Title: The effects of caffeine, taurine or caffeine-taurine co-ingestion on repeat-sprint cycling performance and physiological responses

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Caffeine, taurine and cycling performance

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Abstract

Purpose: This study investigated the effects of caffeine (C), taurine (T), caffeine and taurine co-ingestion (C+T) or placebo (P) on repeated Wingate cycling performance and associated physiological responses.

Methods: Seven male team sports players participated in a randomised, single-blind, cross-over study, where they completed three Wingate tests, each separated by 2-min, an hour after ingesting: C (5 mg/kg BM), T (50 mg/kg BM), C+T (5 mg/kg BM + 50 mg/kg BM) or P (5 mg/kg BM) in a gelatine capsule. Performance was measured on an ergometer, whilst blood lactate, perceived exertion, heart rate (HR), mean arterial pressure (MAP) and rate pressure product (RPP) were measured at rest (pre-supplement), baseline (1-h post-supplement) and during and after exercise.

Results:

Magnitude-based inferences revealed that all of the supplements increased (*small* to *moderate, likely to very likely*) mean peak power (MPP), peak power (PP) and mean power (MP) compared to P, with greater MPP, PP and MP in T compared to C (*small, possible*). Intra-sprint fatigue index ($\%FI_{Intra}$) was greater in T compared to P and C (*moderate, likely*), whilst inter-sprint fatigue index ($\%FI_{Inter}$) was lower in T compared to C (*small, possible*). C and C+T increased HR, MAP and RPP compared to P and T at baseline (moderate to *very large, likely to most likely*); however, these only remained higher in C compared to all conditions in the final sprint.

Conclusions: T elicited greater improvements in performance compared to P, C or C+T, whilst reducing the typical chronotropic and pressor effects of C.

Key words: Stimulants; fatigue; repeat-sprint; ergogenic

Introduction

Taurine, a sulfur-containing amino acid, is one of the primary ingredients in the most popular energy drinks.[1] In addition, most energy drinks contain caffeine, a methylxanthine drug commonly consumed by athletes as an ergogenic aid.[2] Caffeine ingestion (3–6 mg/kg body mass) has been shown to improve performance across a variety of events,[2] notably during intermittent, sprint performance.[3-4] Whilst the role of caffeine as an ergogenic aid has been well-researched, the effects of taurine on performance are not thoroughly understood. There has been limited research examining the effect of isolated taurine ingestion on performance in healthy human participants, with one study reporting improvements in 3 km time-trial performance after acute supplementation.[5] However, others have reported no effects of acute taurine supplementation on prolonged endurance performance[6] or 'unclear' effects on anaerobic capacity.[7] The effect of acute, isolated taurine supplementation on performance during intermittent, high-intensity exercise has not yet been investigated.

Little is understood about the efficacy of caffeine and taurine co-ingestion on high-intensity intermittent performance, which is surprising given the high concentration of these ingredients in popular energy drinks and their purported effects. However, there are many similarities in the sites of action and proposed mechanisms of taurine and caffeine, which could alter their efficacy. For example, both caffeine[8] and taurine[9-11] are reported to regulate intracellular Ca^{2+} handling and the sensitivity of myofibrils to Ca^{2+} in skeletal muscle fibres. One mechanism of action shared by caffeine and taurine appears to be potentiation of ryanodine receptors.[10] Whilst the capacity of caffeine to effect muscle force production via myofibrillar calcium handling at physiological concentrations (- 70 μM) is still a topic of some debate,[8] *in vitro* studies have shown that taurine's effects on peak force (~29 %) and rate of force development (~28 %) is augmented in the presence of a physiological dose of caffeine.[10] Both taurine and caffeine also have established, yet separate roles in the control of cardiovascular (CV) responses during rest and exercise.[11-14] The specific roles of both caffeine and taurine on the CV system could be important for increasing capacity during intermittent exercise and recovery from intermittent bouts, which relies on the maintenance of cardiac output.[15-16] Lastly, taurine and caffeine are known to act on the central nervous system (CNS) but have distinctly different mechanisms, with caffeine relying on antagonism of adenosine receptors[17] to induce wakefulness, alertness[18] and enhance information processing.[19] This is in contrast to the suggested role of taurine as an extrasynaptic $GABA_A$ receptor agonist, which can increase network activity at various sites in the brain, such as the thalamus,[20] which can reduce anxiety.

Based on the above reasoning, it is feasible that the isolated effects of caffeine and taurine could interact *in vivo*, but it is not known how this might manifest during repeat-sprint performance. Therefore, the purpose of this study was to investigate the effect of caffeine (C), taurine (T), caffeine and taurine co-ingestion (C+T) or placebo (P) on repeated (× 3) Wingate cycling performance and associated physiological responses. It was hypothesized that all conditions would enhance performance compared to placebo but that the combined properties of caffeine and taurine would lead to an improved performance and reduced CV response during the intermittent protocol.

Methods

Participants

Seven male University team sports players provided written informed to take part in the study (Age 20.8 ± 0.9 years; stature 1.76 ± 0.11 m; body mass 86.3 ± 10.2 kg). Given the typical

effect sizes (Cohen's d = 0.3-1.0) reported using caffeine and taurine across the various dependent variables in this study, G*Power (Version 3.0.10) was used to calculate an *a-priori* sample size of seven, which was sufficient to identify differences between groups with a statistical power of 0.80. Given the statistical approach of the study, we also used Hopkins' method (http://www.sportsci.org/2006/wghss.htm) to estimate sample size for magnitude-based inferences, based on peak power reliability data from our laboratory. A sample size of 6 participants was generated based on a smallest important change of 25 W (0.2 × between subject SD) and a typical error of 15 W. The chances of type I and II errors were deemed to be 5 %. The participants were instructed to maintain their normal, self-selected, diet throughout testing and reported this on the day of each trial. The participants did not eat within 2 hours of the trial. The participants were also provided with an extensive list of dietary sources containing caffeine and taurine, which they were instructed to avoid in the 24-h prior to testing. The participants abstained from strenuous exercise in the 48-h before testing. Institutional ethical approval was given for this study, which was conducted in accordance with the 1964 Helsinki declaration.

Design

All participants reported to the laboratory on five separate occasions. During visit 1, the participants were familiarised with the ergometer and Wingate procedure. The all-out maximal nature of Wingate cycling tests was emphasized during this time. The bike was fitted to the participant during this visit, which remained consistent for the remainder of the study. On visits 2, 3, 4 and 5, the participants performed three 30-s Wingates, separated by 2-min of active recovery. The trial was conducted using a randomised, single-blind, cross-over design. All trials were conducted at the same time of day and separated by 48-h.

Procedure

On arrival at the laboratory, the participants rested for 10-min prior to the measurement of resting heart rate (HR) (Polar FT1, Polar Electro Oy, Kempele, Finland), blood lactate concentration (B[La]) and blood pressure (BP) (OMRON Healthcare Europe B.V. Hoofddrop, Netherlands). Blood pressure was measured by occluding the left brachial artery of participants and reported as the mean arterial pressure (MAP) (MAP = DBP + 0.33 (SBP–DBP)). Rate pressure product (RPP) was also reported (Systolic pressure x HR) as an indication of myocardial oxygen demand. A lancet was used to extract a capillary blood sample from the lobe of the ear to measure B[La], which was measured using a calibrated analyser (Biosen C Line, EKF diagnostic GmbH, Barleben, Germany). For all B[La] measurements, two samples were taken and the mean was calculated. Before each trial day, the participants' body mass (kg) was recorded using a Portable Scale (MPMS-230, Marsden Weighing Group, Oxfordshire, UK) to allow for the correct dose of supplement and calculation of power output (W/kg) for the subsequent four trials.

Supplementation

All of the supplements were prepared in a powder form, which were measured using an analytical balance (Precisa 125A, Precisa Gravimetrics AG, Zurich, Switzerland) and ingested in a gelatine capsule. The capsules contained one of the following: caffeine (C) (5 mg/kg BM), taurine (T) (50 mg/kg BM), caffeine + taurine (C+T) (5 mg/kg BM + 50 mg/kg BM) or a placebo (P) (maltodextrin) (5 mg/kg BM). The dosages of caffeine[2] and taurine[21] followed the recommendations of recent studies. All supplements were sourced from the same company (My Protein, Manchester, UK). After ingestion, the participants rested in a seated position for 1-h in a quiet room and were observed by the investigators, after which baseline (post-supplement) measurements of B[La], HR and BP were taken. We hereafter

refer to post-supplement measurements as 'baseline'. The 1-h timing was chosen as this accounted for the peak plasma availability of both taurine[22] and caffeine[23] after oral administration.

Wingate protocol

All tests were conducted indoors using an electronically braked cycle ergometer (Lode Excalibur Sport, Lode B.V. Medical Technology, Groningen, The Netherlands). The Wingate protocol was conducted at a load corresponding to 0.075 kg × BM and uncorrected power output was reported. Each participant completed a 5-min warm-up at 0.9 W/kg, cycling at 80 revolutions per minute (rev/min). After 3-min of the warm-up, a 5-s sprint was performed at a load equal to the Wingate test. After the warm-up, a 3-min passive recovery stage was provided to allow for any final stretching and water. The exercise protocol consisted of three 30-s Wingate tests, preceded by a 2-min active recovery. During the active recovery (0.9 W/kg), the participants maintained a cadence of 65 rev/min. A countdown of "3, 2, 1 - GO" was given at the beginning of each test. The participant cycled as fast as possible for 30-s with standardised, non-specific verbal encouragement from the investigators. Recordings of B[La], were taken 1-min into each 2-min recovery. This procedure was repeated for the following two Wingate tests. The performance variables measured on the ergometer were: peak power (the highest power (PP) output attained over 1-s during the three Wingate tests); mean peak power (mean of the PP across the three Wingate tests; MPP), mean power (average power output of the three Wingate tests; MP), mean intra-sprint fatigue index (percentage difference between maximal and minimal power output during all of the three 30-s Wingate tests combined; $\%FI_{Intra}$) and inter-sprint fatigue index (percentage change in mean power output between the three Wingate tests; $\%FI_{Inter}$).[24]

Heart rate was recorded from the start to the end of exercise and readings were recorded, alongside a rating of perceived exertion (RPE; 6-20) in the 5-sec after each sprint using a 6-20 Borg scale. The 'final' HR hereafter describes the recording after the last Wingate sprint in each trial. Blood lactate concentration was measured 1-min after each sprint. The HR, B[La] and RPE were reported as a mean of all three Wingate tests (i.e. mean exercising HR, B[La] and RPE. Blood pressure (for reporting of MAP and RPP) was measured for a third and final time immediately after the final Wingate test, after which a 5-min cool-down was completed. The following three trials were carried out in an identical manner, using one of the four experimental conditions.

Statistical analysis

Based on best-practice recommendations for research in sports nutrition[2], effect sizes (ES) and magnitude-based inferences (MBIs) were used to identify mechanistic differences in the dependent variables between the four experimental conditions (P, C, T and C+T). Effect sizes were defined as; trivial = 0.2; small = 0.21–0.6; moderate = 0.61–1.2; large = 1.21–1.99; very large > 2.0.[25] Raw data were log-transformed to account for non-uniformity of effects. Threshold probabilities for a substantial effect based on the 90% confidence limits were: <0.5% *most unlikely*, 0.5–5% *very unlikely*, 5–25% *unlikely*, 25–75% *possibly*, 75–95% *likely*, 95–99.5% *very likely*, 99.5% *most likely*. Thresholds for the magnitude of the observed change in the dependent variables were determined as the within-participant standard deviation × 0.2 (*small*) 0.6 (*moderate*) and 1.2 (*large*). Effects with confidence limits across a *likely small* positive or negative change were classified as *unclear*. The uncertainty of effects was based on 90% confidence limits for all variables. A custom spreadsheet designed for cross-over trials was used to perform all of the calculations (http://www.sportsci.org/.).

Results

Differences between experimental conditions for resting HR, resting MAP, resting RPP and resting B[La] were all mechanistically *unclear*, with ES ranging from *trivial* to *small*. The only exception at rest was the *moderate, yet unclear,* differences in B[La] between T and both C and C+T (Table 1). Post-supplementation, there were *very large, most likely* differences in HR between C and T and *moderate, likely* differences between C and P, P and T, and C+T and T. This translated to the findings for MAP, with baseline *small, possible* differences between C and T (Table 1). During exercise, there were *small, possible* differences for mean exercising HR between C and P and *small, possible* differences between C and C+T, with all other comparisons being *trivial-small* and *unclear* (Table 1). The final exercising HR was also different between C and C+T (*small, likely*), P and C+T, T and C+T and T and C (*small, possible*), with all other comparisons being *trivial*. This translated to *small, possible* differences in final MAP and final RPP between C and P, T and C+T, whilst all other comparisons were *unclear* (Table 1). All comparisons of exercising RPE were *unclear (Table 1).*

**********Insert Table 1 here**********

There were *moderate, very likely* differences in MPP between C and P, T and P and C+T and P. There were *small, possible* differences in MPP between T and C (Figure 1).

*******Insert Figure 1 here*******

There were *moderate, likely* differences in PP between T and P and C+T and P. PP was different (*small, likely*) between C and P, whilst there were *small, possible* differences between T and C (Figure 2).

*******Insert Figure 2 here*******

There were *moderate, very likely* differences in MP between T and P, with *small likely* differences in MP between C and P and C+T and P. Similar *small,* yet *possible* differences in MP were apparent between T and C (Figure 3).

*******Insert Figure 3 here*******

There were *small, possible* differences in $\%FI_{Inter}$ between C and P and T and C. There were *small, likely* differences in $\%FI_{Inter}$ between C+T and P. Similar *small,* yet *unclear* differences were apparent between C+T and T (Figure 4).

*******Insert Figure 4 here*******

There were *moderate, likely* differences for $\%FI_{Intra}$ between T and P and T and C. C+T showed *small, unclear* differences to P and C but *moderate, possible* differences to P (Figure 5).

*******Insert Figure 5 here*******

Figure 6 shows the power profile for a representative participant during the three Wingate tests across each of the experimental conditions.

*******Insert Figure 6 here*******

There were no trial order effects for any performance measures found between consecutive trials, with all ES < 0.2 (*trivial*).

Discussion

In partial support of our hypothesis, we found that isolated caffeine, taurine and caffeine+taurine supplementation can improve performance during repeated Wingate tasks compared to placebo, by increasing MP, PP and MPP (Figures 1-3). Whilst it is known that caffeine may induce changes of this type,[3-4] this is the first study to report improvements after isolated or co-ingested taurine supplementation. Moreover, the MP, PP and MPP achieved in the taurine condition was *possibly* greater (ES = *small*) than the caffeine condition (Figures 1-3). The higher PP achieved in the taurine condition resulted in a greater intra-sprint fatigue

index compared to the caffeine and caffeine+taurine conditions. In other words, the taurine supplement permitted a higher power output at the expense of power maintenance within each Wingate sprint, whereas the caffeine-containing conditions did not increase power production to the same level but maintained power more effectively within sprints. However, this was not true for the inter-sprint fatigue index, where taurine supplementation improved the maintenance of power output across the three Wingate sprints (Figures 4 and 6). In mammalian studies, high levels of endogenous taurine have been reported in skeletal muscle,[26] which is reduced after exhaustive exercise.[27] Taurine depletion *in vitro* has been shown to reduce force output and increase the rate of fatigue during repeated stimulation of mouse skeletal muscle.[11] The primary mode of action in skeletal muscle appears to be through intracellular membrane stabilisation, increased Ca^{2+} uptake and release and increased sensitivity of the contractile filaments to Ca^{2+}; contributing to enhanced force production.[9-11] Taurine-depleted muscle fibres are suggested to fatigue faster than non-depleted muscle fibres due to altered SR-Ca^{2+} handling.[11] Indeed, suppression of Ca^{2+} release or reuptake is an established cause of peripheral muscle fatigue.[28] These proposed fatigue mechanisms could support the higher PP achieved in the taurine group (i.e. greater Ca^{2+} release) and the resultant greater fatigue (i.e. greater depletion and decreased availability, alongside a transient reduction in taurine concentration) within each Wingate sprint ($\%FI_{Intra}$); a mechanistic process that would be less useful for endurance-type exercise, as reported elsewhere[6]. Whilst the superior $\%FI_{Inter}$ in the taurine condition might seem at odds with these findings, it is entirely feasible that the 2-min recovery period between sprints was sufficient for the restoration of SR-Ca^{2+} before commencing the subsequent sprint. Indeed, the apparent inhibition of recovery between sprints in the caffeine+taurine condition compared to taurine alone might be related to a similar mechanism, whereby Ca^{2+} reuptake is interrupted by the competition for the same molecular site.

Research has highlighted the ergogenic effects of caffeine in repeated high-intensity exercise.[3-4] The combination of caffeine and taurine increased PP, MPP, MP (Figures 1-3) compared to placebo and guarded against the reduction in power within each Wingate test (Figure 5). *In vitro* studies have showed that physiological concentrations of taurine can improve force (~29 %) and rate of force development (~28 %) in the presence of caffeine.[10] On this basis, it has been proposed that the isolated effects of caffeine and taurine could interact to augment high-intensity physical performance. However, others have shown no change in force production, rate of fatigue or acute recovery after repeated stimulations of

isolated mouse skeletal muscle with caffeine and taurine co-ingestion compared to caffeine alone, with no effect of isolated taurine.[29] Using doses of taurine that were larger than that of a typical energy drink (50 mg/kg BM *vs*. ~15-35 mg/kg BM),[6-7] appeared to exaggerate the effects on repeated-sprint performance, such that that taurine supplementation alone elicited the greatest effects on power output. By implication, this also suggests that caffeine, for unknown reasons, inhibited the effect of taurine in this study. Further research is required to understand the mechanisms that explain this phenomenon during repeat-sprint cycling; however, this could be linked to the shared molecular target that both caffeine and taurine potentially act on to alter Ca^{2+} dynamics in skeletal muscle, which appears to be dependent on muscle fibre type.[11,29]

Cardiovascular responses (MAP, HR and RPP) were highest in caffeine-containing conditions, 1-h after supplementation (baseline) (Table 1). This can be explained by the chronotropic effects that can be elicited by caffeine, contributing toward the acute, centrally-mediated, increases in blood pressure observed after ingestion.[17] However, during exercise and the final exercising measurements, HR, MAP and RPP were higher in the caffeine condition compared to placebo, taurine or caffeine+taurine. It is known that isolated taurine administration does not increase HR or blood pressure but does exert inotropic actions on the cardiac musculature[12-14] particularly when Ca^{2+} concentration is reduced, as can be observed during exhaustive exercise.[26] If taurine supplementation increased myocardial contractility and, in turn diastolic filling time per cardiac cycle, during intermittent cycling, the lower cardiac frequency (HR) might be anticipated. Indeed, such characteristics have been associated with increased recovery from exercise.[16] This provides one possible explanation for the ergogenic effects of taurine in this study.

It is likely that the baseline increases in HR, MAP and RPP reflect the acute effects of caffeine on the heart in caffeine-containing conditions but that the introduction of taurine (caffeine+taurine) blunted this effect at later exercising periods (Table 1). There are two potential reasons for this delayed response. Firstly, it is known that exercise-induced increases in reactive oxygen species (ROS) trigger a release of taurine from muscle during exercise.[30] Therefore, it is possible that the interactive effects of caffeine and taurine on the cardiovascular system might be exercise-induced. Secondly, peak plasma levels of taurine occur approximately 1 to 2.5-h (mean = 1.5-h) after oral ingestion,[22] whereas peak plasma caffeine concentration is typically reached between 0.25 to 1-h (mean = 0.5-h) after

ingestion.[23] Since both supplements were administered simultaneously in the current study, it is possible that the actions of taurine on the cardiovascular system were delayed and, thus, did not induce physiological changes until after baseline conditions. Whilst more research is needed to elucidate the mechanisms that caused this response, our findings suggest that oral ingestion of taurine is capable of lowering BP and HR.

Co-ingestion of taurine and caffeine has been shown to reduce HR, perhaps facilitated by taurine in response to caffeine-induced pressor effect.[14] Our baseline data shows that caffeine+taurine increased HR but, after exercise, HR and other cardiovascular responses were lower than caffeine alone (Table 1). We are unsure why our data only agree with previous studies[14] after our participants took part in physical exercise but various methodological differences prevent direct comparisons. For example, Bichler et al.[14] did not conduct their study on exercising participants and administered lower oral doses of taurine and caffeine. Whilst further research is required to elucidate the cardiovascular effects of caffeine and taurine co-ingestion, our findings suggest that taurine can counteract the effect of caffeine on HR, MAP and RPP, as demonstrated by differences between caffeine and caffeine+taurine at various time-points (Table 1), without compromising performance during repeat-sprint cycling.

There were some limitations to this study. We have primarily focussed on peripheral causes of fatigue, without acknowledging the wider roles of both caffeine and taurine on the central nervous system.[17,20] It would have been useful to measure the relative contributions of central and peripheral sources of fatigue in this study in order to identify the mechanisms that facilitate the notable performance improvements with taurine supplementation, as well as qualifying our discussion of mechanism, which have centred on Ca^{2+} handling in the muscle. Future research should investigate the underlying mechanisms further. We also did not take venous blood samples in this study to test for plasma caffeine or taurine concentration, nor did we follow a double-blind research design. The reasons for these choices related to participant recruitment and health and safety concerns whilst providing supplements. Our laboratory is currently working on methods to avoid venous blood sampling for verification of plasma caffeine and taurine in studies such as this.

Practical applications

The superior PP, MPP and MP observed after taurine supplementation has logical importance during track cycling events. The ability to generate a high peak power may help in sprinting, standing starts or even translate into other power-based sports. Taurine supplementation might also ameliorate performance during short, high-intensity events, based on the ~3% difference in the inter-sprint fatigue index between taurine and caffeine conditions.

Conclusion

Oral ingestion of taurine elicited at *small-to-moderate* improvements in repeat-Wingate cycling compared to other conditions. Whilst taurine ingestion led to a greater rate of fatigue within each Wingate sprint, power output was maintained more effectively between successive sprints compared to caffeine or caffeine+taurine co-ingestion. Caffeine-containing supplements increased baseline (post supplementation) cardiovascular responses compared to taurine and placebo conditions but the interaction of taurine and caffeine resulted in a lowered HR, MAP and RPP in response to exercise compared to caffeine alone. Further research is needed to establish whether this effect is exercise-induced and to reveal the underlying mechanisms that explain the current findings.

References

1. McLellan TM, Lieberman HR. Do energy drinks contain active components other than caffeine?. *Nut Res*. 2012; 70(12):730-744.
2. Burke LM. Caffeine and sports performance. *Appl Physiol Nutr Metab.* 2008; 33(6):1319-1334.
3. Stuart GR, Hopkins WG, Cook C, Cairns SP. Multiple effects of caffeine on simulated high-intensity team-sport performance. *Med Sci Sports Exerc*. 2005; 37(11):1998-2005.
4. Mohr M, Nielsen JJ, Bangsbo J. Caffeine intake improves intense intermittent exercise performance and reduces muscle interstitial potassium accumulation. *J Appl Physiol.* 2011; 111(5):1372-1379.
5. Balshaw TG, Bampouras TM, Barry TJ, Sparks SA. The effect of acute taurine ingestion on 3-km running performance in trained middle-distance runners. *Amino Acids*. 2013; 44(2):555-561.
6. Rutherford JA, Spriet LL, Stellingwerff T. The effect of acute taurine ingestion on endurance performance and metabolism in well-trained cyclists. *Int J Sport Nutr Exerc Metab.* 2010; 20(4):322-329.
7. Milioni F, Malta Ede S, Rocha LG et al. Acute administration of high doses of taurine does not substantially improve high-intensity running performance and the effect on maximal accumulated oxygen deficit is unclear. *Appl Physiol Nutr Metab*. 2016; 41(5):498-503
8. Tallis J, Duncan MJ, James RS. What can isolated skeletal muscle experiments tell us about the effects of caffeine on exercise performance? Br J Pharmacol. 2015; 172:3703–3713.
9. Galler S, Hutzler C, Haller T. Effects of taurine on Ca^{2+}-dependent force development of skinned muscle fibre preparations. *J Exp Biol.* 1990;152(1):255-264.
10. Bakker AJ, Berg HM. Effect of taurine on sarcoplasmic reticulum function and force in skinned fast-twitch skeletal muscle fibres of the rat. J Physiol. 2002;538(1):185-194.
11. Hamilton EJ, Berg HM, Easton CJ, Bakker AJ. The effect of taurine depletion on the contractile properties and fatigue in fast-twitch skeletal muscle of the mouse. *Amino Acids.* 2006;31(3):273-278.
12. Doerner JM, Kuetting DL, Luetkens JA, et al. Caffeine and taurine containing energy drink increases left ventricular contractility in healthy volunteers. *Int J Cardiovasc Imaging*. 2015; 31(3):595-601.
13. Hajsadeghi S, Mohammadpour F, Manteghi MJ, et al. Effects of energy drinks on blood pressure, heart rate, and electrocardiographic parameters: An experimental study on healthy young adults. *Anatol J Cardiol*. 2016;16(2):94-99.
14. Bichler A, Swenson A, Harris MA. A combination of caffeine and taurine has no effect on short term memory but induces changes in heart rate and mean arterial blood pressure. *Amino Acids*. 2006;31(4):471-476.
15. Crisafulli A, Carta C, Melis F et al. Haemodynamic responses following intermittent supramaximal exercise in athletes. *Antonio Exp Physiol.* 2004;89(6):665–674.
16. Lavine SJ, Walsh T. Exercise Tolerance and the Post Exercise Diastolic Filling Pattern in Patients With the Resting Impaired Relaxation. *Cardiol Res.* 2011;2(4):139-149.
17. Fredholm BB, Battig K, Holmen J, Nehlig A, Zvartau EE. Actions of caffeine in the brain with special reference to factors that contribute to its widespread use. *Pharmacol Rev*. 1999;51(1):83-133.
18. Schuh KJ, Griffiths RR. Caffeine reinforcement—the role of withdrawal. *Psychopharmacology*. 1997;130(4):320–326.
19. Kenemans JL, Lorist MM. Caffeine and selective visual processing. *Pharmacol. Biochem Behav*. 1995;52(3):461–471.
20. Jia F, Yue M, Chandra D et al. Taurine Is a Potent Activator of Extrasynaptic GABAA Receptors in the Thalamus. *J Neurosci.* 2008;28(1):106 -115.
21. Da Silva LA, Tromm CB, Bom KF et al. Effects of taurine supplementation following eccentric exercise in young adults. *Appl Physiol Nutr Metab*. 2013;39(1):101-104.

22. Ghandforoush-Sattari M, Mashayekhi S, Krishna CV, Thompson JP, Routledge PA. Pharmacokinetics of Oral Taurine in Healthy Volunteers. *J Amino Acids*. 2010, 346237. doi: 10.4061/2010/346237
23. Arnaud MJ, Welsch C. Theophylline and caffeine metabolism in man. In: Reitbrock N, Woodcock BG and Staib, AH eds. *Theophylline and Other Methylxanthines.* Zurich: Friedr. Vieweg and Sons; 1982:135–148.
24. Fitzsimons M, Dawson B, Ware D, Wilkinson A. Cycling and running tests of repeated sprint ability. *Aust J Sci Med Spor*t.1993.25:82–87.
25. Batterham AM, Hopkins WG. Making meaningful inferences about magnitudes. *Int J Sports Physiol Perform.* 2006;1:50–57.
26. Huxtable JR. Physiological actions of taurine. *Physiol Rev.*1992;72:101-163.
27. Matsuzaki Y, Miyazaki T, Miyakawa S, Bouscarel B, Ikegami T, Tanaka N. Decreased taurine concentration in skeletal muscles after exercise for various times. *Med Sci Sports Exerc*. 2002;34:793-797
28. Westerblad H, Allen DG. Recent advances in the understanding of skeletal muscle fatigue. *Curr Opin Rheumatol*. 2002;14:648–652.
29. Tallis J, Higgins MF, Cox VM, Duncan MJ, James RS. Does a physiological concentration of taurine increase acute muscle power output, time to fatigue, and recovery in isolated mouse soleus (slow) muscle with or without the presence of caffeine? *Can J Physiol Pharmacol*. 2014;92(1):42-49.
30. Cuisinier C, Michotte De Welle J, Verbeeck RK et al. Role of taurine in osmoregulation during endurance exercise. *Eur J Appl Physiol*.2002;87(6):489-95.

Table 1. Effect sizes and magnitude-based inferences for resting, baseline, and exercising heart rate (HR), blood lactate (B[La]), mean arterial pressure (MAP), rate pressure product (RPP) and rating of perceived exertion (RPE) between placebo (P), caffeine (C), taurine (T) and caffeine+taurine (C+T) conditions (n = 7). Mean ± SD are reported.

	Placebo (P)	Caffeine (C)	Taurine (T)	Caffeine + Taurine (C+T)	Direction, effect size and mechanistic inference
HR					
Resting HR (b/min)	75.3 ± 12.5	76.0 ± 8.2	74.7 ± 12.2	76.6 ± 11.2	$P<C^{\dagger E}$; $P>T^{\dagger E}$; $P<C+T^{\dagger E}$; $C>T^{\dagger E}$; $C<C+T^{\dagger E}$; $T<C+T^{\dagger E}$
Baseline HR (b/min)	73.0 ± 11.3	79.1 ± 14.7	66.9 ± 13.5	74.0 ± 12.9	$P<C^{\ddagger C}$; $P>T^{\ddagger C}$; $P<C+T^{\dagger E}$; $C>T^{*A}$; $C>C+T^{\ddagger E}$; $T<C+T^{¥C}$
Mean exercising HR (b/min)	159.6 ± 26.1	164.9 ± 26.4	161.5 ± 29.9	158.2 ± 25.1	$P<C^{\ddagger D}$; $P<T^{\dagger C}$; $P<C+T^{\dagger E}$; $C>T^{\dagger E}$; $C>C+T^{\ddagger D}$; $T>C+T^{\dagger E}$
Final HR (b/min)	166.7 ± 21.3	169.8 ± 23.8	166.0 ± 23.0	163.3 ± 22.4	$P<C^{\ddagger E}$; $P<T^{\dagger E}$; $P>C+T^{\ddagger D}$; $C>T^{\ddagger D}$; $C>C+T^{\ddagger C}$; $T>C+T^{\ddagger D}$
MAP					
Resting MAP (mmHg)	89.7 ± 12.5	90.9 ± 10.2	92.7 ± 6.5	92.4 ± 8.2	$P<C^{\dagger E}$; $P<T^{\ddagger E}$; $P<C+T^{\ddagger E}$; $C<T^{\dagger E}$; $C<C+T^{\dagger E}$; $T>C+T^{\dagger E}$
Baseline MAP (mmHg)	92.2 ± 12.3	95.7 ± 8.3	90.6 ± 7.6	94.5 ± 9.8	$P<C^{\ddagger E}$; $P>T^{\dagger E}$; $P<C+T^{\ddagger E}$; $C>T^{\ddagger D}$; $C>C+T^{\dagger E}$; $T<C+T^{\ddagger E}$
Final MAP (mmHg)	88.4 ± 9.7	94.4 ± 19.0	87.3 ± 5.1	88.5 ± 6.1	$P<C^{\ddagger C}$; $P>T^{\dagger E}$; $P<C+T^{\dagger E}$; $C>T^{\ddagger D}$; $C>C+T^{\ddagger D}$; $T<C+T^{\dagger E}$
RPP					
Resting RPP (mmHg/b/min)	9981 ± 1548	9525 ± 1623	9977 ± 1626	9454 ± 1513	$P>C^{\ddagger E}$; $P>T^{\dagger E}$; $P>C+T^{\ddagger E}$; $C<T^{\ddagger E}$; $C>C+T^{\dagger E}$; $T>C+T^{\ddagger E}$
Baseline RPP (mmHg/b/min)	8870 ± 1243	10636 ± 2134	8645 ± 1327	9688 ± 2240	$P<C^{¥B}$; $P>T^{\dagger E}$; $P<C+T^{\ddagger E}$; $C>T^{¥B}$; $C>C+T^{¥C}$; $T<C+T^{¥E}$
Final RPP (mmHg/b/min)	22311 ± 3809	23921 ± 5312	22150 ± 4531	22120 ± 4338	$P<C^{\ddagger D}$; $P>T^{\dagger E}$; $P<C+T^{\dagger E}$; $C>T^{\ddagger D}$; $C>C+T^{\ddagger D}$; $T>C+T^{\dagger E}$
B[La]					
Resting B[La] (mmol/L)	1.2 ± 0.3	1.5 ± 0.8	1.0 ± 0.2	1.5 ± 0.5	$P<C^{\ddagger E}$; $P>T^{\ddagger E}$; $P<C+T^{\ddagger E}$; $C>T^{¥E}$; $C\sim C+T^{\ddagger E}$; $T<C+T^{¥E}$
Baseline B[La] (mmol/L)	1.1 ± 0.6	1.2 ± 0.2	0.8 ± 0.1	1.0 ± 0.1	$P<C^{\ddagger C}$; $P>T^{\ddagger E}$; $P>C+T^{\dagger E}$; $C>T^{¥A}$; $C>C+T^{\ddagger D}$; $T<C+T^{\ddagger B}$
Mean exercising B[La] (mmol/L)	8.9 ± 1.6	9.7 ± 1.9	8.6 ± 1.7	8.8 ± 1.8	$P<C^{\ddagger E}$; $P>T^{\ddagger E}$; $P>C+T^{\dagger E}$; $C>T^{\ddagger C}$; $C>C+T^{\ddagger C}$; $T<C+T^{\dagger E}$
RPE					
Mean exercising RPE (6-20)	18 ± 1	17 ± 1	17 ± 1	17 ± 1	$P>C^{\ddagger E}$; $P>T^{\ddagger E}$; $P>C+T^{\ddagger E}$; $C\sim T^{\dagger E}$; $C\sim C+T^{\dagger E}$; $T\sim C+T^{\dagger E}$

Note: Mechanistic inferences: [A] = Most likely; [B] = Very likely; [C] = likely; [D] = Possibly; [E] = Unclear. Qualitative outcome is reported between experimental conditions. Effect sizes (d): † = Trivial; ‡ = Small; ¥ = Moderate; * = Large or Very Large. > = mean is larger than; < = mean is smaller than; ~ = mean is equal. Symbols are used in all following Figures

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Figure 2. Mean ± SD for peak power (PP) across the three Wingate tests between conditions (*n* = 7). Only small-large differences are presented for clarity.

Figure 3. Mean ± SD for mean power (MP) across the three Wingate tests between conditions (*n* = 7). Only small-large differences are presented for clarity.

Figure 4. Mean ± SD for the inter-sprint fatigue index ($\%FI_{Inter}$) across the three Wingate tests between conditions (*n* = 7). Only small-large differences are presented for clarity.

Figure 5. Mean ± SD for the intra-sprint fatigue index ($\%FI_{Intra}$) across the three Wingate tests between conditions (*n* = 7). Only small-large differences are presented for clarity.

Figure 6. Power output of a representative participant during repeated Wingate tests (x 3) in the four experimental conditions (T = Taurine; C+T = Caffeine + Taurine; C = Caffeine; P = Placebo).

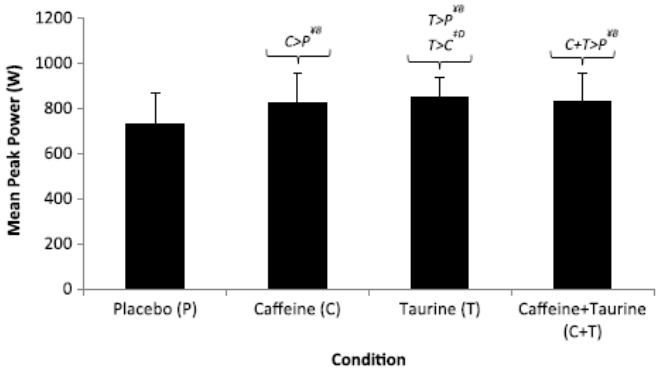

Figure 1 — Mean ± SD for mean peak power across the 3 Wingate tests between conditions ($n = 7$). Only small-large differences are presented for clarity. Note: Mechanistic inferences: [A]Most likely; [B]very likely; [C]likely; [D]possibly; [E]unclear. Qualitative outcome is reported between experimental conditions. Effect sizes (d): †Trivial; ‡small; ¥moderate; *large or very large. >= mean is larger than; <= mean is smaller than; ~= mean is equal.

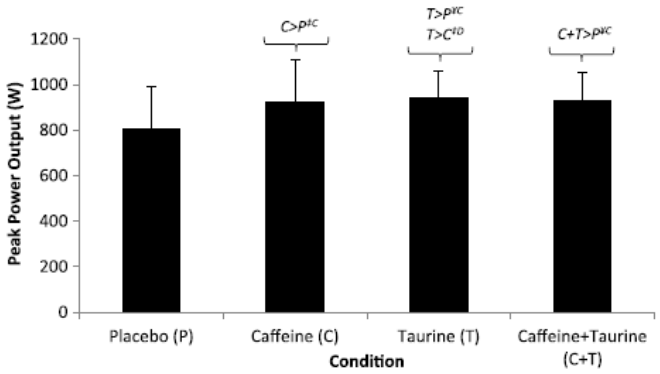

Figure 2 — Mean ± SD for peak power across the 3 Wingate tests between conditions ($n = 7$). Only small-large differences are presented for clarity. Note: Mechanistic inferences: [A]Most likely; [B]very likely; [C]likely; [D]possibly; [E]unclear. Qualitative outcome is reported between experimental conditions. Effect sizes (d): †Trivial; ‡small; ¥moderate; *large or very large. >= mean is larger than; <= mean is smaller than; ~= mean is equal.

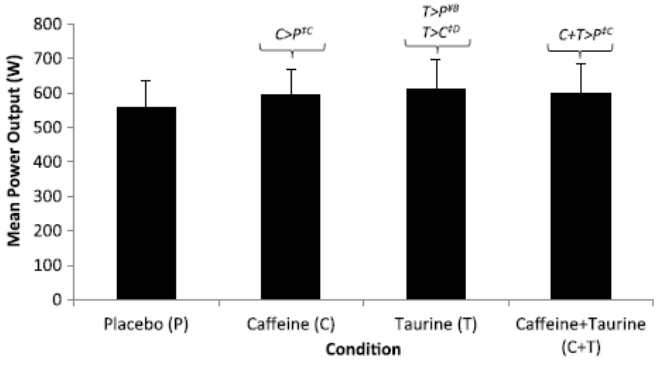

Figure 3 — Mean ± SD for mean power across the 3 Wingate tests between conditions ($n = 7$). Only small-large differences are presented for clarity. Note: Mechanistic inferences: [A]Most likely; [B]very likely; [C]likely; [D]possibly; [E]unclear. Qualitative outcome is reported between experimental conditions. Effect sizes (d): †Trivial; ‡small; ¥moderate; *large or very large. >= mean is larger than; <= mean is smaller than; ~= mean is equal.

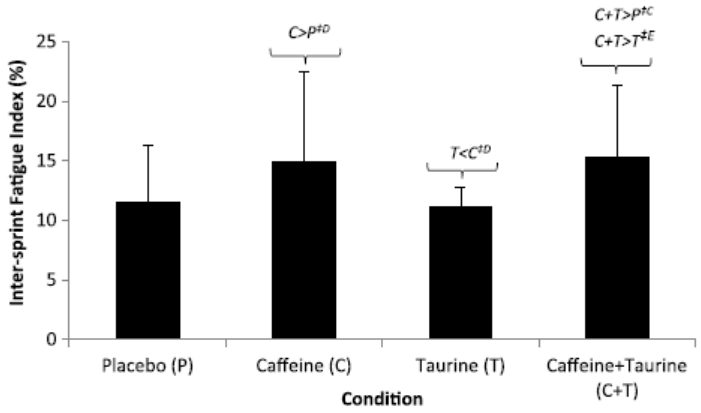

Figure 4 — Mean ± SD for the intersprint fatigue index ($\%FI_{Inter}$) across the 3 Wingate tests between conditions ($n = 7$). Only small-large differences are presented for clarity. Note: Mechanistic inferences: [A]Most likely; [B]very likely; [C]likely; [D]possibly; [E]unclear. Qualitative outcome is reported between experimental conditions. Effect sizes (d): †Trivial; ‡small; ¥moderate; *large or very large. > = mean is larger than; < = mean is smaller than; ~ = mean is equal.

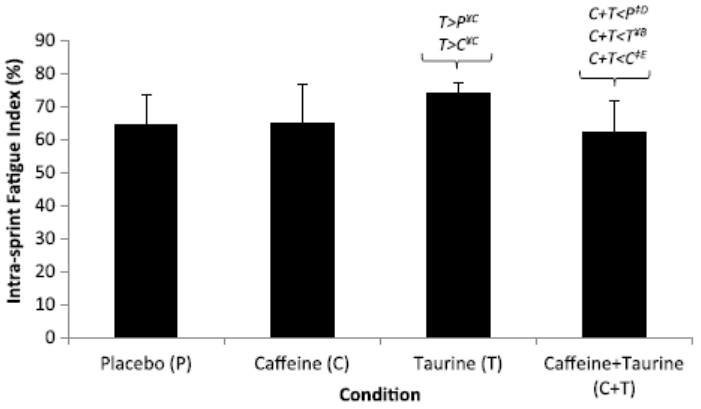

Figure 5 — Mean ± SD for the intrasprint fatigue index ($\%FI_{Intra}$) across the 3 Wingate tests between conditions ($n = 7$). Only small-large differences are presented for clarity. Note: Mechanistic inferences: [A]Most likely; [B]very likely; [C]likely; [D]possibly; [E]unclear. Qualitative outcome is reported between experimental conditions. Effect sizes (d): †Trivial; ‡small; ¥moderate; *large or very large. > = mean is larger than; < = mean is smaller than; ~ = mean is equal.

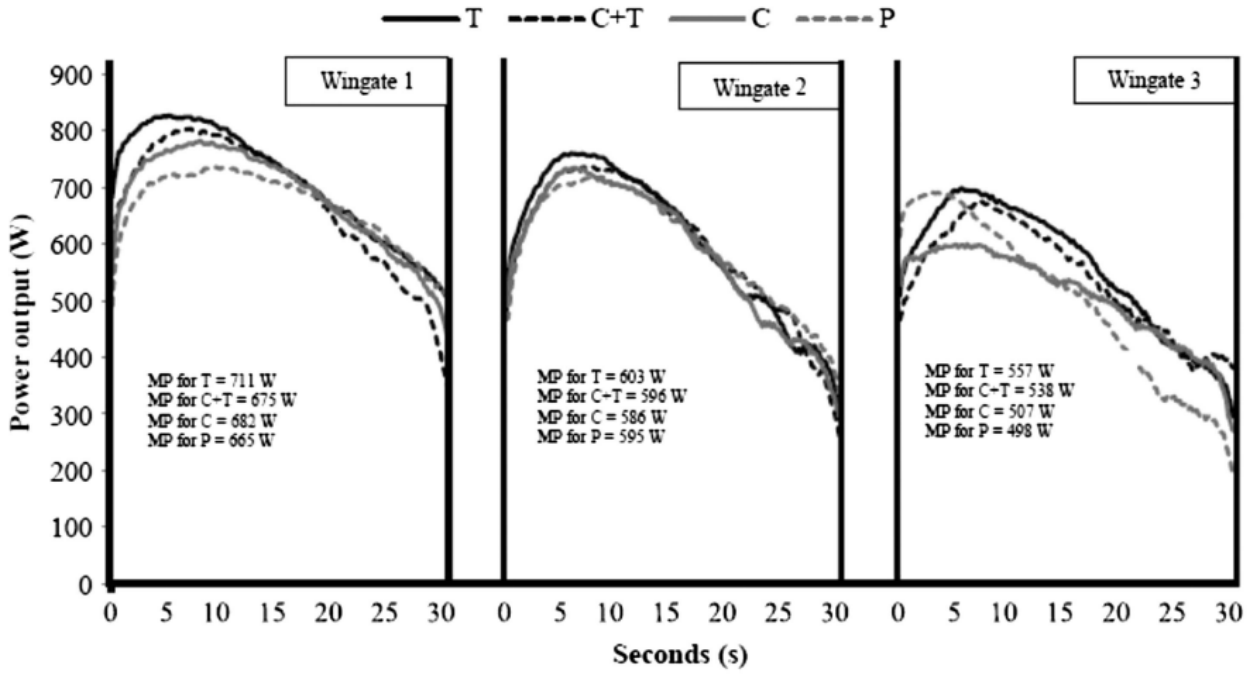

Figure 6 — Power output of a representative participant during repeated Wingate tests (×3) in the 4 experimental conditions (T, taurine; C+T, caffeine + taurine; C, caffeine; P, placebo).

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