A Comparison of Caffeine Versus Pseudoephedrine on Cycling Time-Trial Performance

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Both caffeine (CAF) and pseudoephedrine (PSE) are proposed to be central nervous system stimulants. However, during competition, CAF is a permitted substance, whereas PSE is a banned substance at urinary levels >150 μg·ml⁻¹. As a result, this study aimed to compare the effect of CAF versus PSE use on cycling time trial (TT) performance to explore whether the legal stimulant was any less ergogenic than the banned substance. Here, 10 well-trained male cyclists or triathletes were recruited for participation. All athletes were required to attend the laboratory on four separate occasions—including a familiarization trial and three experimental trials, which required participants to complete a simulated 40 km (1,200 kJ) cycling TT after the ingestion of either 200 mg CAF, 180 mg PSE or a nonnutritive placebo (PLA). The results showed that the total time taken and the mean power produced during each TT was not significantly different (p > .05) between trials, despite a 1.3% faster overall time (~57 s) after CAF consumption. Interestingly, the time taken to complete the second half of the TT was significantly faster (p < .05) in CAF as compared with PSE (by 99 s), with magnitude based inferences suggesting a 91% beneficial effect of CAF during the second half of the TT. This investigation further confirms the ergogenic benefits of CAF use during TT performances and further suggests this legal CNS stimulant has a better influence than a supra-therapeutic dose of PSE.

Keywords: ergogenic aid, endurance performance, doping

Pseudoephedrine (PSE) is a sympathomimetic drug commonly used as a therapeutic decongestant for the treatment of cold and flu. However, PSE in a central nervous system (CNS) stimulant and as such has previously suggested as an ergogenic aid to athletic performance. With this in mind, in 2010, the World Anti-Doping Agency (WADA) moved to place PSE onto the prohibited substance list. However, due to its ubiquitous nature in many cold and flu medications, rather than a complete ban on the use of this substance, an upper threshold limit of 150 μg·ml⁻¹ in urine was established. Despite the suggestion of an upper limit for detection, the individual response and excretion time of PSE from the system seems to be wildly variable, and as such, the advice from WADA to athletes is to stop taking therapeutic doses of PSE during the 24 hr before competition (World Anti-Doping Agency, 2010).

Pseudoephedrine acts as a stimulant, and increases heart rate (HR), blood pressure (BP), bronchiole tube dilation, and rate of liver glycogenolysis (Bouchard et al., 2002). Such changes are mediated via catecholamine neurotransmitters (Jones, 2008), potentially explaining the ergogenic effect of these drugs. To date, research into PSE and sports performance has found that therapeutic doses up to 120 mg have limited ergogenic potential (Chester et al., 2003; Chu et al., 2002; Hodges et al., 2006). However, when these doses are increased (>180 mg), the influence of PSE on performance has been shown equivocal. Previously reported benefits of PSE include increased isometric knee extension strength (8.6%), increased peak anaerobic power (2.8%; Gill et al., 2000) and improved 1,500 m running time trial performance (5.79 s; Hodges et al., 2006). In contrast, separate investigations have failed to show any performance benefits in 800-m running time trial performance when a supra-therapeutic dose of 2.5 mg·kg⁻¹ was used (Berry & Wagner, 2012), with similar outcomes also shown during aerobic-based cycling performance (Betteridge et al., 2010). As such, it remains controversial as to whether a supra-therapeutic dose of PSE actually improves athletic performance.

Conversely, caffeine (CAF) is an alternative ergogenic aid, also known for its effect as a stimulant; however, this drug is not considered a banned substance by WADA. It is proposed that CAF increases alertness, in addition to decreasing fatigue and perceptual effort via its effect as an antagonist on the adenosine receptors (Bouchard et al., 2002; Cox et al., 2002; Sinclair & Geiger, 2000). To date, the use of CAF to improve athletic performance has been widely reported (Bruce et al., 2000; Cox et al., 2002; Ivy et al., 2009), utilizing dosage regimes of 3–6 mg·kg⁻¹, ingested 60–90 min before exercise (Graham, 2001). As a result of the suggested influences of CAF on the CNS, it is possible that the use of this stimulant is similar in its effect on athletic performance as that of PSE. As such, it was the aim of this investigation to determine if similar ergogenic

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effects could be obtained through the use of CAF (a legal stimulant) in comparison with PSE (a banned substance) during a 40 km cycling time trial (TT).

**Methods**

Ten endurance-trained males were recruited from local cycling and triathlon clubs to participate in this investigation (age: 30 ± 2 y, body mass: 79.10 ± 1.65 kg and VO2peak: 58.9 ± 2.0 ml·kg·min−1). All participants were reported as regular CAF users; however, a 48-hr washout period requiring the abstinence of CAF-containing foods and beverages was enforced before each trial, to exert a level of CAF use control between participants. Furthermore, athletes were also asked to avoid strenuous exercise for 24 hr before each trial, and no food or beverages other than water were to be consumed within 2 hr of arrival at the laboratory. Written informed consent was given by each participant before commencement of this study. Ethical approval was granted by the Human Ethics Committee of the University of Western Australia.

One familiarization and three experimental cycling TT’s were completed on a stationary bicycle ergometer, each at the same time of day and separated by a period of 7 days. The three experimental trials were administered in a randomized, double-blind, repeated measures fashion, requiring the pre-TT administration of CAF, PSE, or a placebo (PLA) taken 60 min before the commencement of the TT. The CAF was administered at a dose of 200 mg using No-Doz Awakeners (Key Pharmaceuticals, New South Wales, Australia). The PLA was administered at a dose of 180 mg using Chemists’ Own Sinus Relief (Pseudoephedrine Hydrochloride, Victoria, Australia). All supplements used here were provided as an “off-the-shelf” preparation and no active ingredient conformational analysis was performed. Supplements were provided to athletes in concealed gelatin capsules; hence, there were no overt indicators evident to the athlete as to the type of supplement they were taking. Absolute supplement doses were used here to better reflect the external validity of an athlete consuming the entire dose of a commercially available product rather than a relative dose, which would be impractical in a field-based situation. However, for clarity and comparison, the relative doses provided here were 2.5 ± 0.1 mg·kg−1 of CAF, and 2.3 ± 0.1 mg·kg−1 of PSE.

The initial familiarization session included a graded exercise test (GXT) to determine each athlete’s peak oxygen consumption (VO2peak). The methods used to determine VO2peak in this laboratory have been described previously (Peeling et al., 2005). For each of the three experimental sessions, upon arrival at the laboratory, an earlobe blood sample was collected into a 35μL heparinized glass capillary tube, and analyzed for blood lactate (BLa) concentration using a blood gas analyzer (ABL 625; Radiometer Medical A/S, Copenhagen, Denmark). Before all earlobe blood sampling, the collection site was sterilized with an alcohol swab and the initial blood droplet discarded. Subsequently, the participant was administered their randomized drug treatment, before commencing a 50 min period of seated rest. Next, participants completed an 8-min warm-up consisting of 2 min of cycling at a self-selected gear and cadence, two 15-s accelerations to 300 W with 45 s of active recovery between sets, three 30-s accelerations to a perceived TT pace (with 30 s of active recovery between sets), followed by a 1-min free spinning effort at self-selected gear and cadence. Subsequent to the warm-up, a 2-min rest period was allowed before the cycle TT commenced.

The cycling TT required athletes to complete a given amount of work in the fastest time possible. Previously, it has been documented that trained athletes complete 600 kJ of work in ~30 min at an intensity of 80–82% VO2max (Hawley et al., 2000). Therefore, 1,200 kJ of work was chosen to elicit an exercise time of ~60 min at this intensity. A calibrated wind-braked cycle ergometer (Evolution Pty. Ltd., Adelaide, Australia) was used during the GXT and TT to record mean power output, the amount of work completed (kJ), and the elapsed time of work completion. During each cycle TT, participants were provided feedback indicating the percentage of total work completed (every 5%), but were blinded to all other data output.

During the cycle TT, the participants’ HR, the elapsed cycle time, and the mean power output were visible only to the researcher. The HR (Polar RS200, Finland) was measured and recorded at 20% intervals of total work completed (i.e., 240 kJ of work). At the end of each 20% work interval, a capillary blood sample was collected from the earlobe and immediately analyzed for BLa. Participants were concurrently asked to rate their perceived exertion levels using the Borg Perceptual Scale (Borg, 1982). Immediately following the cycle TT completion, a final capillary blood sample was collected and analyzed for BLa, thus ending the experimental trial. During the first cycle TT, participants were allowed to drink water ad libitum; however, this volume was recorded and provided as a mandatory volume to be consumed during subsequent trials. Additionally, at the conclusion of each trial, all participants were asked to report which supplement they thought they were given before that performance. The data from this survey showed that 3 out of 10 correctly guessed when they were using caffeine, and 4 out of 10 correctly guessed when they were given the PLA or the PSE.

The following results are reported as mean ± SEM. Repeated-measures ANOVA was conducted to explore the effect of CAF and PSE on cycling TT performance, BLa, mean power output, HR and RPE. In the event of a main effect, paired-samples t tests were used to clarify where differences occurred. The alpha level was set at $p \leq .05$. In addition, effect sizes for data trends are expressed in Cohen units, and the likelihood that a true effect was substantially beneficial, trivial or harmful was reported.
The smallest worthwhile effect was taken as 0.2. If the percentage chance that the effect was beneficial and harmful were both >5%, the true effect was assessed as unclear (could be beneficial or harmful); otherwise, the chances of benefit or harm were assessed as follows: <1% almost certainly not; 1–5% very unlikely; 5–25% unlikely; 25–75% possibly; 75–95% likely; 95–99% very likely; >99% almost certainly (Batterham & Hopkins, 2006).

Results

The total time taken to complete each cycle time trial was not significantly different between conditions (Table 1). However, it should be noted that the cycle TT of the CAF trial was 57 s faster than that of the PSE and 58 s faster than that of the PLA. When split into two 600 kJ sections, it becomes evident that the time taken to complete second half of the TT was significantly slower in PSE as compared with CAF (p ≤ .05). The magnitude based inferences suggested that CAF ingestion had a 91% likely beneficial effect in enhancing the performance time in the second half of the TT as compared with PSE (by 99 s), and a 51% likely beneficial effect as compared with the PLA (by 48 s; Table 2). The overall mean power output was not significantly different between trials (Table 1). However, mean power output for the second half of the TT was significantly lower in the PSE as compared with CAF and PLA (p ≤ .05).

The mean HR for the CAF, PSE, and PLA trials were 166 ± 3, 157 ± 3 and 162 ± 3 bpm, respectively. Mean HR was significantly lower in the PSE as compared with both the CAF and PLA trials (p ≤ .05). The mean RPE was 15 ± 1 for each trial, with no significant differences recorded between trials. The mean BLa during the TT was not significantly different between trials (Table 3); however, the immediately post-TT BLa was significantly lower in the PSE as compared with both CAF and PLA (p ≤ .05).

Discussion

This study showed that, under controlled conditions, the ingestion of 200 mg CAF or 180 mg PSE independently, did not significantly improve overall 1200 kJ (~40 km) simulated cycling TT performance. However, the cycling TT of the CAF trial was ~57 s quicker than the PSE and PLA trials, supported by a significantly higher mean power output and a faster time taken to complete the second half of the TT. These results suggested a likely beneficial impact of consuming CAF for the back-end of a ~40 km cycling TT effort.

Initially, it was anticipated from previous work investigating PSE (Gill et al., 2000; Hodges et al., 2006) or CAF (Cox et al., 2002; Kovacs et al., 1998) that both of these substances in isolation may improve cycling TT performance. Contrary to these previous positive findings however, this study showed that the isolated effect of PSE resulted in a lack of any performance enhancing effect (even when consumed in supra-therapeutic doses). Alternatively, although CAF was unable to statistically influence overall TT performance, a 1.3% improvement

| Table 1 | Time and Mean Power Output During the First Half, Second Half, and Total Time Trial |
|---------|---------------------------------|---------------------------------|---------------------------------|
|         | CAF (Time (s) ± Power (W))      | PSE (Time (s) ± Power (W))      | PLA (Time (s) ± Power (W))      |
| First half of TT | 2,228 ± 78 273.4 ± 9.6 | 2,186 ± 88 278.9 ± 11.2 | 2,238 ± 92 273.4 ± 11.3 |
| Second half of TT | 2,211 ± 75 275.5 ± 8.8 | 2,310 ± 73a 263.1 ± 8.1a | 2,259 ± 74 269.4 ± 8.4 |
| Total | 4,439 ± 153 274.4 ± 8.8 | 4,496 ± 152 271.0 ± 9.2 | 4,497 ± 153 271.4 ± 9.1 |

aSignificantly different to CAF (p ≤ .05).

| Table 2 | Effect Size and Magnitude of Effect Outcomes for the First Half, Second Half, and Total Time Trial for the Caffeine (CAF) vs. Pseudoephedrine (PSE), CAF vs. Placebo (PLA), and PSE vs. PLA |
|---------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
|         | CAF vs. PSE | CAF vs. PLA | PSE vs. PLA |
| First half of TT | effect size | 0.15 | −0.03 | −0.18 |
| % chance that effect is beneficial | 2(61/37) | 17(73/10) | 43(56/1) |
| Second half of TT | effect size | −0.43 | −0.2 | 0.22 |
| % chance that effect is beneficial | 91(9/0) | 51(47/2) | 1(43/55) |
| Total TT time | effect size | −0.12 | −0.12 | 0.01 |
| % chance that effect is beneficial | 24(75/1) | 32(63/5) | 3(94/3) |

Note: If the percentage chance that the effect is beneficial and harmful are both >5%, the true effect was assessed as unclear (could be beneficial or harmful). Otherwise, chances of benefit or harm were assessed as followed: <1% almost certainly not; 1–5% very unlikely; 5–25% unlikely; 25–75% possibly; 75–95% likely; 95–99% very likely; and >99% almost certainly.
in 1200 kJ completion time was evident when CAF was consumed, likely explained by the significantly higher mean power output in the second half of the TT. It is possible that the greater second half performance in the CAF trial might be explained by the timing of the CAF ingestion used here (60 min pre-TT) being some 30 min later than those previously suggested to reach peak plasma CAF levels before the start of a competitive situation (Conway et al., 2003). With the potential that the peak plasma CAF levels of the participants in this investigation were not reached until some 30 min into the cycling TT, it may be likely that if the demands of the cycling task were extended (i.e., if the trial were a simulated 80 km, or if CAF was ingested 30 min earlier), the ergogenic effects of CAF ingestion may have resulted in significant overall performance benefits. However, such a strategy of delayed CAF intake requires further attention, and might be considered during races of longer duration (i.e., the cycle-leg of an Ironman triathlon), to exploit the ergogenic benefits of CAF in the latter stages of ultra-distance races.

Immediately post-TT, the BLa levels in the CAF trial were significantly higher as compared with PSE. This is likely due to the greater intensity at which the TT was completed in the second half of the effort. Several CAF studies have shown similar increases in BLa (Kovacs et al., 1998; Graham & Spriet, 1991; Spriet et al., 1992), with most attributing the increase to greater work output and not a direct effect of CAF. (Graham, 2001; Kovacs et al., 1998; Doherty et al., 2004). In addition, this transient increase in BLa has been suggested to have minimal influence on muscle metabolism, and may instead be a reflection of reduced lactate clearance by the liver or resting muscle (Graham, 2001). In contrast, PSE studies have not shown BLa to increase above control levels during exercise (Chester et al., 2003; Hodges et al., 2006; Gillies et al., 1996), similar to the results obtained here.

It has previously been suggested that PSE influences the CNS by binding to cell surface receptors of central and peripheral neurons to prolong the half-life of catecholamine neurotransmitters, resulting in a fatigue-masking effect (Bouchard et al., 2002; Gillies et al., 1996). Although this investigation, and a number of other separate studies have failed to show any ergogenic effect of PSE (Hodges et al., 2003; Chu et al., 2002; Gillies et al., 1996), those that do show a positive outcome have attributed the improvement to such an effect on the CNS (Gill et al., 2000; Hodges et al., 2006). In the present investigation however, PSE and CAF ingestion did not result in any perceptual enhancements of fatigue resistance (as suggested by the lack of difference in RPE) during the TT performance—an outcome that is similar to previous research (Chester et al., 2003). The results here revealed that the RPE during the PSE trial did not differ from that recorded in the PLA, albeit with the dose of PSE being higher than that given during previous investigations (Hodges et al., 2003; Chester et al., 2003; Gillies et al., 1996). Such results may be due to the nature of PSE being unable to cross the blood-brain barrier directly; therefore relying on an indirect effect on the CNS (Bouchard et al., 2002). Conversely, CAF is a psychomotor stimulant previously shown to reduce or maintain RPE to provide an ergogenic effect (Bruce et al., 2000; Cox et al., 2002). Although mean power output during the second half of the TT was significantly faster in CAF, the mean RPE for each trial was not significantly different. This may be explained by the action of CAF on the CNS through adenosine receptor antagonism (Sinclair & Geiger, 2000), with receptors found in regions of the brain associated with locomotor activity (Jones, 2008). To this end, CAF may have enabled the individual to perform a greater amount of work in the second half of the TT without a corresponding increase in the perception of effort.

Pseudoephedrine exerts its effects by directly stimulating adrenergic receptors on certain tissues, such as b1 adrenoreceptors on cardiac muscle to increase the rate of contraction (Bouchard et al., 2002). Mixed findings exist on the impact of PSE on exercise HR (Hodges et al., 2003; Gill et al., 2000; Hodges et al., 2006); however, the present investigation showed that the mean HR was significantly lower during PSE as compared with PLA. Similar to PSE, CAF also acts to increase HR by preventing the slowing of atrial-ventricular nodal conduction via binding to adenosine receptors (Sinclair & Geiger, 2000). Increases in HR upon CAF ingestion are thus expected, and was demonstrated here by the highest mean HR recorded within the CAF trial. Regardless of such outcomes, it is doubtful that the increased HR in the CAF trial seen here was causal of the improved TT performance, but rather that such an outcome is a consequence of the higher intensity at which the second half of the CAF trial was performed.

A practical limitation of the current study is that an absolute dose of CAF or PSE independent of body weight was administered here, as compared with the majority of previous studies where dosage was weight dependent (for review see: Graham, 2001). Although an individually determined dose of supplement may have shown more optimal outcome, from a practical application, the use of an absolute dose is more relevant to field-based situations due to the commercial availability of CAF or PSE in tablet-form (100 mg and 60 mg per tablet,
Conclusion

In conclusion, the use of 200 mg of CAF resulted in a 1.3% improvement (~57 s) in 1,200 kJ cycling TT performance when compared with 180 mg of PSE and a PLA trial of no stimulant administration at all. Although the overall performance time was not statistically different between trials, the CAF supplement resulted in a significantly faster second half of the TT as compared with PSE, with a 91% likely beneficial impact. These results favorably show that the effects of the legal stimulant CAF are likely better than that of the banned substance PSE. Hence, an adverse finding of PSE misuse in athletes may not have incurred a performance gain any better than that achievable via legal means.

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References


