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A combination of caffeine and taurine has no effect on short term memory but induces changes in heart rate and mean arterial blood pressure

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Summary. Red Bull energy drink has become extraordinarily popular amongst college students for use as a study aid. We investigated the combined effects of Red Bull's two active ingredients, caffeine and taurine, on short term memory. Studies on the effects of these two neuromodulators on memory have yielded mixed results, and their combined actions have not yet been investigated. In this double-blind study, college student subjects consumed either caffeine and taurine pills or a placebo and then completed a memory assessment. Heart rate and blood pressure were monitored throughout the testing period. The combination of caffeine and taurine had no effect on short term memory, but did cause a significant decline in heart rate and an increase in mean arterial blood pressure. The heart rate decline may have been caused by pressure-induced bradycardia that was triggered by caffeine ingestion and perhaps enhanced by the actions of taurine.

Keywords: Caffeine – Taurine – Red Bull – Short term memory – Pressure-induced bradycardia

Introduction

Energy drinks have recently exploded onto the mainstream US market and are popular amongst athletes, partygoers, and college students. At the top of the list is Red Bull, an energy drink containing caffeine and taurine that sold 1.5 billion cans in 2004. The makers of Red Bull claim that it ''gives you wings,'' by improving performance, concentration and reaction speed, vigilance, emotional status, and stimulating metabolism (Red Bull North America, 2005). Red Bull's makers credit its active ingredients, caffeine and taurine, for producing these effects and recommend drinking Red Bull before tests. Many college students drink Red Bull while studying and before exams because they believe it improves their memory and performance.

Carefully controlled studies on Red Bull's effects, particularly its influence on short term memory, are limited. Alford et al. (2001) found that human subjects who consumed Red Bull had improved performance on an immediate recall memory test in which subjects were given one minute to memorize a list of 22 two-digit numbers, then given another minute to recall as many of the numbers as possible. These authors also found that Red Bull ingestion improved anaerobic performance, aerobic endurance, reaction time, and concentration. In another study, however, Red Bull consumption was shown to have no effect on human verbal or spatial memory compared to placebo (Warburton et al., 2001).

To our knowledge only these two studies have evaluated Red Bull's effect on memory. Neither of these studies, however, isolated Red Bull's active ingredients, caffeine and taurine. Both studies had test subjects consume a 250 ml can of the Red Bull energy drink, which contains a variety of other ingredients, including glucuronolactone, niacin, vitamins B6 and B12, sucrose, and glucose. A study on the effects of a caffeine/taurine combination on short term explicit memory is lacking.

Caffeine effects

Individually, both caffeine and taurine have been shown to impact cognitive function, including memory, but results are mixed. Caffeine is a CNS-stimulating drug that acts as an adenosine receptor antagonist in the brain (Smit and Rogers, 2000). Adenosine antagonism contributes to stimulation of muscarinic cholinergic receptors; these receptors have been linked to improvement in higher cognitive functions such as memory (Riedel et al., 1995). Additionally, adenosine antagonism has been implicated as a

contributor to some of the physiological effects associated with caffeine consumption, such as a direct cardioacceleratory effect, and increased blood pressure and respiration rate (Suleman and Siddiqui, 1997–2004).

A consensus on caffeine's impact on memory has not yet been reached. Studies indicate that caffeine improves reaction time, endurance, and cognitive performance in human subjects (Battig et al., 1984; Smit and Rogers, 2000; Lieberman, 2001). Riedel et al. (1995) found that caffeine improved both short and long term memory in human subjects with scopolamine-induced memory impairment. Additionally, caffeine was demonstrated to reduce the worsening of memory associated with time of day in older adults (Ryan et al., 2002). Numerous other studies, however, have indicated that caffeine has no significant impact on memory function (Vojtechovsky, 1972; Loke, 1988; Mitchell and Redman, 1992). A number of factors may contribute to the discrepancies between studies, including the time of day subjects were tested (Mitchell and Redman, 1992; Ryan et al., 2002) and the dosage of caffeine administered (Loke, 1988). It has been proposed that the benefits of caffeine consumption are simply a reversal of caffeine withdrawal symptoms, so that only regular caffeine users experience significant effects (Rogers et al., 2003). If this is true, failure to control for the caffeine usage habits of test subjects may have contributed to these studies' variable results.

Taurine effects

Taurine is a non-essential amino acid that is found in high concentrations in the brain and acts as both a neuromodulator and a neurotransmitter (Huxtable, 1992; Rivas-Aranciba et al., 2000). It is also present in high quantities in mammalian hearts, where it has been shown to increase cardiac stroke volume (Baum and Weis, 2001) and may have anti-hypertensive activity (Huxtable, 1992).

It is believed that taurine may play a role in memory function through modulation of N-methyl-D-asparate (NMDA) receptors (Saransaari and Oja, 1993), but no studies in humans have established a concrete link between taurine and memory improvement. Studies in rodents have demonstrated that taurine improves chemically-disrupted memory function (Rivas-Aranciba et al., 2000; Vohra and Hui, 2000).

Current study

While research indicates that caffeine and taurine may individually enhance memory, the combined effects of caffeine and taurine on short term memory are unknown. In light of this research void and the immense popularity of using Red Bull as a study aid amongst college students, we investigated whether the caffeine and taurine present in Red Bull energy drink improve short term explicit memory.

We hypothesized that consumption of caffeine and taurine in concentrations equivalent to those in one 250 ml serving of Red Bull energy drink would significantly increase short term explicit memory performance (due to a combined neuromodulatory effect) as compared to test performance after consuming a placebo. We tested this hypothesis by having 14 human subjects complete a memory assessment on two occasions: once after consuming caffeine and taurine pills in amounts equivalent to those found in one 250 ml Red Bull beverage, and once after consuming a placebo (sugar pills). Drugs were administered in a double-blind manner. Subject heart rate and blood pressure were also monitored throughout the trials in order to assess the cardiovascular effects of the caffeine/taurine combination.

Materials and methods

Subjects

Fourteen undergraduate student volunteers (8 female and 6 male), aged 18 to 23 (mean age 20.5 ± 1.5 SD), participated in the study. The subjects reported no histories of heart conditions or allergies to caffeine or taurine. All subjects were moderate (2–4 caffeinated beverages/day) or infrequent (0–1 caffeinated beverage/day) caffeine consumers. They were instructed to abstain from caffeine and taurine consumption for 24 h prior to testing, and on the day of testing all subjects reported in writing that they had done so. Informed written consent was obtained from all subjects and the experimental protocol was approved by the UW-Madison Health Sciences Institutional Review Board.

Procedure overview

Each subject came in for testing on two occasions that were separated by a minimum of 24 and a maximum of 240 h. During one trial they received the active treatment, 100 mg caffeine and 1000 mg taurine, both in pill form. These are nearly equivalent to the 80 mg caffeine and 1000 mg taurine amounts found in a standard 250 ml can of Red Bull energy drink. During the other trial subjects received two placebo sugar pills. The treatments were administered in a double-blind fashion and the order of treatment was randomized. Subjects completed a short term memory exam 45 min after ingesting a treatment. Subject heart rate and blood pressure were measured on three occasions throughout the trials using an Omron automatic digital blood pressure monitor (model HEM-747IC). Mean arterial blood pressure (MABP) was calculated from systolic and diastolic values, where $\text{MABP} = \text{diastolic BP} + (0.333 * (\text{systolic-diastolic BP}))$. Figure 1 summarizes the trial events.

Baseline measurements

Each subject was tested individually in a small, quiet room. When subjects arrived in the testing room, they were instructed to sit down and read or

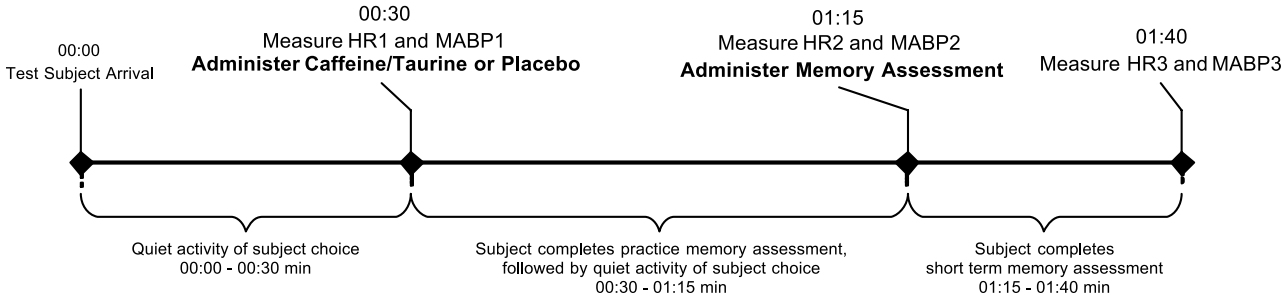

Fig. 1. Timeline for subject testing session. Time 00:00 represents subjects' arrival to test room. HR1 and MABP1 represent the first time these parameters were measured 30 min after subject arrival, HR2 and MABP2 were measured 1 h and 15 min after arrival, HR3 and MABP3 1 h and 40 min after arrival. Each session lasted 1 h and 40 min

study quietly for 30 min after which resting heart rate and blood pressure were measured (HR1 and MABP1, respectively; see Fig. 1). At this point, the subjects received the test drugs (either the caffeine/taurine treatment or placebo) which were put into pharmaceutical containers that did not allow the proctors or the subjects to know which drug was contained inside.

Memory assessment

During the 45 min quiet period following treatment administration, subjects completed an abbreviated practice version of the Experimental Comparative Prediction Battery, a short term explicit memory test. This test was created by the Educational Testing Service and requires subjects to study a list of 35 sentences, each approximately eight words long, for five minutes. Subjects are then presented with the same list of sentences in a different order, with one word omitted from each sentence. Subjects have five minutes to write the missing word in each sentence. (The abbreviated practice version contains only five sentences, and subjects had one minute to study them and one minute to fill in omitted words.) After completion of the practice test, subjects were instructed to study quietly for the remainder of the 45 min to allow time for the treatments to take effect (Alford et al., 2001).

At the end of the 45 min quiet period, heart rate and blood pressure were measured again (HR2 and MABP2; see Fig. 1). Subjects were given five minutes to study the full 35 sentence list and then were instructed to stop studying and play the card game Solitaire for 15 min so that all subjects were as equivalently focused as possible before the actual test was administered. Subjects were then given the full memory assessment, and upon completion of the test, physiological parameters were measured a final time (HR3 and MABP3). Each subject returned within ten days of their first test date for their second testing session, in which they were given the other study drug and a different version of both the practice test and the memory test. While the specific random facts memorized were different on the two tests, the format and difficulty level of the two tests were identical.

Data analysis

Data were analyzed using SPSS version 12.0 for Windows. Differences between placebo memory test performance and caffeine/taurine test performance were examined using the nonparametric Wilcoxon Signed Ranks test. The Wilcoxon test was also used to evaluate changes in heart rate and mean arterial blood pressure during the course of the test for both placebo and treatment trials. Differences were considered significant if p-value <0.05.

Results

Consuming caffeine and taurine in combination did not significantly change performance on the memory assess-

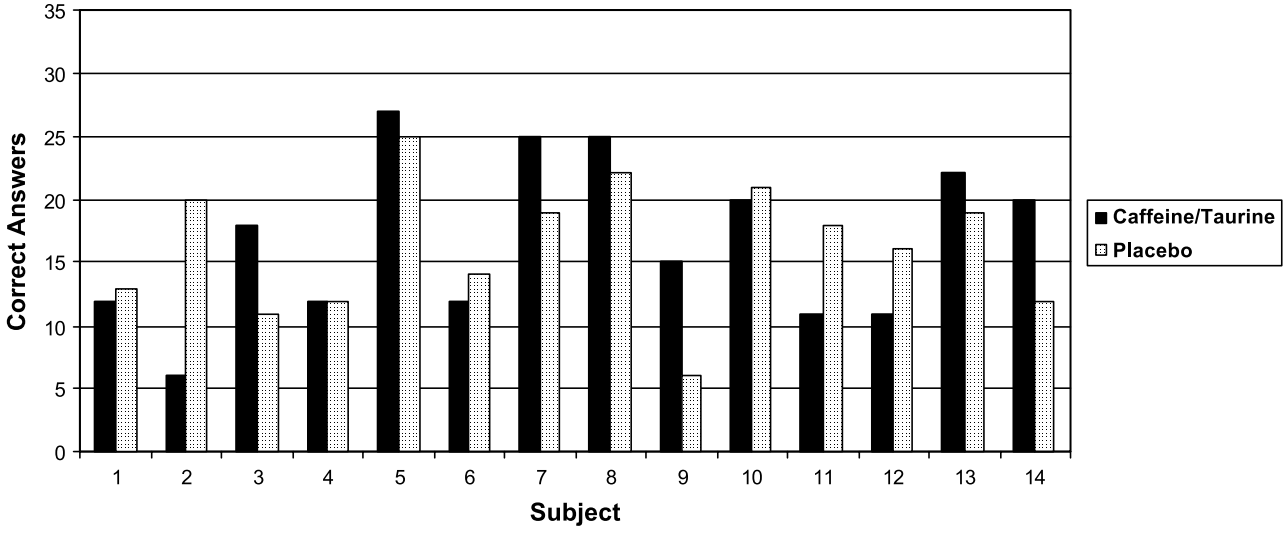

Fig. 2. Each subject's raw memory assessment score (out of 35 possible) under both caffeine/taurine treatment and placebo conditions. There was no significant difference between the trial test scores ($T = 36$, 2-tailed $p = 0.51$)

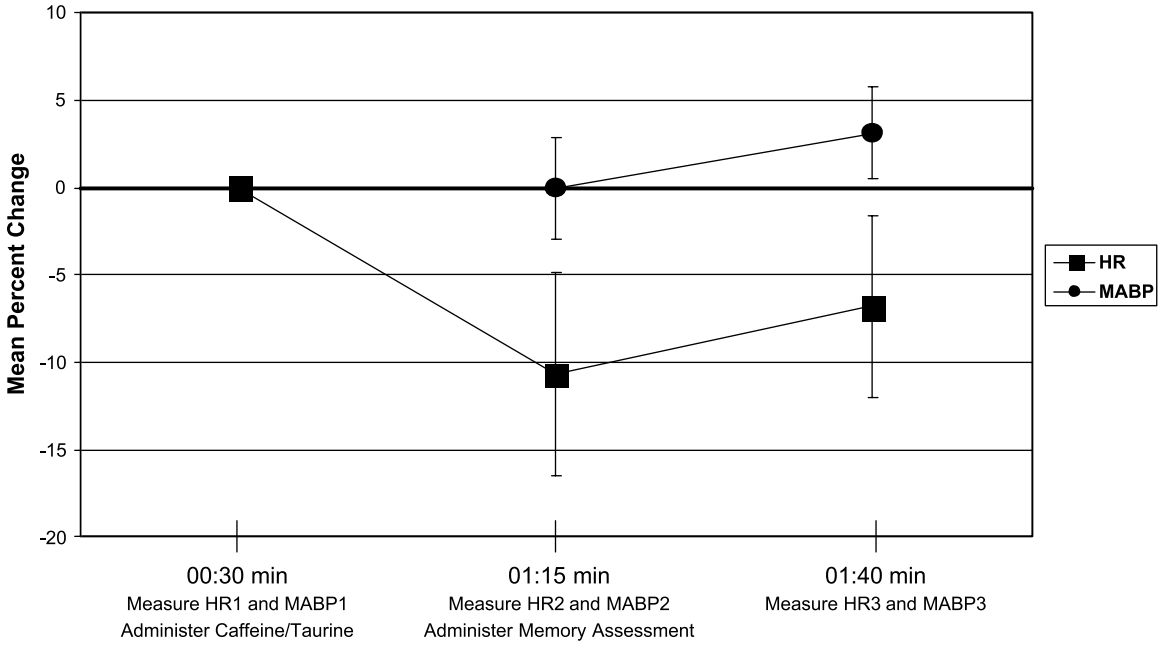

Fig. 3. Average percent changes in subject heart rate and mean arterial blood pressure after caffeine/taurine ingestion over the course of the trial. Error bars represent a 95% confidence interval

ment as compared to placebo ($T = 36$, 2-tailed $p = 0.51$, with the ranks for greater caffeine/taurine test score totaling 55 and the ranks for greater placebo test score totaling 36; see Fig. 2). A comparison of test scores for all subjects between day one and day two of testing showed no significant differences ($T = 33.5$, $p = 0.40$), indicating that subjects did not improve their memory assessment scores with experience.

Heart rate significantly decreased by an average of 8.1 beats/min (10.7%) in the 45 min after caffeine and taurine were ingested (comparison of HR1 vs. HR2: $T = 6$, 2-tailed $p = 0.006$; see Fig. 3). Heart rate increased slightly but insignificantly by an average of 2.1 beats/min (3.9%) after the completion of the memory assessment (comparison of HR2 vs. HR3: $T = 28.5$, 2-tailed $p = 0.23$). For the placebo trial, heart rate did not significantly change throughout the testing period (comparison of placebo HR1 vs. HR2: $T = 34$, $p = 0.42$; for HR2 vs. HR3: $T = 36.5$, $p = 0.84$). There were no significant differences in resting heart rates between day one and day two of testing (comparison of HR1 on days one and two: $T = 31$, 2-tailed $p = 0.18$).

Ingesting caffeine and taurine did not significantly change MABP in the 45 min following drug administration (comparison of MABP1 vs. MABP2: $T = 51$, 2-tailed $p = 0.93$), but MABP did increase modestly but significantly by 2.8 mm Hg (3.2%) after completion of the memory assessment (comparison of MABP2 vs. MABP3: $T = 9$, 2-tailed $p = 0.03$; see Fig. 3). During the placebo trial MABP did not change significantly. Resting MABP values did not differ significantly between day one and day two (comparison of MABP1 on days one and two: $T = 40$, 2-tailed $p = 0.70$).

Heart rate and blood pressure did not undergo any significant changes throughout the placebo trials, indicating the testing environment and the memory assessment alone did not induce changes in these physiological parameters. Further, the non-significant difference between resting heart rate (HR1) and blood pressure (MABP1) on the two different days, before subjects had consumed either placebo or caffeine/taurine, is evidence that these physiological parameters were repeatable in our subjects.

Discussion

Our results suggest that a combination of caffeine and taurine in amounts similar to those in one 250 ml serving of Red Bull energy drink have no effect on short term memory in young college students. These results are consistent with studies demonstrating that ingesting caffeine or taurine individually does not impact short term memory in humans (Vojtechovsky, 1972; Loke, 1988; Mitchell and Redman, 1992). There may be no combined neuromodulatory effect of caffeine and taurine on short term explicit memory, as we had originally hypothesized.

Several other studies, however, have observed improvement in memory after caffeine or taurine consumption (Riedel et al., 1995; Rivas-Aranciba et al., 2000; Vohra and Hui, 2000; Ryan et al., 2002). There are, however, multiple forms of memory besides short-term recall. Simple short term recall may not be representative of the type of memory students utilize when studying for or taking exams. It is possible that a combination of caffeine and taurine can improve other types of memory function.

Cardiovascular effects

While the primary goal of our study was to test how a combination of caffeine and taurine impacted short term memory, we found that ingestion of these drugs significantly decreased heart rate an average of 8.1 beats/min within 45 min. Mean arterial blood pressure also increased but only after subjects took a memory test. Consumption of caffeine increases cardioacceleratory signals, which should increase heart rate (Suleman and Siddiqui, 1997–2004). Numerous studies, however, have shown that caffeine consumption can cause heart rate to decline through pressure-induced reflex bradycardia (Suleman and Siddiqui, 1997–2004). Caffeine-induced heart rate decline may also result from direct central vagal stimulation (Whitsett et al., 1984). The caffeine dosage used in our study (~1.1–2.2 mg/kg) was lower than that used in other studies (2.2–8.8 mg/kg), though the average heart rate decline we observed was equal to or greater than that seen previously (Pincomb et al., 1987, 1991; Robertson et al., 1978; Suleman and Siddiqui, 1997–2004; Sung et al., 1990; Whitsett et al., 1984). It may be that the taurine facilitated pressure-induced reflex bradycardia, which has been observed in rats (Yang and Lin, 1983). Further, taurine has also been shown to increase cardiac stroke volume (Baum and Weis, 2001), which would also enhance pressure-induced reflex bradycardia.

After completing the memory assessment, test subject mean arterial blood pressure (MABP3) was significantly increased by an average of 2.8 mm Hg, and heart rate began to return to resting levels but was still significantly lower than them (Fig. 3). This might indicate that caffeine and taurine in combination with a stressful event (such as taking a test) elevate blood pressure and possibly heart rate, likely in conjunction with catecholamine release from the adrenal glands (Charmandari et al., 2005; Robertson et al., 1978). The combination of caffeine and psychological stress has been shown to increase blood pressure (Pincomb et al., 1987).

Limitations and implications for future studies

While we found no evidence that a caffeine/taurine combination affects short term memory, our results do prompt additional interesting questions. We therefore suggest that future studies on the combined effects of caffeine and taurine:

- test subjects who refrain from caffeine and taurine consumption for longer than 24 h prior to testing to better ensure that subjects are free of residual caffeine and taurine.
- conduct trials at the same time of day to control for time of day effects on memory or caffeine withdrawal symptoms (Mitchell and Redman, 1992).
- control for subject food intake 24 h prior to testing as this may affect caffeine and taurine absorption rates.
- compare how caffeine and taurine affect habitual caffeine consumers and non-users. Many of caffeine's effects might simply be a reversal of withdrawal symptoms (Rogers et al., 2003); therefore, non-habitual users might be less likely to feel an effect from consuming caffeine and taurine.
- repeat the current study with the addition of caffeine-alone and taurine-alone treatments, in order to elucidate their individual effects on memory.
- examine whether the absence of an effect of caffeine/taurine on memory observed here would also be seen in larger, more diverse subject groups representing both college and non-college participants.
- amend subject exclusion criteria such that alcohol consumption is prohibited within 24 h prior to testing, use of CNS-active compounds, and pregnancy, due to their effects on cardiovascular physiology.

It is important to recognize that the actual Red Bull energy drink also contains other ingredients such as glucuronolactone and other sugars. One study did find that consuming Red Bull energy drink improved short-term memory (Alford et al., 2001), and a recently published study reported that subjects who drank a beverage containing caffeine and glucose, as well as ginkgo and ginseng herbal flavorings, had improved performance on a secondary memory assessment compared to placebo (Scholey and Kennedy, 2004). It is therefore possible that Red Bull's other ingredients impact memory, either alone or in conjunction with caffeine and taurine.

In conclusion, our study represents the only research to date on the combined effects of caffeine and taurine on human memory. Our results show that the combination of these two neuromodulators, in concentrations equivalent

to those found in one 250 ml serving of the Red Bull energy drink, does not improve performance on tasks requiring short term recall of simple facts but does modulate cardiovascular physiology.

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