absent), Taurine (present, absent), and Time (blocks 1–5) as within-participant variables and Glucose (present, absent) as a between-participant variable. An effect was deemed statistically significant if the likelihood of its occurrence by chance was $p<0.05$. When an ANOVA yielded a significant main effect, post-hoc tests using the Bonferroni correction were conducted. Because the sample consisted of more women than men, post-hoc analyses assessed gender differences on all behavioral and physiological parameters. All statistical analyses were performed using SPSS 12.0.

3. Results

3.1. Withdrawal questionnaire (WQ)

Analysis of the headache/poor mood subscale revealed main effects for Caffeine $F(1,46)=77.062$, $p<0.01$ (caffeine<no caffeine), taurine $F(1,46)=44.311$ $p<0.01$ (taurine<no taurine), and Time $F(1,46)=17.294$, $p<0.01$ (60 min post-intake<120 minutes; Fig. 2). A caffeine × time interaction $F(1,46)=52.100$, $p<0.01$ revealed that feelings of headache/poor mood decreased from baseline to 60 and 120 min following caffeine intake $F(1,46)=13.076$, $p<0.01$, but increased from baseline to 60 and 120 min following no caffeine intake $F(1,46)=7.428$, $p<0.01$. A time × gender interaction $F(1,44)=7.401$, $p<0.01$ showed that feelings of headache/poor mood were lower 60 than 120 min post-intake in women $F(1,29)=28.266$, $p<0.01$ but not men.

Analysis of the Physical Symptoms subscale indicated main effects of taurine $F(1,46)=5.443$, $p<0.05$ (taurine > no taurine), Time $F(1,46)=11.793$, $p<0.01$ (60 minutes<120 minutes), and a caffeine × taurine × time interaction $F(1,46)=4.358$, $p<0.05$. Taurine had no effect in combination with caffeine intake, but in the absence of caffeine intake, a main effect of taurine $F(1,46)=9.629$, $p<0.01$ showed that taurine increased the magnitude of withdrawal symptoms. A taurine × time interaction $F(1,46)=9.033$, $p<0.01$ indicated that taurine increased the magnitude of physical symptoms at 120 min post-intake $F(1,46)=12.153$, $p<0.01$.

Analysis of the activity subscale showed main effects of Caffeine $F(1,46)=7.062$, $p<0.05$ (caffeine > no caffeine) and time

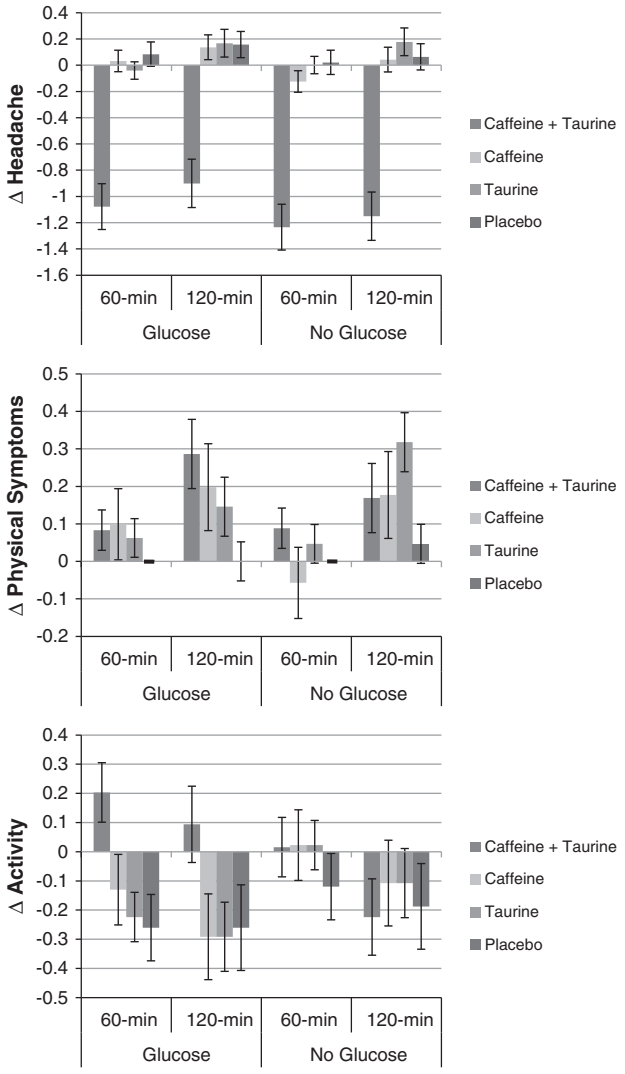

Fig. 2. WQ difference change-from-baseline means (SE). The graph represents change from baseline to 60 and 120 min post-intake for each treatment combination (n = 48; 24 glucose, 24 no-glucose).

$F(1,46) = 4.384$, $p < 0.05$ (60 min > 120 min). A time × gender interaction $F(1,44) = 6.683$, $p < 0.05$ showed that feelings of activity were lower 120 than 60 min post-intake in women $F(1,29) = 8.734$, $p < 0.01$ but not men. Treatments did not influence tiredness or flu-like symptoms.

3.2. Profile of mood states (POMS) questionnaire

Analysis of the Tension subscale indicated a Caffeine x Drink interaction $F(1,46) = 5.043$, $p < 0.05$, such that feelings of tension were higher following caffeine intake when consumed with glucose $F(1,23) = 9.666$, $p < 0.01$ (caffeine = 2.312 ± .738; no caffeine = .302 ± .482) but not without glucose. A caffeine × time interaction $F(1,46) = 11.596$, $p < 0.01$ revealed that caffeine increased feelings of tension 120 min post-intake $F(1,46) = 8.560$, $p < 0.01$ but not 60 min post intake (Fig. 3). A time × gender interaction $F(1,44) = 6.805$, $p < 0.05$ showed that feelings of tension were lower 120 than 60 min post-intake in women $F(1,29) = 14.835$, $p < 0.01$ but not men.

Analysis of the Vigor subscale revealed a main effect of Caffeine $F(1,46) = 4.854$, $p < 0.05$ (caffeine > no caffeine). A caffeine × taurine interaction $F(1,46) = 6.879$, $p < 0.05$ showed that taurine intake had no effect in combination with caffeine intake, but taurine intake lowered feelings of vigor in the absence of caffeine intake $F(1,46) = 4.329$, $p < 0.05$.

Analysis of the Fatigue subscale indicated main effects of taurine $F(1,46) = 4.706$, $p < 0.05$ (taurine < no taurine) and Time $F(1,46) = 18.200$, $p < 0.01$ (120 min = .135 ± .405; 120 min = 1.813 ± .503). A caffeine × taurine × time interaction $F(1,46) = 6.834$, $p < .05$ showed that between baseline and 60 min post-intake, caffeine decreased feelings of fatigue $F(1,46) = 11.272$, $p < 0.01$. Between baseline and 120 min post-intake, caffeine and taurine in combination only, increased feelings of fatigue $F(1,46) = 10.780$, $p < 0.01$.

Main effects of time were found for anger $F(1,46) = 7.087$, $p < 0.05$ (60 min = −.344 ± .358; 120 min = .734 ± .327), confusion $F(1,46) = 8.036$, $p < 0.01$ (60 min = −.712 ± .278; 120 min = .417 ± .240), and total mood disturbance $F(1,46) = 11.110$, $p < 0.01$ (60 min = .625 ± 1.291; 120 min = 6.936 ± 1.767). A time × gender interaction $F(1,44) = 4.235$, $p < 0.05$ showed that feelings of anger were lower 120 than 60 min post-intake in women $F(1,29) = 8.922$, $p < 0.01$ but not men. No differences were found for the depression subscale as a function of intake of caffeine, taurine or glucose.

3.3. ANT

Analysis of the orienting system showed a taurine × glucose interaction $F(1,46) = 4.680$, $p < 0.05$, such that taurine increased the orienting system score in combination with glucose (1,23) = 9.012, $p < 0.01$, but

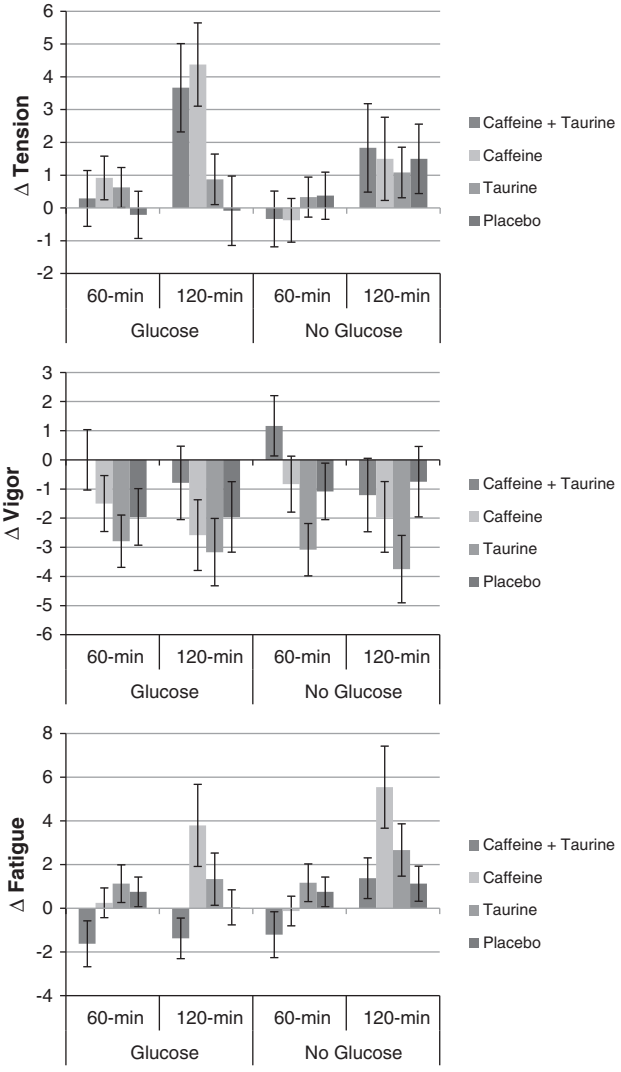

Fig. 3. POMS change-from-baseline means (SE). The graph represents change from baseline to 60 and 120 min post-intake for each treatment combination (n = 48; 24 glucose, 24 no-glucose).

Table 1
Effects of caffeine, taurine, and glucose on ANT performance and simple and choice reaction time (n = 48; 24 glucose, 24 no-glucose). Mean (SD) are shown for each parameter. Note that in the ANT, higher difference scores in the alerting and orienting networks indicate greater performance; conversely, lower difference scores in the executive control network indicate greater performance. Reaction time task values are collapsed across time, as there were no significant Treatment × Time interactions.

	Caffeine + taurine	Caffeine	Taurine	Placebo
ANT alerting				
Glucose	56.92 ± 32.67	54.79 ± 23.85	45.83 ± 28.94	43.38 ± 18.73
No glucose	38.79 ± 27.76	44.71 ± 25.13	44.92 ± 29.88	39.00 ± 19.27
ANT orienting				
Glucose	44.04 ± 19.93	29.71 ± 14.21	39.46 ± 17.71	36.00 ± 13.63
No glucose	31.42 ± 12.47	31.46 ± 10.06	30.96 ± 31.46	33.04 ± 14.00
ANT executive function				
Glucose	84.21 ± 26.05	87.46 ± 26.51	96.38 ± 30.31	97.08 ± 22.31
No glucose	87.67 ± 31.81	81.71 ± 21.41	86.42 ± 27.01	93.04 ± 25.65
SRT reaction time (ms)				
Glucose	181.35 ± 13.61	185.73 ± 14.32	195.18 ± 17.14	213.89 ± 19.96
No glucose	154.27 ± 13.61	158.37 ± 14.32	159.58 ± 17.14	160.12 ± 19.96
CRT accuracy				
Glucose	0.96 ± 0.00	0.96 ± 0.01	0.97 ± 0.00	0.96 ± 0.01
No glucose	0.96 ± 0.00	0.96 ± 0.01	0.96 ± 0.00	0.95 ± 0.01
CRT reaction time (ms)				
Glucose	439.43 ± 14.76	425.79 ± 12.90	434.29 ± 13.62	460.32 ± 20.42
No glucose	386.21 ± 14.76	390.76 ± 12.90	393.37 ± 13.62	409.32 ± 20.42

had no effect without glucose (Table 1). Analysis of the executive control system revealed a main effect of Caffeine $F(1,46) = 7.184$, $p<0.05$, such that executive control score was higher following caffeine intake than placebo. No effects of caffeine, taurine or glucose were found for the alerting system.[1]

3.4. N-back

Across all stimulus types, analyses revealed main effects of Load (all $p<0.01$), in which hit rate and sensitivity (d′) were greater in the 1-back and 2-back than 3-back loads, and reaction time was lower in the 1-back and 2-back compared to 3-back load. Each stimulus type is considered in turn, below.

3.4.1. Verbal

There was a main effect of caffeine on reaction time such that reaction time was lower following caffeine intake than placebo $F(1,44) = 5.592$, $p<0.05$, and a caffeine × taurine × load $F(2,88) = 4.453$, $p<.05$ interaction (Table 2). At the 1-Back load, a caffeine × taurine interaction $F(1,46) = 5.714$, $p<0.05$ showed that taurine reduced response time only in the absence of caffeine. No effects were found at the 2-Back load. For the 3-Back Load, a main effect of Caffeine $F(1,46) = 7.714$, $p<0.01$ indicated that reaction time was lower following caffeine than placebo. No effects were found for hit rate or d′.

3.4.2. Spatial

Analysis of d' revealed a main effect of Caffeine, such that caffeine increased sensitivity relative to placebo $F(1,46) = 7.641$, $p<0.01$. Neither hit rate nor reaction time differed as a function of dietary variables.

3.4.3. Object

Analysis of hit rate showed a caffeine × glucose interaction $F(1,46) = 4.450$, $p<0.05$, such that caffeine and glucose, only in combination, increased hit rate. Reaction time indicated a taurine × load interaction $F(2,84) = 3.546$, $p<0.05$. Reaction time was lower following taurine than placebo only at the 3-Back load. Analysis of sensitivity revealed a main effect of Caffeine $F(1,46) = 5.122$, $p<0.05$, such that d' was higher following caffeine intake than placebo intake.

3.5. Reaction time task

Analysis of the simple reaction time (SRT) task showed no effects for accuracy (accuracy was at ceiling). Analysis of reaction time indicated main effects of Caffeine $F(1,46) = 4.617$, $p<0.05$ (caffeine < no caffeine) and Time $F(4,184) = 3.161$, $p<0.05$, such that response time increased as the experiment progressed (Table 1).

Analysis of the choice reaction time (CRT) task revealed main effects of taurine $F(1,46) = 4.701$, $p<0.05$ (taurine > no taurine) and time $F(4,184) = 3.112$, $p<0.05$ for accuracy, such that accuracy increased over time. Analysis of reaction time showed Main effects for Caffeine $F(1,46) = 5.144$, $p<0.05$ (caffeine < no caffeine), Glucose $F(1,46) = 6.006$, $p<0.05$ (glucose > no glucose) and Time $F(4,184) = 3.789$, $p<0.01$, such that response time increased as the experiment progressed.

3.6. Cortisol

No differences were found for salivary cortisol concentration.

3.7. Heart rate

Analysis of heart rate indicated a main effect of Time $F(2,66) = 9.784$, $p<0.01$, such that heart rate was higher at baseline than all subsequent time points. There were no differences in heart rate as a function of treatment or time.

4. Discussion

4.1. Withdrawal symptoms and mood

Results from the WQ revealed that caffeine reduced headache symptoms and tiredness and increased alertness, suggesting that participants began test sessions in a withdrawal state and that caffeine intake mitigated withdrawal symptoms. Additionally, results from the POMS demonstrated that caffeine reduced feelings of fatigue and increased feelings of tension and vigor. These findings are consistent with the literature on caffeine effects on withdrawal symptoms (Addicott and Laurienti, 2009; Lane, 1997; Lane and Phillips-Brute, 1998). Taurine intake reduced feelings of headache and increased caffeine withdrawal symptoms (e.g. lightheaded, jittery), but caffeine reversed this effect. Glucose potentiated caffeine-induced feelings of tension. We found no gender differences in any cognitive tasks or physiological measures, and no gender by treatment interactions on mood or withdrawal symptoms. However, gender by time interactions showed that women, but not men, had heightened feelings of tension, anger, and activity 60 than 120 min post-intake and heightened headache symptoms 120 than 60 min post-intake. To our knowledge only two previous studies evaluated gender differences in caffeine effects. One study found no gender differences (Amendola et al., 1998) and the other found that caffeinated coffee led to greater arousing effects in men than women and decaffeinated coffee led to greater arousing effects in women, which the authors interpreted to indicate that women are more prone to placebo effect than men (Adan et al., 2008). Although survey studies generally find that men consume more energy drinks than women (e.g. Miller, 2008), limited available studies assess the interaction between energy drinks and gender on mood and cognition, which should be explored in future research. The treatment effects on mood are consistent with previous research (Addicott and Laurienti, 2009; Brunyé et al., 2010a; Lane, 1997; Phillips-Bute and Lane, 1998). To our knowledge this is the first report of caffeine by glucose interaction on mood or of any effect of taurine on mood.

[1] Post-hoc analyses revealed that glucose versus placebo induced overall slower response times during conditions involving neutral flankers $F(1,44) = 4.463$, $p<0.05$. We thank an anonymous reviewer for this suggestion.

Table 2
N-Back hit rate, reaction time, and sensitivity means (SD) for each treatment combination (n = 48; 24 glucose, 24 no-glucose).

	Measure	Caffeine + taurine	Caffeine	Taurine	Placebo
Verbal					
Glucose	RT (ms)	737.92 ± 38.20	710.20 ± 39.24	761.37 ± 43.91	772.96 ± 36.95
No glucose	RT (ms)	679.67 ± 36.57	700.34 ± 37.57	701.21 ± 42.04	731.09 ± 35.38
Object					
Glucose	Sensitivity	2.62 ± 0.16	2.73 ± 0.22	2.39 ± 0.26	1.86 ± 0.30
No glucose	Sensitivity	2.71 ± 0.16	2.44 ± 0.22	2.30 ± 0.26	2.33 ± 0.30
Spatial					
Glucose	Hit rate	0.85 ± 0.03	0.86 ± 0.03	0.82 ± 0.04	0.77 ± 0.03
	RT (ms)	715.00 ± 41.65	735.45 ± 42.57	721.58 ± 41.47	736.02 ± 39.98
	Sensitivity	2.88 ± 0.17	2.77 ± 0.23	2.53 ± 0.25	2.03 ± 0.28
No glucose	Hit rate	0.82 ± 0.03	0.81 ± 0.03	0.82 ± 0.04	0.85 ± 0.03
	RT (ms)	689.65 ± 41.65	709.81 ± 42.57	677.18 ± 41.47	706.72 ± 39.98
	Sensitivity	2.70 ± 0.17	2.52 ± 0.23	2.45 ± 0.25	2.49 ± 0.28

4.2. Cognitive tasks

4.2.1. Caffeine

Results from the cognitive tasks showed that caffeine reduced reaction time on the simple and choice reaction time tasks and verbal N-Back Task, particularly at the highest (3-Back) load. Additionally, caffeine increased d′ on the spatial and object N-Back tasks, and enhanced attention (executive control system). Whether caffeine enhances cognition or rather reverses withdrawal-induced cognitive impairment may depend on the specific cognitive domain. Caffeine withdrawal may play a role in psychomotor performance (Attwood et al., 2007; Hewlett and Smith, 2007), however there is less evidence that caffeine's influence on higher cognitive domains including attention and working memory are the result of reversal of caffeine withdrawal (Brunyé et al., 2010a,b; Smith et al., 2006). In the present study, a dose less than half of what the average participant normally consumed was sufficient to improve psychomotor performance.

Previous studies have found that caffeine (250 mg) improved N-Back working memory performance in moderate to high caffeine consumers (mean approximately 375 mg/day) following 30 h caffeine abstinence as well as after normal caffeine consumption (Addicott and Laurienti, 2009). However, following 12 h caffeine abstinence, a lower dose of caffeine (100 mg) had no effect on N-Back performance in moderate caffeine consumers despite significant blood oxygenation level-dependent (BOLD) regional brain activity, in which the working memory task itself increased BOLD activity in frontal and parietal cortices and caffeine increased activity in the bilateral middle and inferior frontal cortex to the right anterior cingulated gyrus, areas associated with attention and executive control (Koppelstaetter et al., 2008). The present data indicated that caffeine, with and without taurine, enhanced spatial working memory and, in combination with glucose, object working memory performance, furthering the literature, as Koppelstaetter et al. (2008) and Addicott and Laurienti (2009) assessed only verbal working memory.

In recently published studies in our lab, overnight caffeine withdrawn low- (less than 100 mg/day) and high- (greater than 300 mg/day) caffeine consumers consumed 0, 100, 200, or 400 mg caffeine and 20 min later completed the ANT. In low consumers, caffeine enhanced alerting system scores beginning and asymptoting at 200 mg and enhanced executive function system scores at 200 and 400 mg (Brunyé et al., 2010a). In high consumers, caffeine enhanced alerting system and executive function system but not orienting system scores, and only at the 400 mg dose (Brunyé et al., 2010a). The ANT data support recent studies from our lab showing that caffeine enhanced executive function system, and furthered previous work by showing that when habitual consumers abstain for longer periods of time, this effect is seen at a lower dose (Brunyé et al., 2010a,b).

4.2.2. Taurine

Taurine increased accuracy on the choice response task. Taurine reduced response time on the verbal N-Back at the lowest (1-Back) load, in the absence of caffeine intake, and on the object N-Back at the highest (3-Back) load, regardless of caffeine intake. While work in the animal literature supports taurine's influence on reaction time, showing taurine (400 mg/kg i.p.) extenuated locomotor-increasing effects of caffeine (2–10 mg/kg i.p.) in mice (Kimura et al., 2009), the effect should be interpreted with some caution as taurine did not show reaction time effects for the simple or choice reaction time tasks which directly measure psychomotor performance.

4.2.3. Glucose

The cognitive effects of glucose were limited to slowing reaction time in the choice reaction time task as well as neutral stimuli in the ANT, enhancing object working memory in combination with caffeine, and enhancing attention (in particular, orienting system) in combination with taurine. To our knowledge, this is the first study to report an interaction between glucose and taurine. Furthermore, only one previous study assessed the interactive effects of caffeine and glucose, and found that caffeine and glucose, alone and together, reduced reaction time and together improved sustained attention and verbal working memory (Adan and Serra-Grabulosa, 2010). Our results are consistent with their finding that together caffeine and glucose improved working memory. Additionally, slowed reaction time in the afternoon is consistent with previous findings that some aspects of cognitive performance are impaired in the afternoon (i.e. post-lunch dip; for review, see Kanarek, 1997).

In previous research, glucose improved some aspects of cognitive performance, notably spatial, logical, short- and long-term memory, however results are often inconsistent (for review, see Gorby et al., 2010; Hoyland et al., 2008). This inconsistency may be due to differences in study participants and design. Glucose seems to have greater enhancing effect in older adults than younger adults (Meikle et al., 2004). Glucose also has greater enhancing effects in tasks with high levels of difficulty or that require divided attention (Korol, 2002). A recent review suggested glucose facilitates long-term memory, but there is less evidence to support effects on short-term memory or other cognitive domains including attention and psychomotor performance, suggesting that cognitive load in the form of delay period augments glucose effects (Hoyland et al., 2008). Furthermore, studies that employed dual task paradigms tended to show greater facilitatory effects than those that did not. For example, few studies found glucose effects on verbal short-term memory using a free recall task, but multiple studies by Sunram-Lea and colleagues found that glucose facilitated short-term memory when attention was divided by a secondary task (Sunram-Lea et al., 2001, 2002). The present study did not entail delay periods between memory and testing, or dual task paradigms, which might account for sparse findings relative to previous studies. A cohesive

mechanism to explain how glucose enhances cognitive performance has not yet been established. One possible mechanism is that glucose stimulates the synthesis of neurotransmitters including acetylcholine (Ach), glutamate and gamma-aminobutyric acid (GABA; Messier, 2004). The role of the hippocampus in episodic memory is well-established (Smith et al., 2011). Glucose-mediated hippocampal Ach neurotransmission may account for the facilitatory effect of glucose on memory and attention.

Two previous studies have assessed the effects of ingesting carbohydrate in the afternoon (rather than as the lunchtime meal). One study found that glucose enhanced memory and attention (Kanarek and Swinney, 1990). The second found that glucose enhanced memory but impaired performance on a secondary attention task (Mahoney et al., 2007). Although we did not find main effects of glucose, the interaction results are in line with these studies. Given that the glycemic load in the lunch was moderate, it is possible that there was not enough time between lunch consumption and treatment to see any beneficial effects of additional carbohydrate.

4.3. Physiological measures

We found no treatment effects on heart rate or cortisol. While some work has shown caffeine effects on cortisol in habitual consumers (Lane, 1994), our results are consistent with previous studies on habitual caffeine consumers that found few to no effects of caffeine on heart rate (Green and Suls, 1996; Koppelstaetter et al., 2008; Lane, 1997) and cortisol (Lovallo et al., 2005). The inclusion criterion for this study was habitual caffeine consumption of at least 200 mg/day. However, participants averaged over 500 mg/day. Therefore, it is possible that the 200 mg dose was not sufficient to produce changes in physiological response.

4.4. Limitations

One concern of the present research involves the interval between treatment intake and completion of the cognitive tasks, particularly the Attention Network Task which was administered 30-minutes post-intake. Caffeine and glucose reach peak plasma concentrations within 30 min (Blanchard and Sawers, 1983; Kennedy and Scholey, 2000). However, taurine does not reach peak plasma concentration until at least 60-minutes post-intake (Ghandforoush-Sattari et al., 2010), which may partially account for the limited effects of taurine on the Attention Network Task. Another limitation regards the study design, particularly our choice to include glucose as a between-subjects factor. Previous between-group studies that found cognitive effects of glucose intake typically had larger samples (for review, see Gilsenan et al., 2009), which may account for our limited findings of glucose effects. Finally, although we were able to compare differences between the treatment days and placebo days as well as assess caffeine withdrawal levels, we could not determine the effects of caffeine withdrawal compared to performance following the normal caffeine consumption. A "normal consumption" condition would allow us to more effectively evaluate whether differences due to caffeine are attributed to cognitive enhancement or reversal of caffeine withdrawal-induced cognitive impairment. Another limitation is that given participants' mean caffeine intake of over 500 mg/day, the 200 mg caffeine dose may not have been sufficient to see cognitive effects that were different from placebo. Conversely, the present dose is ecologically relevant in that it reflects the caffeine content of commonly consumed energy drinks and was administered in similar ratios to glucose and taurine consistent with those drinks. In order to better determine whether caffeine, taurine, and glucose have effects above and beyond what we found in the present study, experiments should be conducted with non-habitual caffeine consumers in the morning following an overnight fast. These conditions would better control for differences in caffeine withdrawal, cortisol response, and previous glucose intake. However, the present study's design more accurately reflects real-world situations in which energy drinks are frequently consumed in the afternoon and evening (i.e. maintaining alertness while studying and driving; Attila and Cakir, 2011; Malinauskas et al., 2007).

5. Conclusion

Caffeine had the most consistent effects on cognitive performance (i.e. improvements in all cognitive domains assessed, especially attention, in particular cognitive control, working memory, and psychomotor performance). Taurine intake opposed caffeine effects on mood, including reducing feelings of vigor and increasing caffeine withdrawal symptoms. Additionally, although taurine had various effects on cognitive performance, the results are not sufficiently consistent to conclude an overall beneficial effect, e.g. taurine improved reaction time on certain loads/stimuli types in the N-Back task, but did not influence response time tasks directly assessing psychomotor performance. The effects of glucose on cognitive performance, while generally consistent with the literature, do not provide overwhelming evidence for the beneficial effects of glucose. However, as previously acknowledged, a stronger design in regard to glucose is needed to further elucidate in cognitive enhancement following energy drink consumption. In conclusion, the present data suggest that the caffeine content, but not the taurine or glucose in energy drinks drives cognitive performance improvements in executive control, working memory, and psychomotor performance, at least in caffeine-withdrawn habitual caffeine consumers.

Acknowledgement

We would like to thank Neha Kumar for her careful assistance with data collection and scoring.

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