The Effect of Caffeine on Endurance Performance in Trained Female Cyclists

by

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ABSTRACT

Caffeine has been established as ergogenic to endurance exercise in men, but this effect had not been demonstrated in women. The purpose of this study was to investigate the effect of caffeine on endurance performance in trained female cyclists. Eight women (VO_2max = 56.1±4.1 $mL \cdot kg^{-1} \cdot min^{-1}$) cycled to exhaustion at 80% VO_2max following ingestion of 5 mg/kg caffeine during the follicular phase of their menstrual cycle. Time to exhaustion was significantly prolonged from 68.4 to 77.2 minutes (13.2%) in the caffeine trial ($p<0.05$). Subjectively, caffeine habituation did not appear to influence the ergogenic effect, while use of oral contraceptives appeared to moderate the effect. Heart rate, oxygen consumption, ventilation, and perceived exertion were unaffected by caffeine ingestion, suggesting these variables are not critical to caffeine's mechanism of action in women. Further investigation into mediating factors may help to elucidate the mechanism through which caffeine prolongs time to exhaustion.

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Many, many thanks to my participants and volunteers for enduring the exercise tests and for continued interest in the study. To all my family and friends who believed in me, especially Ian and Sean, thank you – I would not have finished this in "one-piece" without you.

DEDICATION

To my parents, Donna Jean and Hugh MacLeod. You believed in me, taught me to succeed, and supported me unconditionally, always. I could not have accomplished any of this without you. It is with pride, and surprise, that I find myself following in your footsteps.

INTRODUCTION

In both the competitive and recreational worlds of endurance sport, athletes strive for improvements in performance and often turn to nutritional supplements to enhance their training and competitive results. One such supplement is caffeine. This drug is legal, publicly accepted, inexpensive, and readily available in many beverages and foods as well as over-the-counter stimulants and analgesics. Purported to enhance endurance performance, caffeine is commonly consumed by athletes (Delbeke & Debachere, 1984; Martin, Roussos, Perry, & Salzwedel, 1997). While evidence for caffeine's effect on exercise performance exists, the mechanisms of action and potential differences between types of exercise or between men and women are not fully elucidated.

Caffeine and Exercise

Caffeine is a well-known central nervous system (CNS) stimulant that has a complex array of metabolic and physiological effects (see Review of Literature, Appendix A). As an adenosine receptor antagonist, caffeine blocks inhibitory (A_1 receptor mediated) signals in adipocytes, brain, heart, and kidney tissues and stimulatory (A_2 receptor mediated) signals in brain, platelets, liver, and smooth muscle (Graham, 1997). During endurance exercise, caffeine's action may involve any or all of these tissues and is potentially complex. It is notable that the role of adenosine receptors in skeletal muscle, where caffeine's action could be the most relevant during exercise, has yet to be clarified.

Studies have shown that caffeine ingestion can enhance exercise *endurance* (i.e., prolong the duration of sustained work and delay onset of fatigue) and/or exercise *intensity* (i.e., enhance the power output). In studies measuring effects on endurance, early work demonstrated that 330 mg of caffeine (approximately 4.7 mg/kg) prolonged cycling at 80% VO_2max by 19.5% over the placebo time of 75.5 minutes (Costill, Dalsky, & Fink, 1978). Many subsequent studies have shown that caffeine administered at dosages of 4.45 to 13.0 mg/kg one hour before exercise can delay fatigue by 20 to 50% during bouts of both running (Graham, Hibbert, & Sathasivam, 1998; Sasaki, Takaoka, & Ishiko, 1987) and cycling (Denadai & Denadai, 1998; Greer, Friars, & Graham, 2000; Spriet et al., 1992) to exhaustion at intensities near 80% VO_2max. This improvement was shown to be

independent of both modality (Graham & Spriet, 1991) and dosage (Graham & Spriet, 1995; Pasman, van Baak, Jeukendrup, & de Haan, 1995). Caffeine has also been reported to significantly improve time-trial performance (i.e., exercise intensity) during cross-country skiing (Berglund & Hemmingsson, 1982) and cycling time trials (Cox et al., 2002; Kovacs, Stegen, & Brouns, 1998).

Elucidating the precise mechanism(s) through which caffeine enhances exercise performance and/or delays fatigue is a challenge because the potential effects of this drug are very complex. A wide range of metabolic, neural, and neuroendocrine pathways that can affect endurance exercise (e.g., cardiovascular regulation, endocrine secretion, and sympathetic activity) are sensitive to caffeine and its metabolites (Graham, 1997). As well, given the lack of knowledge concerning the CNS pathways associated with caffeine's effects, at rest, in exercise, or in relation to fatigue, it is difficult to identify potential central site(s) of its action to improve exercise performance.

Early studies attributed caffeine's ergogenic action to a caffeine-induced rise in circulating epinephrine, lipolysis and free fatty acid (FFA) mobilization, and subsequent glycogen sparing (Costill et al., 1978; Essig, Costill, & Van Handel, 1980; Ivy, Costill, Fink, & Lower, 1979) as well as to an altered perception of effort (Costill et al., 1978). More recent research (see Review of Literature, Appendix A) presents findings that are not consistent with these theories and allude to the existence of an alternate mechanism.

Sex Differences

To date, most studies of caffeine and exercise have been limited to the study of trained male subjects. However, men and women differ in their hormonal, metabolic, sympathetic, and neuromuscular activity during submaximal exercise (Tarnopolsky, 1999). The few studies that have included women and men have not always reported comparative effects. In an investigation which employed four male and four female participants, sex-specific performance results were not reported (Cadarette, Levine, Berube, Posner, & Evans, 1983). Graham (Graham, 2001) later noted that the placebo plasma caffeine levels in this study were sufficiently high to elicit ergogenic benefit,

making the results difficult to interpret. Another, more recent, study that included a notable proportion of women (8 of 23) also failed to report sex-specific results (Bell & McLellan, 2002).

Only one study was found that compared the effect of caffeine on endurance performance in male and female subjects (Butts & Crowell, 1985). These authors reported that, in both 13 male and 15 female participants, cycling time to exhaustion at 70-75% VO_2max was not changed by 300 mg of caffeine (approximately 5 mg/kg). Although not statistically significant, they also reported that caffeine had a greater fatigue-delaying effect in women (14.4%) than in men (3.1%). These results may be confounded somewhat by methodology, as they added caffeine to decaffeinated coffee, which has more recently been shown to moderate caffeine's ergogenic action (Graham et al., 1998).

Consequently, the ergogenic benefit of caffeine has yet to be demonstrated in women. The purpose of this thesis was therefore to investigate the effect of caffeine on the endurance cycling performance of female athletes.

The specific research question addressed by the present study was:

> *What is the effect of 5 mg/kg caffeine, ingested as a single dose one hour prior to exercise, on the total time to exhaustion in trained female athletes cycling at 80% VO_2max?*

Hypothesis (H_1)

Caffeine ingestion will prolong time to exhaustion in female athletes cycling at 80% VO_2max.

Assumptions

1) Subjects provided a maximal effort on all tests.
2) Subjects reported honestly in questionnaires and diaries.
3) Placebo and caffeine tests to exhaustion were performed during the follicular phase of the same menstrual cycle (defined by self-report).

Delimitations

1) Participants were trained female cyclists (18 to 40 years of age) who had a minimum of 18 months of endurance-based cycling experience at a competitive level.
1) A single dose of caffeine (5 mg/kg) dissolved in lemonade was ingested one hour prior to exercise.
2) Participants cycled to exhaustion at an exercise intensity equal to that which elicited approximately 80% VO_2max.
3) Exercise testing was performed during the follicular phase of the menstrual cycle.

Limitations

1) Plasma caffeine levels were not measured.
2) Pre-exercise nutrition, fatigue, and caffeine status varied among subjects.
3) Oral contraceptive use and caffeine habituation were reported but not controlled.
4) Reproductive hormone levels were not measured.

Operational Definitions

Endurance performance	*Total exercise time (minutes and seconds) from the onset of exercise to exhaustion at a work load eliciting 80% VO_2max*
Exhaustion	*Voluntary cessation of exercise or an inability to maintain a minimum of 40 rpm for more than 10 seconds*
Habitual caffeine consumption	*Caffeine consumption equal to or greater than 1 cup of coffee per day (approximately 125 mg)*
Follicular phase	*The 10 days following the first day of menses, or the seven days during which oral contraceptive users are not ingesting hormones*
Trained	*Minimum of 18 months experience in endurance-based cycle training in either road or mountain biking with a minimum VO_2max of 48 $mL \cdot kg^{-1} \cdot min^{-1}$*

METHODS

Subjects

Sixteen trained female cyclists volunteered to participate in this research. Eight were excluded for one or more of the following reasons: inability to schedule all tests; illness; failure to meet minimum training criteria; amenorrhea; and/or caffeine ingestion prior to an exercise trial. Table 1 provides the physical characteristics of the eight women who met the eligibility criteria and completed each test appropriately. All were eumenorrheic with a self-reported cycle length ranging from 28 to 34 days. The experimental procedures and potential risks of the study were described to each subject individually, both verbally and in writing and informed consent was received from each subject prior to participation in each testing session (Appendix B). Ethics approval was obtained from the Human Research Ethics Committee at the University of Victoria.

Pre-experimental protocol

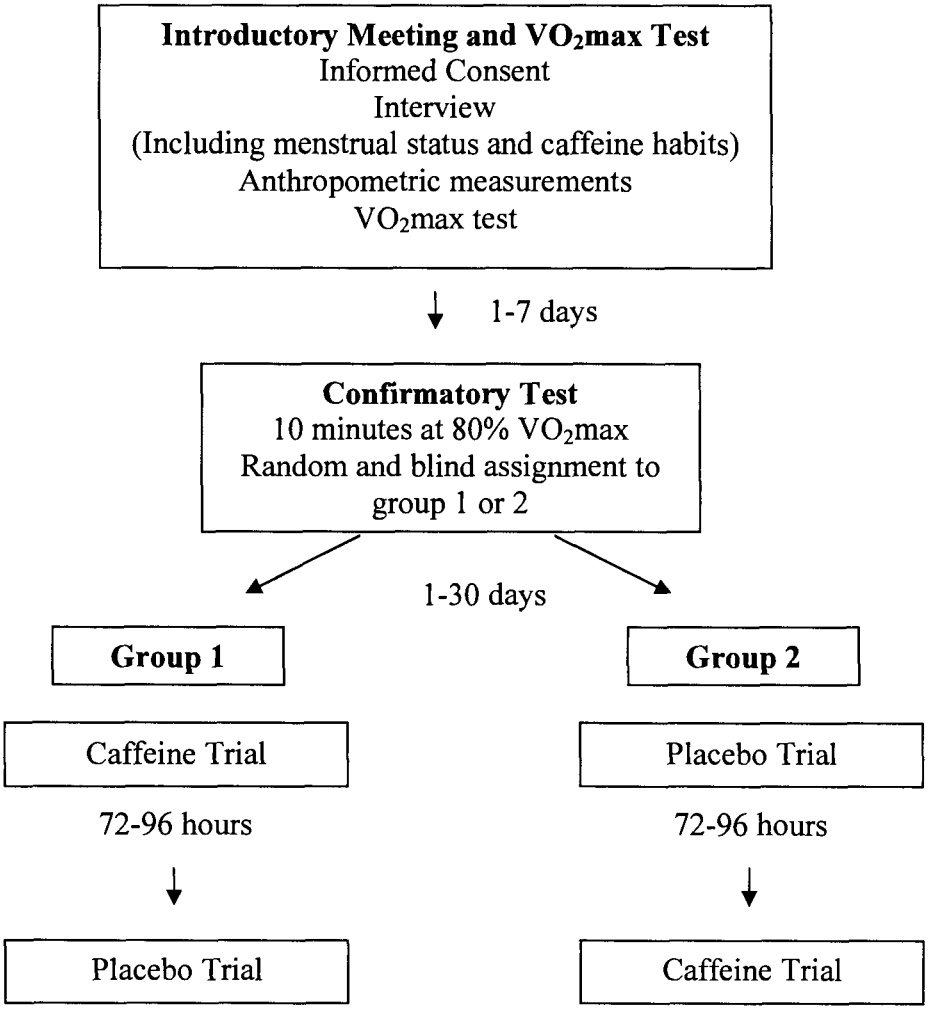
Figure 1 provides a diagrammatic representation of the research design and timing of data collection. Each subject reported to the laboratory twice, within 14 days, prior to the beginning of the exercise experiment. On the first visit, an individual interview was conducted and anthropometric measurements, including height, weight, and skin folds at five sites (triceps, biceps, subscapular, iliac crest, and calf) were taken using the Canadian Physical Activity, Fitness, and Lifestyle Appraisal protocol (CSEP, 1998) as descriptive measures of the subjects (Table 1).

Table 1: Physical characteristics, aerobic power, and ventilatory threshold (VT) of individual subjects.

Subject	Age (yr)	Height (cm)	Weight (kg)	SO5S (mm)	VO_2max ($mL \cdot kg^{-1} \cdot min^{-1}$)	PO at 80% VO_2max (Watts)	VT Estimate ($mL \cdot kg^{-1} \cdot min^{-1}$)	VT Estimate (%VO_2max)
1	25	162	59.6	56.8	60.2	210	47.7	79.2
2	37	156	50.2	27.1	59.9	195	48.5	81.0
3	30	169	59.1	29.7	59.0	225	48.9	82.9
4	19	164	64.8	61.9	48.6	195	38.7	79.6
5	23	169.5	76.1	79.6	56.3	275	43.4	77.1
6	22	166	54.7	44.7	55.5	210	44.7	80.5
7	29	162	57.0	49.0	57.8	205	45.2	78.2
8	21	162	60.4	67.0	51.8	200	40.3	77.8
Mean (SD)	25.8 (5.9)	163.8 (4.4)	60.2 (7.7)	52.0 (18.1)	56.1 (4.1)	214.4 (26.4)	44.7 (3.7)	79.5 (1.9)

Following a standardized 10 minute warm up and 10 minute stretching period, a graded cycling exercise test to exhaustion (VO_2max) was performed on a Lode Excalibur Sport (version 2.1) electronically braked cycle ergometer (Lode BV, Groningen, The Netherlands). Expired gas samples were collected with a Vmax 2900 metabolic cart (Sensor Medics) calibrated using primary standards and standard procedures. Gas samples were analyzed using the mixing chamber protocol (averaged over 20 seconds). Heart rate was measured using a Polar S610 monitor and manually recorded every minute. VO_2max was characterized by at least two of the following criteria: a plateau in heart rate; attainment of predicted maximum heart rate (220 - age); a rise in VO_2 of less than 2 $mL \cdot kg^{-1} \cdot min^{-1}$ with an increase in work load; and/or a respiratory exchange ratio of greater than 1.15. The position of all ergometer settings were recorded and maintained throughout all subsequent testing sessions.

Figure 1: Diagrammatic representation of experimental design.



Ventilatory threshold (VT) was estimated from the VO_2max test data (V_E vs power output), as was the wattage required to elicit 80% VO_2max. During the second visit, subjects cycled for 10 minutes at this wattage to ensure they would be cycling at an appropriate intensity during the endurance test. Adjustments were made to this load if necessary. During this session, subjects were familiarized with the modified Borg Scale of perceived exertion (Burdon, Juniper, Killian, Hargrave, & Campbell, 1982). This instrument is presented in Appendix C.

Subjects reported to the laboratory on two further occasions to perform the experimental endurance exercise trials during which they cycled to exhaustion following ingestion of a

placebo (Minute Maid lemonade – 10% Real Juice variety) or caffeine (5 mg/kg in Minute Maid lemonade). These sessions took place during the follicular phase of each subject's menstrual cycle, determined by self-report from the first day of menstruation (for oral contraceptive non-users) or the first of seven days without exogenous hormone ingestion (for oral contraceptive users). Trials were separated by 72-96 hours and conducted at approximately the same time of day. Assignment to group 1 (caffeine trial first) or group 2 (placebo trial first) was random and double blind. Anhydrous caffeine was purchased from a local pharmacy, weighed on an analytical balance (Mettler-Toledo College B, Greifensee, Switzerland), dissolved in lemonade, and refrigerated 24 hours prior to ingestion. As the caffeine was weighed in advance and the weight of each subject fluctuated by up to 1.1 kg throughout the testing sessions, the dosage of caffeine administered to each subject ranged from 4.89 to 5.05 mg/kg, with an average of 4.97 mg/kg.

Subjects were instructed to maintain normal training programs throughout the study and were encouraged to incorporate the experimental trials into their program as training sessions. They were asked to prepare for each endurance exercise trial as they would for a competition, taking diet, sleep, and physical activity into consideration. To improve consistency between the two trials, subjects were asked to maintain a diary of all activity, fluid, and food intake for forty-eight hours before each trial. They were also instructed to abstain from all caffeine ingestion 24 hours before each exercise test.

Endurance exercise (experimental) protocol

A diagrammatic representation of the experimental exercise protocol is presented in Figure 2. Upon reporting to the laboratory, resting heart rate was measured followed by consumption of the placebo or caffeine drink. Subjects then rested quietly for one hour in the lab during which time they were encouraged to drink water *ad libitum*. Heart rate was recorded every 20 minutes throughout this rest period. One hour after caffeine ingestion, subjects performed their standardized 10 minute warm-up and stretching period. They then cycled to exhaustion at the constant power output previously determined to elicit 80% VO_2max. Heart rate was recorded at the end of every minute throughout the test.

Expired gas was measured in 20 second samples during the first two minutes and for approximately two minutes at six minute intervals throughout the test (beginning at the sixth minute). Final gas samples were taken while the subject was still exercising for approximately two minutes before exhaustion. Ratings of perceived exertion (RPE), as defined by the modified Borg Scale (Burdon et al., 1982) were taken immediately before each expired gas reading, unless the subject was breathing into the metabolic cart. Verbal encouragement was provided only at exhaustion. Information about the duration of any test was not disclosed to the subject until completion of all tests. All data collection instruments are provided in Appendix D.

Data analyses

Time to exhaustion

Total time to exhaustion was tested for treatment (caffeine) effect by one-tailed, paired Student's *t* test and the effect of treatment order was tested using a two-tailed Student's *t* test in using Microsoft Excel 2002. Significance was set at $p < 0.05$. Data are reported as means (standard deviation).

Data management and analyses for heart rate, RPE, VO_2, and V_E

Heart rate was collected every minute throughout the experimental trial and RPE, VO_2, and V_E data were collected at the onset of exercise, at 6 minute intervals throughout the exercise test, and at exhaustion. Data were averaged at each of these time points as follows:

At the onset of exercise (minutes 0-3):

- Heart rate = average of minutes one, two, and three
- RPE = reported at end of minute three
- VO_2 and V_E = average of 20 second measures during minutes one and two

At the 6 minute time point and each interval thereafter (for example):

- Heart rate = average of minutes six, seven, and eight
- RPE = reported at end of minute six
- VO_2 and V_E = average of 20 second measures during minutes seven and eight

At exhaustion (Exh):

- Heart rate = average of last two minutes
- RPE = not collected as subjects were breathing into the metabolic cart
- VO_2 and V_E = average of 20 second measures during the final two minutes of exercise

In an attempt to account for the varying duration of each test, data were standardized by calling exhaustion 100%. Data collected during the first two minutes and last two minutes of the exercise test were used to represent onset of exercise and exhaustion, respectively. The data at intervals between the onset of exercise and exhaustion were grouped into percentile blocks representing 10% intervals calculated from each test's total time to exhaustion. For example, in a 60 minute test, the 10% block represents the time period from 3 minutes (onset) to 6 minutes and the 20% block represents the time period from 10% (6 minutes) to 20% (12 minutes). In some longer tests, two interval readings were averaged in a single block (for example the 40% block of a 98 minute test represents the period from 29 to 39 minutes, and therefore encompasses both the 30 and 36 minutes readings). Any such averaged data did not differ by more than 0.5 (RPE), 2% (HR), or 5% (VO_2 and V_E) with the exception of the RPE value in the 20% block for subject three's caffeine test: RPEs of 3.5 and 5.0 were described at the 12 and 18 minutes readings, respectively, but 5.0 was used to represent the 20% block.

Missing data for VO_2, V_E, and RPE reduced the sample size, such that complete data sets existed for only five subjects for V_E and RPE variables while VO_2 had only four complete sets of data. Statistical analyses of HR, VO_2, V_E, and RPE included an omnibus repeated measures analysis of variance over all blocks as well as a specific contrast between the placebo and caffeine treatments (using a contrast matrix program written for Systat version 9.0). Significance was set at $p < 0.05$.

Figure 2a: Diagrammatic representation of the full experimental trial.

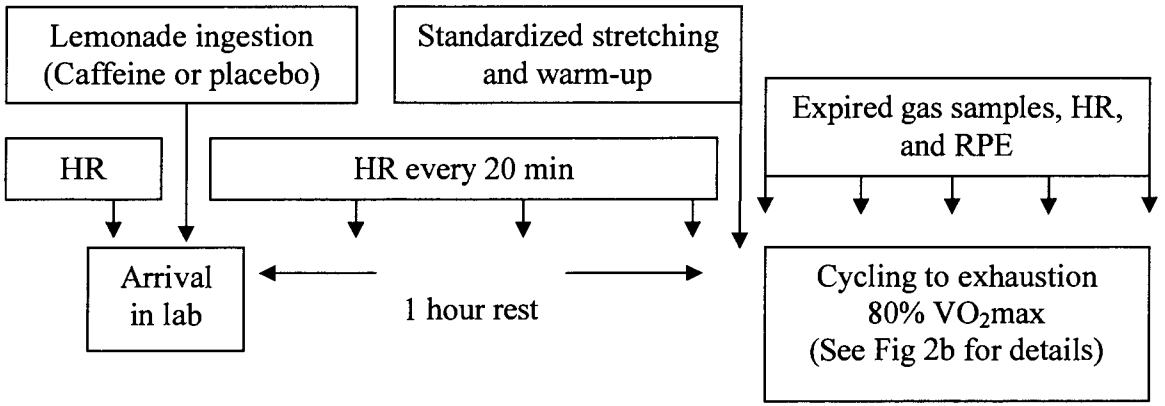
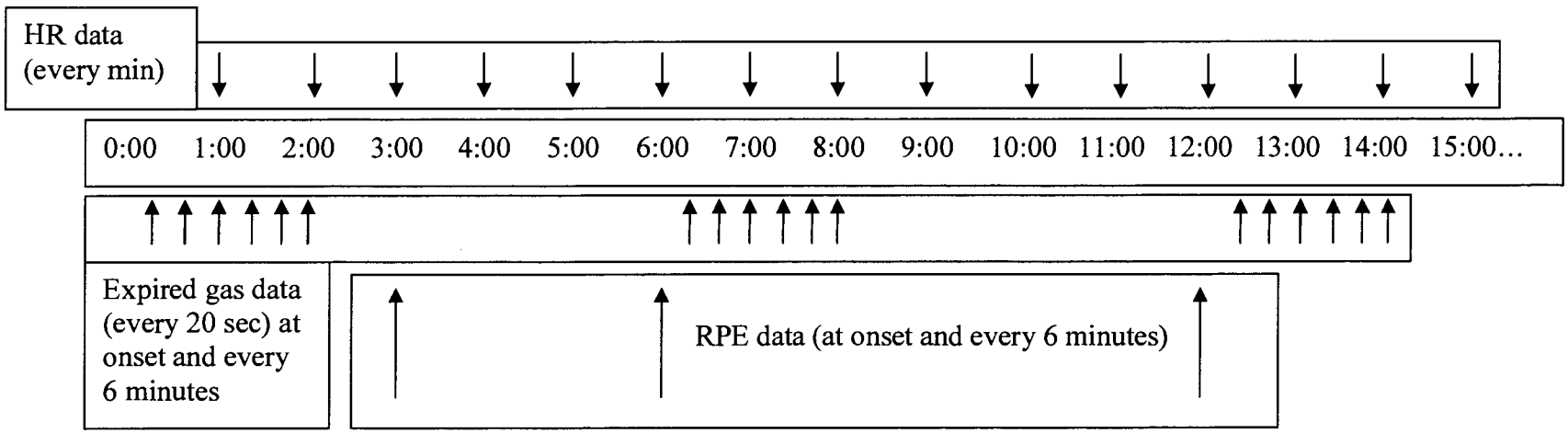


Figure 2b: Diagrammatic representation of experimental trial indicating timing of data collection.

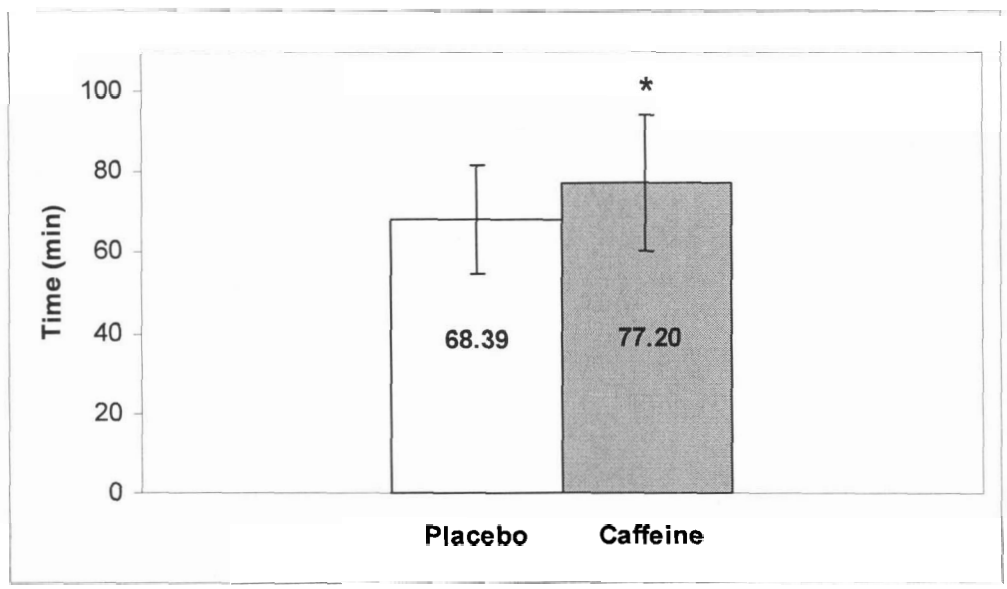


RESULTS

Time to exhaustion

As treatment order did not affect time to exhaustion, data from groups 1 and 2 were combined for all analyses. Figure 3 shows that cycling time to exhaustion following caffeine ingestion (77.2 (16.9) minutes) was significantly prolonged ($p = 0.031$) when compared to the placebo (68.4 (3.4) minutes). This equates to a 13.2 (16.3)% increase in exercise time. Table 2 provides exercise times, caffeine habituation, and oral contraceptive use of individual participants. Subjects varied in their habituation to caffeine (five of eight subjects were habitual consumers) and use of oral contraceptives (50% users). Subjectively, caffeine habituation did not appear to influence the ergogenic effect of caffeine, while it appeared that oral contraceptive use may have a negative effect on caffeine's ergogenic action. Figure 4 presents the mean exercise times of oral contraceptive users (subjects 1 – 4) and non-users (subjects 5 – 8). Although not statistically tested, after consuming caffeine, those not using oral contraceptives prolonged cycling time to exhaustion by 25.2%, while oral contraceptive users experienced virtually no change (note that subject 5 was an oral contraceptive user of only 2 months).

Figure 3: Mean (SD) time to exhaustion in placebo and caffeine treatments (n=8).

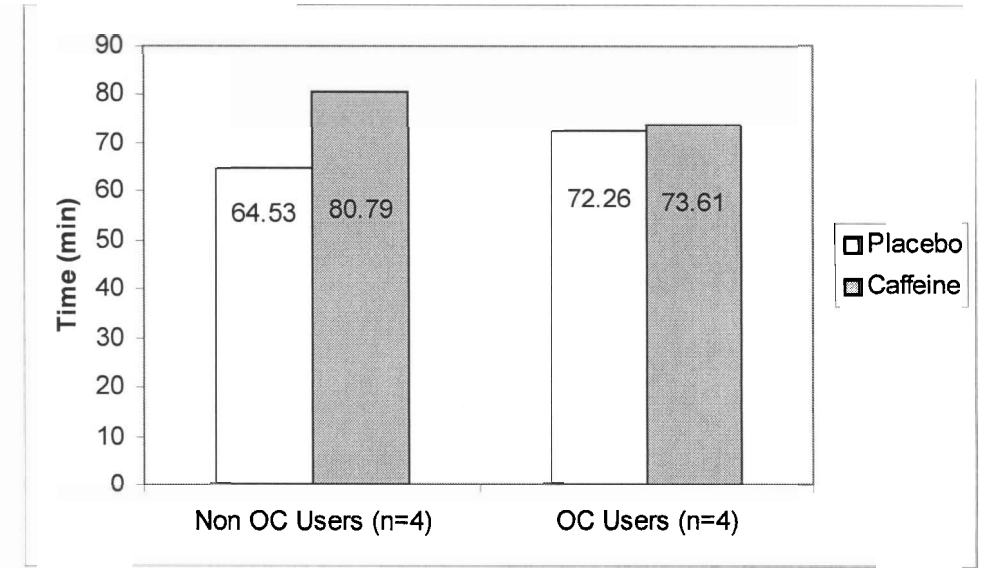


* Denotes statistically different results ($p<0.05$)

Table 2: Individual time to exhaustion in placebo and caffeine treatments with time difference, % change, caffeine habituation, and oral contraceptive (OC) use.

Subject	Group Membership (0=Placebo trial 1st; 1=Caffeine trial 1st)	Placebo (min)	Caffeine (min)	Time Difference (Caffeine – Placebo; min)	% Change	Caffeine Habituation (0=No;1=Yes)	OC Use (0=No; 1=Yes)
1	1	49.27	52.52	3.25	6.6	1	0
2	1	61.92	76.82	14.90	24.1	1	0
3	0	67.43	98.00	30.57	45.3	1	0
4	0	79.50	95.82	16.32	20.5	0	0
5	0	65.55	73.38	7.83	12.0	0	1
6	1	93.05	90.55	-2.50	-2.7	0	1
7	0	72.10	73.10	1.00	1.4	1	1
8	1	58.32	57.40	-0.92	-1.6	1	1
Mean (SD)	50% in each Group	68.39 (13.4)	77.20 (16.9)	8.80 (11.2)	13.2 (16.3)	62.5% Habitual consumers	50% OC Users

Figure 4: Mean times to exhaustion in placebo and caffeine treatments for oral contraceptive (OC) users and non-users.



Heart rate, VO_2, V_E , and RPE

The omnibus repeated measures analysis of variance between and across treatments demonstrated no significant effect of caffeine on heart rate, RPE, VO_2, and V_E throughout the exercise test (Table 3). The statistical analyses included only complete data sets, and therefore differ from the HR, RPE, VO_2, and V_E profiles presented in Figures 5-8, as these graphical representations include all available data. As described in *Data management and analyses for heart rate, RPE, VO_2, and V_E*, missing data in some percentile blocks of VO_2, V_E, and RPE profiles reduced the sample size at these points. Consequently, the sample size of some data points in these graphs varies (see note below figures), although the majority include all subjects.

Table 3: Sample size (n), F statistic, and p value of omnibus repeated measures analysis of variance between placebo and caffeine treatments for heart rate, RPE, VO_2, and V_E.

	Heart rate	RPE	VO_2	V_E
n	8	5	4	5
F statistic	2.481	3.896	0.168	2.418
p value	0.159	0.120	0.709	0.195

The heart rate profiles (Figure 5) of both treatments followed the S curve characteristic of cardiac drift. The caffeine test heart rate appeared to be slightly higher from the 30% block through to exhaustion, but did not reach significance. RPE (Figure 6) increased linearly with increasing time, with no difference between treatments. RPE data were not available at the 90% and 99% blocks, or at exhaustion, as subjects were breathing into the metabolic cart at this time and were unable to speak. As the test was to exhaustion and all subjects reported being unable to continue cycling, it could be inferred that RPE was greater than 9. VO_2 (Figure 7) rose sharply at the onset of exercise and remained steady until exhaustion in both treatments. While there was a tendency for oxygen consumption to be elevated throughout the caffeine test compared to the placebo, this difference was not significant. A sharp rise in V_E (Figure 8) followed by a relatively linear increase was observed for both treatments. V_E appeared to be higher during the caffeine trial, but again this difference did not reach statistical significance. Individual heart rate, VO_2, and V_E standardized raw data is presented in Appendix E.

Figure 5: Mean heart rate (n=8) at % blocks of total time to exhaustion in placebo and caffeine treatments.

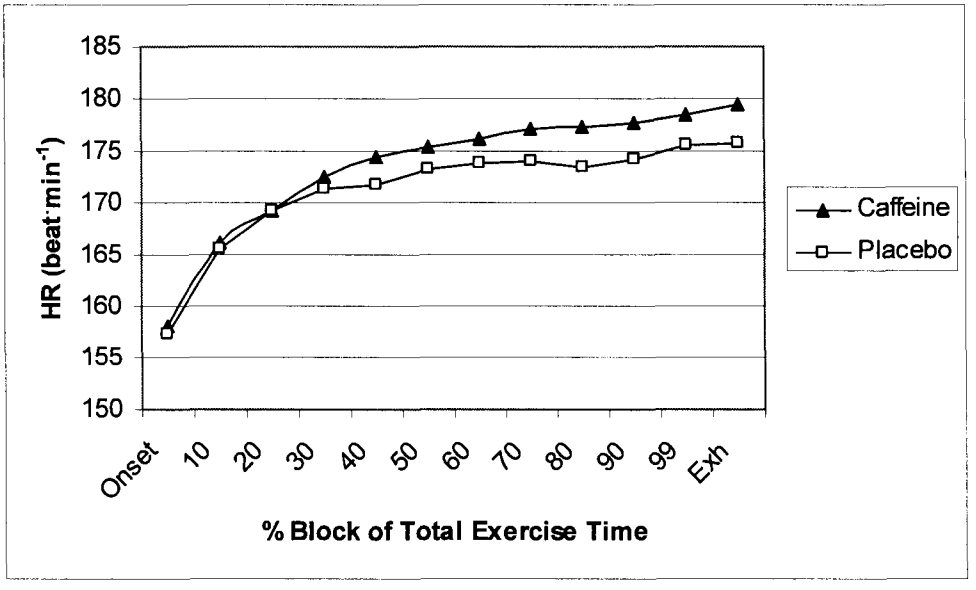
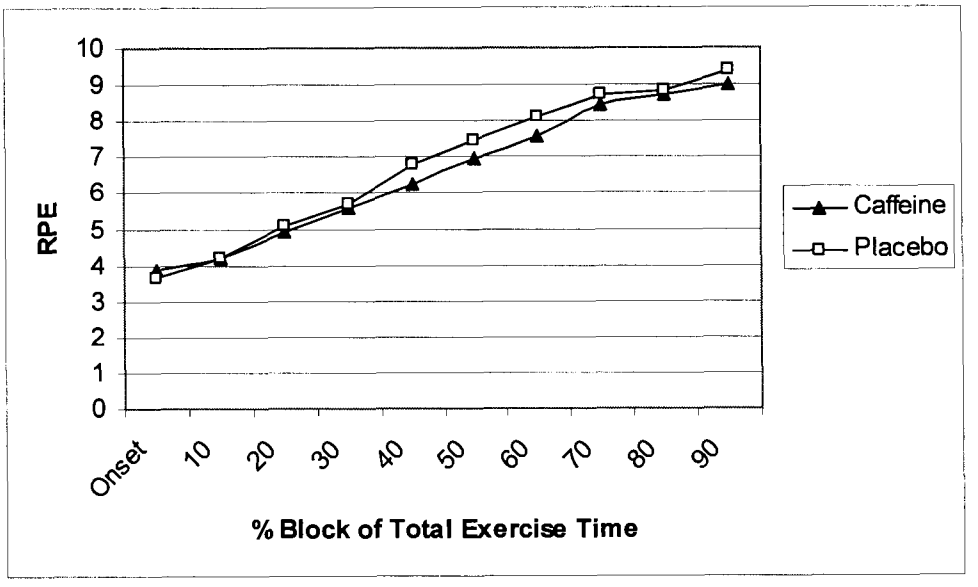
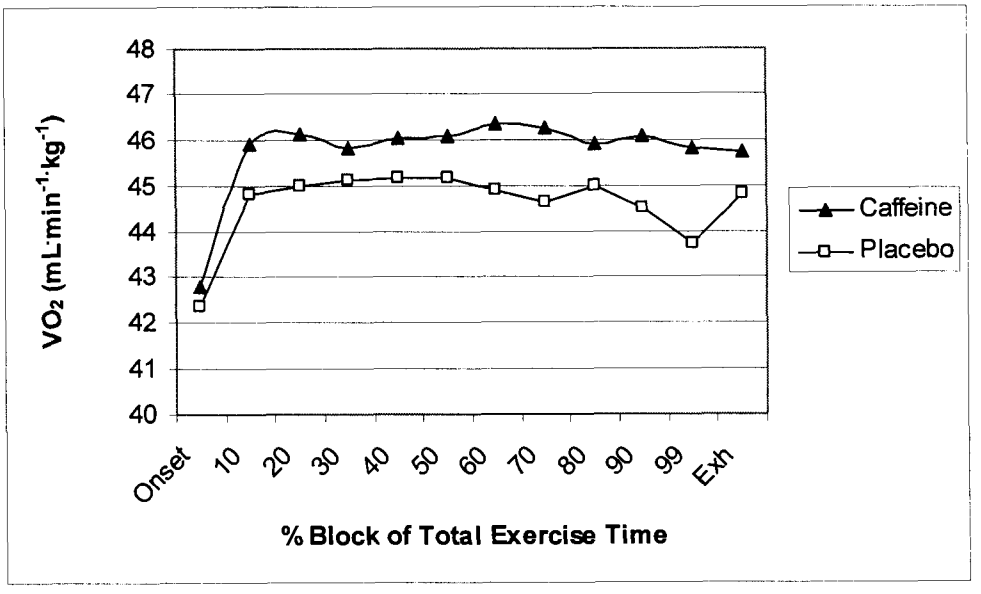


Figure 6: Mean (n=8*) RPE at % blocks of total time to exhaustion in placebo and caffeine treatments.



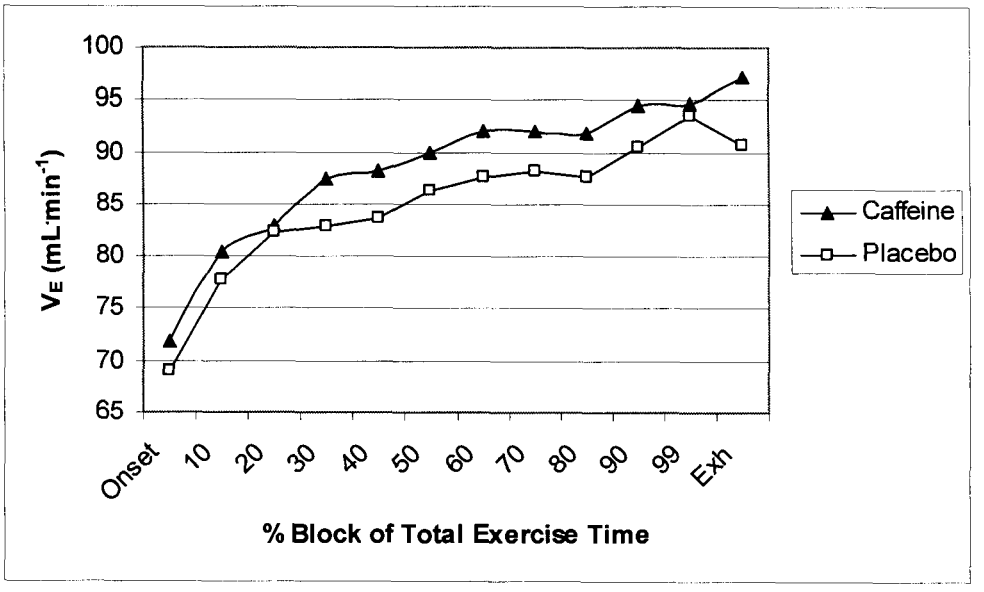
* Placebo: 10% n=7, 60% n=7, 90% n=7; Caffeine: 10% n=7, 80% n=7, 90% n=7

Figure 7: Mean (n=7*) VO_2 at % blocks of total time to exhaustion in placebo and caffeine treatments.



* Placebo: 10% n=6, 60% n=6, 90% n=6, 99% n=5; Caffeine: 10% n=6, 80% n=6

Figure 8: Mean (n=8*) V_E at % blocks of total time to exhaustion in placebo and caffeine treatments.



* Placebo: 10% n=7, 60% n=7, 90% n=7, 99% n=7; Caffeine: 10% n=7, 80% n=7

DISCUSSION

This is the first known study to report that caffeine can significantly enhance endurance exercise performance in women. In trained female cyclists, caffeine ingested one hour prior to cycling at 80% VO_2max prolonged time to exhaustion from 68.4 (13.4) minutes to 77.2 (16.9) minutes ($p<0.05$) (Figure 3). The results support the hypothesis that caffeine ingestion will prolong time to exhaustion in female athletes, although it appears that some women may not be as responsive as others. Caffeine did not significantly affect measures of metabolism or cardiorespiratory function (HR, VO_2, or V_E) or of perceived effort (RPE). Within the limitation of sample size, these preliminary results suggest that these variables are not central to the mechanism(s) through which caffeine enhances endurance exercise performance.

Time to exhaustion

In this study, female athletes tested during the follicular phase of the menstrual cycle showed a mean extension of time to exhaustion of 8.8 (11.2) minutes (13.2 (16.3)%) following caffeine ingestion (5 mg/kg). This result is similar to that of Butts and Crowell (1985), the only other study to report on the effect of caffeine on endurance performance in women. Butts and Crowell demonstrated a non-significant increase of 8.6 minutes (n=15 women; 14.4% over the placebo time of 59.9 (26.6) minutes) in time to exhaustion following caffeine ingestion (300 mg; approximately 4-6 mg/kg). The lack of significance in this result was likely due to a large variation in individual exercise times (reflected by large standard deviations).

This overall effect of caffeine in women is different from that reported in men. Both the present study and Butts and Crowell (1985) found 13-14% increases in time to exhaustion in women. Studies of men indicate 20% to 43% increases in time to exhaustion: placebo times of 24-75 minutes were extended by 5-15 minutes following caffeine ingestion of 3-6 mg/kg (see Review of Literature, Appendix A). This suggests that caffeine has a more potent effect to enhance endurance exercise in men. Caution should be exercised, however, in direct comparison of the results from various studies, as subject characteristics, testing protocols, and equipment differ. Furthermore, Butts and Crowell

(1985) found that the women in their study experienced a greater delay in fatigue than did their male counterparts (14.4% and 3.1%, respectively). A comparison of the effect of caffeine on well-matched men and women during endurance exercise is needed to clarify the role of sex on this ergogenic action.

Not all subjects in the present study exercised longer after consuming caffeine (Table 2). Following caffeine ingestion, four participants experienced improvements of 7.8 to 30.6 minutes (12 to 45%; subjects 1, 2, 3, 4, and 5), one improved by 3.2 minutes (6.6%; subject 1), and three experienced very little change (1.0 to -2.5 minutes; 1.4 to -2.7%; subjects 6, 7, and 8). Small sample sizes and unequal membership in sub-groups based on habitual caffeine consumption or oral contraceptive use prohibited the use of effective statistical analyses of the relationship between time to exhaustion and these variables. Subjectively, it appeared that the delay in fatigue following caffeine ingestion was influenced by the use of oral contraceptives.

Habitual caffeine consumption

Literature addressing the impact of caffeine habituation on the response to this drug during endurance exercise is sparse. Based on his observations of hundreds of subjects (primarily men) Graham (2001) speculated that caffeine non-users do not respond differently to caffeine during exercise, but are more susceptible to the negative effects of high ($\geq$ 9 mg/kg) doses (e.g., jitteriness, lack of focus). Recently, caffeine naïve individuals were found to experience a greater delay in fatigue which lasted longer than habitual consumers (Bell & McLellan, 2002). The results of the present study did not reveal any difference between these groups, although with only three caffeine naïve participants of eight who are divided in their use of oral contraceptives, it is difficult to interpret these findings. Investigation into the responses of caffeine users and non-users during endurance exercise will help to clarify the impact of habituation on caffeine's ergogenic effect. If coupled with information about the effect of chronic caffeine exposure on adenosine receptor number and post-receptor events, insight into caffeine's mechanism of action may also be gained.

Oral contraceptives

Both caffeine and estrogen are metabolized by the same enzymes in the liver (cytochrome P450). It was for this reason that the women in the present study were tested in the follicular phase of the menstrual cycle, when estrogen levels are at lower levels. The administration of ethinyl estradiol, an active component of oral contraceptives, is believed to inhibit caffeine metabolism, effectively impairing caffeine elimination (Balogh et al., 1991; Patwardham, Desmond, Johnson, & Schenker, 1980) and prolonging plasma half life (Rietveld, Broekman, Houben, Eskes, & van Rosum, 1984). Such effects could enhance the ergogenic action of caffeine by prolonging the length of exposure. The data of the present study do not support this speculation.

In the present study, the four subjects who were not using oral contraceptives (OC) cycled an average of 80.79 minutes following caffeine ingestion, a 25.2% increase over their average placebo time of 64.53 minutes (Figure 4). In contrast, three of the four OC users (Table 2) did not exercise longer under the influence of caffeine. It has been shown that the use of OC moderately prolongs the time to reach peak caffeine plasma concentration (Abernethy & Todd, 1985). This may account for the lack of response in OC users exercising only one hour post-ingestion as it may be that caffeine will provide ergogenic benefit to OC users if the exercise is conducted more than one hour post-ingestion. Another possibility is that the OC non-users of this study may have had higher estrogen levels than the OC users, and therefore experienced a greater effect than the OC users. Alternatively, the difference in response to caffeine during endurance performance observed between these two groups may be attributed solely to coincidence.

Three of the four OC users experienced virtually no change in time to exhaustion following caffeine ingestion. One OC non-user (subject 5) delayed fatigue by 7.8 minutes (12.0%). At the time of testing, this subject had completed only two cycles of OC, while the others had completed at least 12. If oral contraceptives alter women's physiology such that caffeine cannot confer ergogenic benefit, it may be that this alteration takes several OC-supported menstrual cycles to manifest. Statistically significant positive trends have been noted between the length of OC use and increases in both mean systolic blood

pressure levels (Yunis & Debert-Ribeiro, 1993) and serum triglycerides (Bloch, 1979). It could be hypothesized that a similar finding would be extended to a caffeine response. Further study of the effect of oral contraceptives on caffeine's ergogenic action is needed.

It should also be noted that subject 8, an OC user who did not demonstrate delayed fatigue after caffeine ingestion, was a mild asthmatic who used Advair prior to both exercise tests. This drug is a combination of flucticasone propionate, an anti-inflammatory glucocorticoid receptor agonist, and salmeterol xinafoate, a selective, long-acting $beta_2$-adrenergic bronchodilator (GlaxoSmithKline, 2003). Fluticasone propionate is metabolized by the cytochrome P450 enzymes and may therefore interfere with caffeine's pharmacokinetics. It is difficult to speculate on whether or not her lack of response to caffeine during exercise was associated with OC and Advair use alone or in combination. Further investigation is required to clarify how interactions between caffeine and other pharmaceuticals affect the physiological and performance effects of caffeine.

When only OC non-users are considered, the extension of exercise time following caffeine ingestion (25.2%) falls into the range of findings from the existing data for men (see Review of Literature, Appendix A). Again, differences in participant characteristics, testing protocols, and equipment preclude direct comparison with these previously reported findings. Sex differences in the metabolic and adrenergic responses to submaximal exercise could produce a sex difference in the response to caffeine during endurance exercise, if caffeine acts through one or both of these mechanisms. The similarity between the 25.2% increase in time to exhaustion observed in OC non-users of this study and the 20 to 43% reported for men following caffeine ingestion of similar dosages might therefore support the contention that caffeine does not act through such mechanisms. A well-controlled study of how sex influences caffeine's effect on endurance performance, plasma metabolites, and circulating hormones would add to our limited understanding of its mechanism of action.

Training Status

It has been suggested that training status may influence the ergogenicity of caffeine,

potentially due to differing responsiveness of trained tissues (e.g., adipose, nervous, or muscle) to this as-yet-unknown stimulus from caffeine, or to the mental discipline of athletes (Graham, 2001). Caffeine has been shown to increase the sprint performance (swimming speed) of trained but not of recreational swimmers (Collomp, Ahmaidi, Chatard, Audran, & Prefaut, 1992). There is no similar comparison of endurance exercise.

In the present study, participants were homogeneous with respect to the operational definition of training status. While the improvement in exercise capacity was similar to that reported by Butts and Crowell (1985), the latter was not significant, likely due to a large variation in exercise times (reflected by large standard deviations). The women of these two studies were of similar age, height, and weight, but differed in their maximal aerobic power, such that those of the present study were more highly trained (mean VO_2max of 56.1 $mL \cdot kg^{-1} \cdot min^{-1}$) compared to the subjects of Butts and Crowell (mean VO_2max of 47.9 $mL \cdot kg^{-1} \cdot min^{-1}$). This large variation in the individual results within Butts and Crowell's study supports the speculation that more highly trained individuals respond more predictably to caffeine (Graham, 2001). Differences in protocols and equipment employed in the two studies, and the lack of control for potentially confounding factors, including caffeine habituation and oral contraceptive use, impede direct comparison and further studies are required to test this hypothesis.

Exercise Intensity

A potentially important aspect of the research investigating the effect of caffeine on endurance performance is that exercise intensity has typically been set relative to VO_2max. At the most commonly employed exercise intensity of 80% VO_2max, subjects could be exercising below, at, or above their anaerobic threshold. Consequently, they may differ greatly in their exercise metabolism, as energy supply may be derived from either aerobic or anaerobic systems. Should caffeine exert its ergogenic effect through metabolic actions, such a discrepancy may have a significant impact on experimental results. In the present investigation, anaerobic threshold was estimated from ventilatory threshold during the VO_2max test (Table 1). From this calculation, it is estimated that all subjects were working within 3% of their anaerobic threshold. The results of this study therefore do not

provide enough information to discuss the effect of exercise intensity on the ergogenic action of caffeine and more research is needed to investigate this query.

Heart rate, RPE, VO_2, and V_E

Caffeine ingestion did not have a significant effect on heart rate, RPE, VO_2 or V_E during exercise. This is consistent with data from Butts and Crowell (1985), although their results may have been moderated by the decaffeinated coffee in which their caffeine was administered. Some research employing male subjects has found that heart rate and VO_2 are unchanged by caffeine (Bell & McLellan, 2003; Costill et al., 1978; Graham, Helge, MacLean, Kiens, & Richter, 2000; Roy, Bosman, & Tarnopolsky, 2001), while VO_2 was reported to be slightly but significantly elevated in two studies (Bell & McLellan, 2002, 2003). RPE has consistently been reported to be lowered by caffeine in studies employing male participants (Bell & McLellan, 2002, 2003; Costill et al., 1978; Denadai & Denadai, 1998; Jacobson, Febbraio, Arkinstall, & Hawley, 2001). V_E is typically not reported, but has been elevated during exercise following caffeine ingestion (Jacobson et al., 2001; Spriet et al., 1992).

The sparse and variable nature of these findings make it difficult to interpret these results. In the present study, the lack of caffeine effect on heart rate, RPE, VO_2, and V_E suggests that the rate of metabolism, cardiorespiratory function, and the perception of effort are not central to caffeine's mechanism of action in women. However, the small sample size in this study may have masked any caffeine effect on these measures. Further studies with a greater number of subjects are needed to confirm these results.

Caffeine's mechanism of action during endurance exercise may be associated with the central nervous system. This speculation is in part supported by the theory that the development of fatigue during endurance exercise is mediated through the CNS (Lepers, Maffiuletti, Rochette, Brugniaux, & Millet, 2002; St Clair Gibson et al., 2003; St Clair Gibson, Lambert, & Noakes, 2001). St Clair Gibson et al. (2001, 2003) describe fatigue as "the conscious awareness of changes in subconscious homeostatic control systems" that results in inhibited efferent neural command. The origin(s) of this sensation have yet

to be localized to particular CNS structures, but are thought to lie in command centres "upstream" of the motor cortex. Thus, the role of caffeine to enhance exercise performance may lie, at least in part, in its central effects to inhibit fatigue.

Application to sport performance

It is recognized that endurance athletes typically race to cover a set distance faster, rather than to cover the most distance possible prior to ceasing due to fatigue. The total time to exhaustion protocol employed in the present study, as well as the majority of existing literature, provides a measure of fatigue and is valuable when attempting to ascertain the mechanism(s) responsible for an ergogenic effect. Time trials, on the other hand, give a much better indication of how a supplement, such as caffeine, will affect the performance of an athlete in a specific competitive event.

The results from this study show that fatigue can be delayed in of female athletes cycling at 80% VO_2max following caffeine ingestion. This information does not indicate that time trial performance would be improved in women ingesting caffeine before a competition. It could be valuable from a training perspective as physiological benefits may be gained from cardiorespiratory, skeletal muscle, or connective tissue adaptations to prolonged time at elevated training intensities. It could also be hypothesized that caffeine may improve competitive performance by allowing athletes to exercise at an intensity that, without caffeine, would induce fatigue before completion of the race. A comparison of caffeine's effect on performance at different intensities is necessary to fully support this contention.

The findings of this investigation are limited to trained cyclists exercising during the follicular phase of the menstrual cycle. They provide the basis for further research into the effect of caffeine on endurance performance in a broader population. Such research will offer information that will improve the ability for all women to make informed choices about the use of caffeine in training and sport.

DIRECTIONS FOR FUTURE RESEARCH

This study provides evidence that trained female cyclists are responsive to caffeine during endurance exercise. It appears that some women, possibly oral contraceptive users, may not experience as great an effect from caffeine as other women. Future research should attempt to ascertain what factors modulate this ergogenic action, such as: training status, exercise intensity relative to AT, caffeine habituation, use of oral contraceptives, phase of the menstrual cycle, menopausal status, and hormone replacement therapy. Research of this type is important because it begins to remedy the distinct lack of literature investigating the female response in the area of muscle metabolism, nutrition, and exercise physiology. It will also provide further scientific evidence of caffeine's influence on endurance in women.

To make this type of study more applicable to sport performance, the effect of caffeine in a fixed distance test, such as a time trial, should also be studied. From an ethical perspective, future research should also aim to determine what urinary concentrations are sufficient to enhance performance, so that sport governing bodies may establish appropriate limits, should such limits be deemed necessary. In addition, a comprehensive comparison of the effect of caffeine on well-matched men and women should be undertaken. Caffeine, if studied in conjunction with metabolites and hormones, may prove to be an effective vehicle to research sex differences in metabolism, including the hepatic P450 system, adenosine receptors, and regulation of lipolysis.

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APPENDIX A: REVIEW OF LITERATURE

This literature review describes general background relevant to the research and a detailed review of primary literature related to studies of caffeine and exercise performance in humans.

SECTION 1: BACKGROUND

Caffeine

Caffeine is a naturally occurring plant alkaloid that is present in many beverages and foods, including coffee, tea, cola and chocolate, as well as over-the-counter stimulants and analgesics. Purported to enhance endurance performance, this drug is frequently consumed by athletes seeking to improve their training or competitive results (Delbeke & Debachere, 1984; Martin, Roussos, Perry, & Salzwedel, 1997).

Disposition and mode of action

Early work investigating potential ergogenic aids clearly demonstrated that cycling time to exhaustion was increased (Costill, Dalsky, & Fink, 1978) and that more work could be performed (Ivy, Costill, Fink, & Lower, 1979) following caffeine ingestion. This effect was attributed to methylxanthine-induced increases in circulating epinephrine as well as enhanced (FFA) mobilization and lipolysis. Caffeine was therefore thought to contribute to glycogen sparing at the muscle, thus delaying fatigue (Essig, Costill, & Van Handel, 1980). This original theory is not consistent with many of the findings from more recent research examining the metabolic and physiological effects of caffeine during endurance exercise. Plasma substrate and metabolite levels may not accurately reflect intramuscular levels and, although muscle substrate usage has been reported infrequently in this literature, findings appear to indicate that carbohydrate and fat metabolism are not altered by caffeine ingestion (Graham, Helge, MacLean, Kiens, & Richter, 2000; Greer, Friars, & Graham, 2000).

Caffeine is absorbed readily from mucosal membranes (e.g., intestine, nasal passages). Following oral ingestion, peak plasma concentrations are reached within 15 to 120 minutes. It is metabolized by the liver and cleared by the kidneys, with a half-life of three

to 10 hours in adult humans (Robertson, Wade, Workman, Woosley, & Oates, 1981). Caffeine is metabolized through the hepatic cytochrome P450 system from a trimethylxanthine structure to three methylxanthines—paraxanthine, theophylline and theobromine—all of which have biochemical activity.

The methylxanthines are structurally similar to adenosine and have demonstrated non-selective antagonism at two subtypes (A_1 and A_2) of adenosine receptors (Daly, Bruns, & Snyder, 1981; Zhang & Wells, 1990). The A_1 adenosine receptor subtype is primarily associated with *inhibition* of adenylyl (adenylate) cyclase activity and to increased cellular cyclic adenosine monophosphate (cAMP) levels. As such, antagonism by caffeine at A_1 receptors in white adipocytes, brain, heart, and kidney, leads to disinhibition of adenylate cyclase and to a rise in cAMP. This may modulate one or more of the many cAMP-dependent effects on cellular metabolism. The A_2 receptor subtype is coupled to *stimulation* of adenylyl cyclase activity and to increased cAMP levels. In tissues having A_2 adenosine receptors (e.g., brain, platelets, liver, smooth muscle), therefore, antagonism by caffeine blocks this stimulation, leading to a drop in cAMP levels (Graham, 1997) and to modulation of cAMP-mediated cellular functions. At present, at physiological caffeine concentrations, antagonism of adenosine receptor action and consequent effects on cAMP is proposed as the only important mode of action during exercise (Graham, 2001).

Effects on Substrate Metabolism

Glycogen, Glucose and Lactate

Literature reporting blood glucose and lactate levels following caffeine ingestion is also equivocal. During exercise, some report elevations in both glucose and lactate (Bell & McLellan, 2003; Cox et al., 2002; Graham et al., 2000; Kovacs, Stegen, & Brouns, 1998) while another observed significantly higher glucose and lactate levels only at exhaustion (Greer et al., 2000). Others have demonstrated raised lactate but not glucose levels (Cadarette, Levine, Berube, Posner, & Evans, 1983; Cole et al., 1996; Graham, Hibbert, & Sathasivam, 1998; Graham & Spriet, 1991; Roy, Bosman, & Tarnopolsky, 2001) as well as the converse (Denadai & Denadai, 1998; Greer et al., 2000). Few studies have

reported that neither glucose nor lactate are elevated (Jacobson, Febbraio, Arkinstall, & Hawley, 2001; van Soeren, Sathasivam, Spriet, & Graham, 1993). One study that did not find an increase in lactate did not investigate glucose levels (Hunter, St. Clair Gibson, Collins, Lambert, & Noakes, 2002), while several others have reported no change (Cox et al., 2002; Jacobson et al., 2001; Mohr, van Soeren, Graham, & Kjaer, 1998; van Soeren, Mohr, Kjaer, & Graham, 1996).

There is little evidence that caffeine alters substrate use to preserve muscle glycogen and consequently to delay the onset of fatigue during endurance exercise. Caffeine has been reported to enhance exercise performance under other conditions, such as short-term high intensity exercise, in which the duration of the test dictated that glycogen sparing would not be of ergogenic benefit. MacIntosh and Wright (MacIntosh & Wright, 1995) established that a 6.0 mg/kg dose of caffeine resulted in a significant reduction in 1500-m swim time. It is unlikely that glycogen supply was a limiting factor, as the test lasted less than 25 minutes.

Caffeine has also demonstrated ergogenicity during intense cycling lasting only four to six minutes (Jackman, Wendling, Friars, & Graham, 1996). This study showed that the net reduction in muscle glycogen did not differ between control and caffeine groups and that glycogen depletion was not associated with fatigue. Although unclear at this time, an alternate mechanism must exist for caffeine's effect to facilitate improvements in both short term and endurance exercise.

Free Fatty Acids and Glycerol

As detailed above, muscle metabolism depends primarily on oxidation of fatty acids during aerobic endurance exercise. Caffeine ingestion alone appears to lead to a rise in FFA levels, but studies of the interaction of caffeine with FFA in exercise are equivocal. Some report caffeine-associated increases in FFA only at rest (Casal & Leon, 1985; Graham & Spriet, 1995), others have observed this both at rest and early during exercise (Cole et al., 1996; Graham et al., 2000; Pasman, van Baak, Jeukendrup, & de Haan, 1995) and still others noted the rise in FFA only during exercise (Cadarette et al., 1983;

Cox et al., 2002; Jacobson et al., 2001). In contrast, several studies failed to show any caffeine effect on FFA levels at all (Bell & McLellan, 2002; Denadai & Denadai, 1998; Graham & Spriet, 1991; Greer et al., 2000; Hunter et al., 2002). Elevated FFA levels have been noted in the absence of an increase in epinephrine (Mohr et al., 1998; van Soeren et al., 1996) as well as in the presence of propanolol, an epinephrine antagonist (van Baak & Saris, 2000). Significant improvements in endurance capacity have occurred without any increase in FFA at rest or during exercise (Bell & McLellan, 2003; Denadai & Denadai, 1998; Graham & Spriet, 1991; Greer et al., 2000). Evidence that working muscle is able to use the additional FFA does not exist at this time (to my knowledge).

The reason for the discrepancies among these findings is unclear, but may be related to methodologies and, particularly, to caffeine dosages. For example, Graham and Spriet (1995) showed that FFA levels were increased at rest when caffeine was ingested at 9.0 mg/kg, but not at either 3.0 or 6.0 mg/kg. This finding supports the hypothesis that the FFA response to caffeine—at rest or during exercise—may be dose-dependent, although there is no detailed report to confirm this.

Most studies have shown an elevation of glycerol following caffeine ingestion; however, a few have reported no change in glycerol levels following caffeine intake (Graham et al., 1998; Jacobson et al., 2001; Mohr et al., 1998). In relation to activity levels, studies have reported increases at rest (Graham et al., 2000; van Soeren et al., 1996; van Soeren et al., 1993), both at rest and during exercise (Cole et al., 1996; Graham & Spriet, 1991, 1995; Greer et al., 2000; Kovacs et al., 1998; Pasman et al., 1995), and during exercise alone (Cox et al., 2002; Greer et al., 2000).

Physiological Effects

Overall metabolic rate

Most studies have not reported a caffeine effect on the respiratory exchange ratio (reflecting changes in substrate oxidation) (Bell & McLellan, 2003; Butts & Crowell, 1985; Cadarette et al., 1983; Cole et al., 1996; Cox et al., 2002; Graham et al., 2000; Graham & Spriet, 1991, 1995; Greer et al., 2000; Jacobson et al., 2001; van Soeren et al.,

1993). Most of these studies also reported no caffeine effect on VO_2 (Cadarette et al., 1983; Costill et al., 1978; Graham et al., 2000; Graham & Spriet, 1991; Jacobson et al., 2001; Mohr et al., 1998; van Soeren et al., 1993). Only two have observed a slight elevation in VO_2 following caffeine ingestion (Bell & McLellan, 2002, 2003). These results suggest that alteration of the overall metabolic rate is not central to caffeine's ability to delay fatigue.

Circulating catecholamines

Circulating epinephrine levels are consistently elevated in response to caffeine ingestion. Research has demonstrated increases in plasma epinephrine levels of approximately two-fold both at rest and during exercise, following ingestion of 4.45 to 9.0 mg/kg caffeine (Graham et al., 2000; Graham et al., 1998; Graham & Spriet, 1991; Greer et al., 2000; Spriet et al., 1992). Interestingly, a comparison of caffeine users and nonusers showed that epinephrine was elevated at rest only in caffeine naïve participants, although the exercising epinephrine levels were similar for both groups (van Soeren et al., 1993). Subjects were exercising at 50% VO_2max, and the significance of this at higher intensities is not clear.

Caffeine has also elicited an ergogenic effect without a concomitant rise in epinephrine. In a dose-response study, circulating epinephrine levels were elevated with caffeine doses of 6.0 and 9.0 mg/kg, while fatigue was delayed only at 3.0 and 6.0 mg/kg (Graham & Spriet, 1995). Research employing spinal cord injured subjects with impaired epinephrine responses has shown that caffeine does not elevate epinephrine at rest (van Soeren et al., 1996) or during exercise, where fatigue was significantly delayed during functional stimulation of the paralyzed limb (Mohr et al., 1998). Furthermore, although not statistically significant, caffeine delayed fatigue by 38% when ingested in combination with propanolol, a β-adrenergic receptor blocker (van Baak & Saris, 2000). It is therefore plausible that caffeine acts directly on adipose and other potentially relevant tissues by actions that are not mediated by plasma epinephrine.

Sex Differences

Only two studies have reported caffeine-induced metabolic changes during exercise in women. In a comparison of 4 men and 4 women during exercise to exhaustion, it was demonstrated that the post-exercise FFA and glycerol levels were higher in women, while post-exercise lactate levels were higher in men (Cadarette et al., 1983). This suggests that triglycerides were the primary substrate in women whereas glycogen/glucose was the primary substrate in men.

During steady state running at 75% VO_2max, a study of six women who habitually consumed caffeine demonstrated unchanged lactate but elevated FFA levels at rest and early during exercise as well as a lowered RER early in exercise (Fisher, McMurray, Berry, Mar, & Forsythe, 1986). These changes occurred only after a four day withdrawal from caffeine and were not noted when the same subjects abstained from caffeine consumption only six hours before the test.

The data from these two studies appear to be consistent with the expected sex differences during submaximal exercise: women demonstrate greater lipid oxidation and glycogen sparing (Tarnopolsky, MacDougall, Atkinson, Tarnopolsky, & Sutton, 1990; Tarnopolsky, Atkinson, Phillips, & MacDougall, 1995). They do not, however, support the theory that caffeine alters metabolism during endurance exercise.

Central Nervous System

Caffeine has also been implicated in the improvement of endurance performance by lowering the perceived rating of exertion through a direct action on the central nervous system (CNS) (Bell & McLellan, 2002, 2003; Cole et al., 1996; Cox et al., 2002; Denadai & Denadai, 1998; Jacobson et al., 2001; van Baak & Saris, 2000). However, few well-controlled studies exist to support this theory (Tarnopolsky, 1994). Ergogenic effects have been demonstrated during stimulation of tetraplegic limbs, in which exercise occurs in the absence of conscious thought (Mohr et al., 1998). These results suggest that an altered perception of exertion is not the critical mechanism to the ergogenic effect caffeine has on performance.

A wide range of neural pathways within the CNS, including cardiovascular regulation, endocrine secretion and sympathetic activity, are sensitive to methylxanthines, making caffeine's potential effects very complex (Graham, 1997). Furthermore, the role of adenosine receptors in skeletal muscle, where caffeine's action could be the most relevant, has yet to be clarified, and more detailed research is needed to identify the neural paths most impacted by caffeine's action during endurance exercise.

In summary, it appears that caffeine's effect to improve exercise performance is not related to primary effects on substrate availability or metabolic rate, or simply on CNS stimulation, but rather to a complex interaction of central and peripheral effects. There is not yet sufficient evidence to determine whether there are differential effects in women and men.

Fatigue

Fatigue, defined as the decrease in force production, or inability to regenerate original force accompanied by an increased perception of effort, may be mediated by peripheral (action potential failure, excitation-contraction-coupling failure, or impairment of cross-bridge cycling) or central (decreased neural drive or motor command) mechanisms (St Clair Gibson, Lambert, & Noakes, 2001). During submaximal exercise, fatigue may be the result of substrate depletion, energy compound depletion, or intramuscular factors including acidity, functional changes within the sarcoplasmic reticulum, or altered Na^+/K^+ ATPase pump activity, but no conclusive evidence links any single peripheral factor (e.g., metabolite accumulation, substrate depletion, or cardiorespiratory limitations) directly or exclusively to either the development of fatigue (Fitts, 1994; Noakes, 2000; Spriet, Soderland, Bergstrom, & Hultman, 1987) or the perception of exertion (Hampson, St Clair Gibson, Lambert, & Noakes, 2001).

It is therefore hypothesized that central governing processes regulate skeletal muscle contractions (St Clair Gibson et al., 2003; St Clair Gibson et al., 2001), especially at the end of prolonged cycling (Lepers, Maffiuletti, Rochette, Brugniaux, & Millet, 2002). St Clair Gibson and colleagues (2001, 2003) have suggested that a number of afferent

inputs, together with non-sensory factors such as motivation, are integrated in the brain and lead to the development of the sensation of fatigue. They have therefore redefined fatigue as the conscious awareness of changes in subconscious homeostatic control mechanisms. The pathways involved in this neuromuscular regulation have yet to be identified, but if found to overlap with those influenced by caffeine during endurance exercise (also yet to be identified), may shed light on its elusive mechanisms of both fatigue and caffeine.

SECTION 2: CAFFEINE AND EXERCISE

Time to Exhaustion

Early work demonstrated that 330 mg of caffeine (approximately 4.7 mg/kg) prolonged cycling at 80% VO_2max by 19.5% over the placebo time of 75.5 minutes (Costill et al., 1978). Many subsequent studies have shown that, at intensities of 80 to 85% VO_2max, caffeine administered at dosages of 4.45 to 13.0 mg/kg one hour before exercise can delay fatigue by 20 to 50% during bouts of both running (Graham et al., 1998; Sasaki, Takaoka, & Ishiko, 1987) and cycling (Denadai & Denadai, 1998; Greer et al., 2000; Spriet et al., 1992) to exhaustion for cycling (Table 1) and running (Table 2).

In a well controlled study testing caffeine during both running and cycling, this improvement was shown to be independent of modality (Graham & Spriet, 1991). Two studies demonstrated that caffeine's ergogenic effect during endurance exercise is also independent of dosage, as fatigue was delayed by 22% at both 3.0 and 6.0 mg/kg (Graham & Spriet, 1995) and by 27% at 5.0, 9.0 and 13.0 mg/kg (Pasman et al., 1995). Recently, it was reported that this effect is maintained for up to six hours, such that exercise performed one, three, and six hours post-ingestion is prolonged by an average of 20% relative to the placebo condition (Bell & McLellan, 2002). This group also showed that fatigue is delayed in a subsequent cycle to exhaustion five hours after ingestion (four hours after initial exercise) and that re-dosing with 2.5 mg/kg one hour before the second bout of exercise preserves, but is not necessary for, the ergogenic effect (Bell & McLellan, 2003).

Table 1: Summary of literature investigating the effect of caffeine on time to exhaustion during high intensity endurance cycling.

Authors	Intensity (% VO_2max)	Subjects	Dose (mg/kg)	Performance Results (% improvement / placebo time)	Conclusions / Comments
Cycling					
Bell & McLellan (2003)	80%	9M, Healthy	AM: 5.0 PM: additional redosing of 2.5	Overall: 31.3% / 18 min	Caffeine significantly delayed fatigue; effect was maintained 5h post-ingestion during subsequent cycle to exhaustion; redosing preserved effect, but was not necessary.
Bell & McLellan (2002)	80%	15M, 8F, Active	5.0	Nonusers: 1h: 35% / 24.2 min; 3h: 24% / 25.8 min; 6h: 36% / 23.2 min; Users: 1h: 17% / 23.3 min; 3h: 21% / 23.2min; 6h: 4% / 23.5 min; Overall:20% / 24.0 min	Caffeine significantly delayed fatigue; effect was greater and longer in nonusers.
Greer et al. (2000)	80%	8M, Active	6.0	22% / 33 min	Caffeine significantly prolonged time to exhaustion.
Denadi et al. (1998)	10% above and below AT	8M, Untrained	5.0	Below AT: 43.5% / 32 min; Above AT: 3.9% / 19 min	Caffeine significantly delayed fatigue below but not above AT.
Pasman et al. (1995)	80% Wmax*	9M, Highly trained	5.0, 9.0, 13.0	27% / 47 min	Caffeine significantly delayed fatigue; effect was independent of dose.
Spriet et al. (1992)	80%	8M, Well trained	9.0	27% / 76 min	Caffeine significantly prolonged endurance exercise.
Graham & Spriet (1991)	85%	6M, 1F, Well trained	9.0	44% / 39 min	Caffeine significantly prolonged endurance exercise; effect was independent of modality.
Butts & Crowell (1985)	75%	13M, 15F, Active	300 mg (Men: ~3.3-5.0; Women: ~ 4.0-6.0 mg/kg)	Men: 3.1% / 68 min; Women: 14.4% / 60 min	Non- Significant findings; only research to report gender-specific performance results.
Costill et al. (1978)	80%	7M, 2F, Well trained	330 mg (~4.7 mg/kg)	19.5% / 75 min	Caffeine significantly prolonged endurance exercise.

* Intensity set relative to subjects' maximum power output

Table 2: Summary of literature investigating the effect of caffeine on time to exhaustion during high intensity endurance running.

Authors	Intensity (% VO_2max)	Subjects	Dose (mg/kg)	Performance Results (% improvement / placebo time)	Conclusions / Comments
Running					
Graham et al. (1998)	85%	**8M, 1F, Trained**	4.45	31% / 32 min	Caffeine significantly prolonged endurance exercise; moderating **component exists in** coffee.
Graham & Spriet (1995)	85%	8M, Well trained	3.0, 6.0, 9.0	3 & 6 mg/kg: 22%; 9 mg/kg: 11% (not significant) / 49 min	Caffeine was effective at low but not high doses.
Graham & Spriet (1991)	85%	6M, 1F, Well trained	9.0	51% / 49 min	Caffeine significantly prolonged endurance exercise; effect was independent of modality.
Sasaki et al. (1987)	80%	5M, Trained	6.6	33% / 39 min	Caffeine added to sucrose did not further improve performance.
Cadarette et al. (1983)	80%	4M, 4F, Healthy	L: 2.2 M: 4.4 H: 8.8	M dose: 37.4% / 53 min	Non-significant findings; improvement seen for the group was due primarily to a single female subject who extended her exercise time by nearly 50%.

Time Trial Performance

Investigations into the effect of caffeine on total time to exhaustion are prevalent in caffeine research but do not simulate competitive events, the majority of which are races over a set distance. Time trial experiments more accurately reflect real-life events but have provided more variable results about the effect of caffeine on endurance performance (Table 3).

Table 3: Summary of literature investigating the effect of caffeine on time trial performance.

Authors	Intensity	Subjects	Dose (mg/kg)	Placebo (min)	Improve't (%)	Conclusions / Comments
Significant Results						
Cox et al. (2002)	120 min @ 70%, TT @ 7kJ/kg (cycling)	12M, Highly trained	6.0; 1.0 x 6	29.18	3%	Caffeine enhanced TT independent of timing of intake.
Kovacs et al. (1998)	Set amt of work equiv to ~ 1hr at 70% Wmax (cycling)	15M(?), Trained	150, 225, 320 mg in 7% CES	Water: 62.5; CES: 61.5	225 & 320 mg: 4.4% over CES; 150 mg: 3.4%over water	Caffeine added to CES improves 1 hr TT performance in well-trained athletes; enhancement is not dose-dependent.
Berglund & Hemmingsson (1982)	21 km (XC skiing)	14M(?), Well trained	6.0	~80	Low altitude: 1.7% High altitude: 3.18%	Caffeine can improve performance during 21 km XC skiing at low and even more at high altitudes.
Non-significant Results						
Conway et al. (2003)	90 min @ 68%, TT @ 80% (cycling)	9M, Trained	6.0; 3.0 x 2	28.3	19%	Improvement statistically insignificant, but could be substantial in a race situation.
Hunter et al. (2002)	100 km TT with bouts of 1 and 4 km sprints (cycling)	8M, Highly trained	6.0 with 0.33 every 15 mins during trial in 7% CHO	~150	1.3%	Total time and average power not changed by caffeine ingestion or 7% CHO ingestion.
Jacobson et al. (2000)	120 min @ 70%, TT @ 7kJ/kg (cycling)	8M, Highly trained	6.0 with 2.6 g/kg CHO or 1.2 g/kg FAT	CHO: 30.37; FAT: 33.02	CHO sig faster that FAT; No CAF effect (4.3% CHO)	Caffeine co-ingested with either CHO or FAT has no additive effect on exercise performance.
Cohen et al. (1996)	21 km (running)	5M, 2F, Well trained	5 and 9 mg/kg		Within 1.1%	No effect during 21 km outdoor footrace in hot and humid conditions.

Following ingestion of 6.0 mg/kg caffeine, statistically significant improvements of 1.7% have been reported in cross-country skiing (Berglund & Hemmingsson, 1982) and 3.2% in cycling time trials (performed after 120 minutes of cycling at 70% VO_2max) (Cox et al., 2002), lasting approximately 80 and 30 minutes, respectively. In another cycling time trial lasting roughly one hour, 225 and 320 mg/L of caffeine (approximately 1.8 and 2.6 mg/kg, respectively) added to a 7% carbohydrate-electrolyte solution (CES) also produced improvements of 4.4% over CES alone, and 150 mg/L caffeine (approximately 1.2 mg/kg) in CES produced an improvement of 3.4% over water (Kovacs et al., 1998).

Four time trial experiments did not yield statistically significant results. After cycling at 68% VO_2max for 90 minutes, athletes performed a time trial at 80% VO_2max 4.5 minutes faster than the placebo time of 28.3 minutes following caffeine ingestion of 6 mg/kg (Conway, Orr, & Stannard, 2003). Although not statistically significant, the researchers noted that this result would be substantial in competition. A study examining five male and two female athletes running in high heat and humidity failed to show any improvement over 21 km following caffeine ingestion of either 5.0 or 9.0 mg/kg (Cohen et al., 1996). This may suggest that the benefits of caffeine do not outweigh the negative influences of the environment.

Cyclists performing 100 km rides demonstrated only slightly faster times (1.3%) over 150 minutes after caffeine ingestion of 6.0 mg/kg in 7% carbohydrate solution before exercise with 0.33 mg/kg every 15 minutes during the trial (Hunter et al., 2002). A centrally regulated pacing strategy that was unaffected by caffeine was proposed to explain these results. Interestingly, athletes in this study experienced the fastest trial during the familiarization session when they were permitted their own drinks *ad libitum*. The authors did not offer an explanation for this finding, but the subjects' pacing strategy may have been more conservative when performing the tests with novel protocols.

It has also been shown that caffeine, ingested with 2.6 g/kg carbohydrate before 120 minutes of cycling at 70% VO_2max followed by a time trial of approximately 30 minutes, did not provide any additive effect on performance when compared with carbohydrate

ingestion alone (Jacobson et al., 2001). This is in agreement with the work of Hunter et al. (2002), as well as Sasaki et al (Sasaki et al., 1987), who demonstrated that caffeine did not further improve time to exhaustion with a carbohydrate solution. Kovacs et al. (1998) reported that caffeine ingested with a CES did significantly enhance the time trial performance of cyclists. Each of these studies examined well-trained male subjects with the exception of Cohen et al (1996) who included 2 women in their investigation.

Exercise Intensity

Based on total times to exhaustion of 40 to 75 minutes and time trials of at least 60 minutes, the participants in the majority of the above-mentioned research were likely exercising below their anaerobic threshold (AT). Four of the above-mentioned studies reported exercise times of approximately 20 to 30 minutes, suggesting their subjects were working at or above AT or that they paced themselves through the exercise. As these studies demonstrated significant improvements following caffeine ingestion, it appears that caffeine can effectively delay fatigue and improve time trial performance during high intensity endurance exercise, independent of the relation to AT. It has, however, been reported that, in untrained men, caffeine prolonged time to exhaustion at an intensity 10% below but not above AT (Denadai & Denadai, 1998). A closer examination of the relationship between the ergogenic effect of caffeine and the intensity of exercise is warranted.

Training Status

Most studies reporting on the positive effects of caffeine have employed well trained subjects. Some have, however, demonstrated significant performance results using less trained participants (Bell & McLellan, 2003; Denadai & Denadai, 1998; Greer et al., 2000). A direct comparison of these groups has yet to be made during endurance exercise, but Graham (2001) notes subjectively that trained athletes respond to caffeine more predictably, and hypothesizes that trained tissues are more responsive to caffeine and / or that trained athletes have the mental discipline required to exercise long or hard enough to elicit potential benefits from caffeine ingestion.

Caffeine habituation

Caffeine habituation was previously thought not to moderate caffeine's ergogenic effect (Tarnopolsky, 1994). Recent findings suggest that the ergogenic action of caffeine is both greater and longer in caffeine naïve participants (Bell & McLellan, 2002) and that initial exercise sensitizes caffeine habituated subjects in a second bout of cycling to exhaustion (Bell & McLellan, 2003). To date, these are the only studies to address the impact of habituation on the performance enhancing effect of caffeine and the study of a large group with differing caffeine consumption habits is necessary to confirm the impact on the ergogenic action.

Sex Differences

Although the performance enhancing effects of caffeine are well documented in male subjects, only one study has reported on this ergogenic action in women. Even studies that include female participants often do not report on differences between men and women. For example, Bell and McLellan (2002) included a group of women (eight of 23 subjects) in their study to explore the endurance of caffeine users and nonusers, but did not report gender-specific results.

In one study, Cadarette et al. (Cadarette et al., 1983) employed four male and four female participants to investigate the effects of 2.2, 4.4 and 8.8 mg/kg caffeine on running time to exhaustion at 80% VO_2max; however, they did not report gender-specific performance results. Overall, following ingestion of 4.4 mg/kg caffeine, fatigue was delayed by 37.5%. Other dosages did not produce statistically significant improvement. These researchers noted a single female subject who ran nearly double the time of her placebo test after caffeine ingestion and they suggested this individual accounted almost entirely for the significant improvement seen for the group. Furthermore, as Graham later noted, the placebo plasma caffeine levels of Cadarette's subjects were sufficiently high to elicit an ergogenic effect of their own (Graham, 2001). Neither Cadarette et al. nor Graham offer an explanation for the elevated caffeine in control subjects; one may speculate only that perhaps the researchers neglected to ask the subjects to abstain from caffeine consumption prior to participating in the experiments.

In another study that compared men and women (Butts & Crowell, 1985), cycling time to exhaustion at 70-75% VO_2max was investigated following ingestion of 300 mg (approximately 5 mg/kg) caffeine in 15 female and 13 male subjects. Times to exhaustion increased by 14.4% and 3.1% for the women and the men, respectively. The researchers also noted the difference in magnitude between the genders was primarily due to a single female subject whose trial time was increased by 50% by caffeine. The improvements observed in this study were not statistically significant, likely as caffeine was administered in decaffeinated coffee, which has more recently been shown to moderate the ergogenic action (Graham et al., 1998).

These studies suggest that women may differ from men in their response to caffeine and in its effects on exercise performance. However, they do not provide unequivocal evidence. Given that men and women differ in their hormonal, metabolic, sympathetic, and neuromuscular activity during submaximal exercise (Tarnopolsky, 1999), and so potentially in the effects of caffeine to modulate these systems, a well-controlled study is necessary to establish the performance effects of caffeine in women.

SUMMARY

Caffeine has been well established as an ergogenic aid to well-trained male athletes in endurance exercise settings. The mechanism through which caffeine acts to improve endurance performance is, however, elusive. Metabolic data are equivocal and do not support the original theory that caffeine alters substrate usage and spares muscle glycogen. As an adenosine antagonist, caffeine is known to exert its action directly at specific tissues, including adipose and CNS tissues. Lipolysis is stimulated in adipocytes but caffeine's potential effects within the CNS are numerous and complicated. The role of training status, caffeine habituation, and sex on caffeine's action remains to be explained. Exploration into the impact of these variables on caffeine's ergogenic action may help to elucidate the mechanism through which it exerts its effects to improve exercise performance.

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van Soeren, M., Mohr, T., Kjaer, M., & Graham, T. E. (1996). Acute effects of caffeine ingestion at rest in humans with impaired epinephrine responses. *Journal of Applied Physiology, 80*(3), 999-1005.

van Soeren, M. H., Sathasivam, P., Spriet, L. L., & Graham, T. E. (1993). Caffeine metabolism and epinephrine responses during exercise in users and nonusers. *Journal of Applied Physiology, 75*(2), 805-812.

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APPENDIX B: PARTICIPANT INFORMED CONSENT FORM

UNIVERSITY OF VICTORIA
OFFICE OF THE VICE-PRESIDENT, RESEARCH
HUMAN RESEARCH ETHICS COMMITTEE

Participant Informed Consent Form

The effect of caffeine on endurance performance in trained female cyclists

You are being invited to participate in a study entitled "The effect of caffeine on endurance performance in trained female cyclists" that is being conducted by Meghan MacLeod. I am a graduate student in the School of Physical Education at the University of Victoria and you may contact me if you have any questions or concerns about this study. I can be reached by telephone at 386-8696 or email at meghanm@uvic.ca.

As a graduate student, I am required to conduct research as part of the requirements for a Master of Science degree in Kinesiology. This study is being conducted under the supervision of Dr. Kathy Gaul. You may contact her by telephone at 721-8380 or by email at kgaul@uvic.ca.

The purpose of this research project is to investigate the effect of caffeine on the endurance performance of trained female athletes. Specifically, I am attempting to establish that time to exhaustion during constant load cycling at a high intensity endurance exercise will be prolonged under the influence of caffeine.

Research of this type is important because it will provide women with scientific validation of the effect of caffeine on endurance exercise, where conclusions are currently drawn from research conducted with almost exclusively male participants. It will also begin to remedy the distinct lack of literature related to the female response in the area of muscle metabolism, nutrition, and exercise physiology.

You are being asked to participate in this study because you meet the following criteria:

- You are a healthy women
- Your age is between 20 and 35
- You have a minimum 2 years experience in endurance-based cycling
- You have a high level of aerobic fitness - this will be represented by a maximal oxygen consumption rate (VO_2max) of at least 50 mL/kg·min. If you agree to participate in this study, this will be measured during our first meeting. Should your maximal oxygen consumption rate not meet this criterion, you will be asked to withdraw from the study.

If you agree to voluntarily participate in this research, your participation will include the following:

- An initial individual interview with questions regarding cycling history, menstrual status, and use of oral contraceptives, caffeine habits, and availability for testing (Initial interview and testing session).
- Height, weight, and skin fold measurements at 5 sites throughout the body (triceps, biceps, subscapular, iliac crest, and calf) (Initial interview and testing session).

- Completion of a diary before each testing session detailing recent physical activity as well as recent food, liquid, and caffeine consumption.
- A VO_2max test, which will be a graded exercise test to exhaustion on a cycle ergometer, where the workload will increase every 1-2 minutes (Initial interview and testing session).
- A testing session where you will cycle for 10 minutes at a constant workload at an intensity of 80% of your VO_2max (Confirmatory testing session).
- Completion of 2 physical endurance tests, where you will cycle to exhaustion at the constant workload equivalent to 80% of your VO_2max. At the beginning of each of these testing sessions, you will be given a bottle of lemonade that will, on one occasion, contain a 5 mg/kg dosage of caffeine. Neither you, nor the investigators will be informed about which trial is being performed until the conclusion of the entire study. After drinking the lemonade, you will rest in the Sport and Fitness Centre for one hour before beginning the exercise test.

Participation in this study may cause some inconvenience to you, including the sacrifice of the following:

- Approximately one and a half (1.5) hours during the first interview where the anthropometric measurements and VO_2max test will be performed.
- Approximately one (1) hour during the confirmatory testing session.
- Approximately three (3) hours for each physical endurance testing sessions. These two sessions must take place 4 days apart and must also take place within the first 9 days following your first day of menstruation.

The total involvement of each subject over the 4 testing sessions outlined above is estimated at 8.5 hours and is expected to take place over a period of 3 to 6 weeks. All sessions will take place at the Sport and Fitness Centre (Room 171 in the McKinnon building) at the University of Victoria.

There are some potential risks to you by participating in this research. These include possible physical discomfort or physical injury and possible emotional stress. Potential physical risks include, but are not limited to, muscular discomfort (aches, pains, or acute injuries such as strains or tears) during and/or after exercise sessions, shortness of breath, nausea, dehydration, diarrhea or cramps. Potential emotional stresses include, but are not limited to, alertness, restlessness, agitation, irritability, or insomnia. The risks incurred from the physical tests do not exceed those associated with your regular training. The risks incurred through the ingestion of 5 mg/kg of caffeine are those associated with the consumption of approximately 2 cups of strong coffee.

Physical risks will be minimized through the implementation of warm-up and cool-down procedures before and after every exercise session, encouragement to consume water before, during and after each exercise session and the request to prepare adequately (sleep, nutrition, activity) for each exercise session. Injuries incurred during any part of the protocol will be treated as appropriate (applying ice, for example) and a recommendation to a health care professional will be made. You will be encouraged to perform the tests at a time when the caffeine's effects on sleep or other important tasks are minimized.

The potential benefits of your participation in this research include the following:

- You will be provided with valuable physiological and performance data that can be used to assess your current physical condition and may serve as a comparison following future training.

- You will be provided with information about the effect of caffeine on your endurance performance, which will allow you to make informed decisions about its use during training or competition.
- In the broader community, this study will provide data that may be of value to sport governing bodies when establishing acceptable urinary caffeine levels.
- In the scientific community, as outlined above, this research will begin to remedy the lack of literature investigating the female response in the area of muscle metabolism, nutrition, and exercise physiology. It will provide women with scientific validation of the effect of caffeine on endurance exercise, where conclusions are currently drawn from research conducted with almost exclusively male participants. One of the hopes of this research is to contribute to that state of knowledge, and if successful, this information may help to introduce caffeine as a tool to investigate gender differences in metabolism and exercise physiology.

Your participation in this research must be completely voluntary. If you do decide to participate, you may withdraw at any time without any consequences or any explanation. You may do this by telling me at any of our meetings, or by contacting me by telephone or email at any time. If you do withdraw from the study, your data will not be used and will be destroyed immediately.

In order to assure myself that you are continuing to give your consent to participate in this research, I will request that you sign a Participant Informed Consent Form before every testing session.

In terms of protecting your anonymity, you will be assigned a unique data code to be used in place of your name for identification purposes and collection of all data. As the principal investigator, only myself and my supervisor, Dr. Kathy Gaul, will have access to the coding key, and it will be altered or destroyed (electronic files deleted and paper copies shredded) upon completion of the data collection. No personal information will be released.

Your confidentiality and the confidentiality of the data will be protected by keeping hard copies of data and back-up copies of electronic data (on disk) in a locked filing cabinet. The computer on which data is stored will be password protected. Five years following completion of the study, all data will be destroyed.

As this study is being conducted in partial fulfillment of the requirements for my Masters of Science degree, the results will be communicated as a formal thesis. These results may also be published in a peer-reviewed scientific journal or presented at professional academic conferences.

I will attempt to minimize the motivation you may experience to out-perform either your first, or a particular test. To accomplish this, neither you nor the investigators will have knowledge about what exercise trial you are performing (caffeine or placebo). In addition, any indication of the length of time passed during the test, including the total time to exhaustion, will not be disclosed until completion of the entire data collection. At this time, a summary of your results and the collective average will be provided to you. However, as a participant in this study, you have free access to any of your other information at any time during or following data collection. I am more than willing to discuss your test results with you at a time that is mutually convenient.

In addition to being able to contact me or my supervisor at the above phone numbers, you may verify the ethical approval of this study, or raise any concerns you might have, by contacting the Associate Vice-President, Research at the University of Victoria (250-472-4362).

Your signature below indicates that you understand the above conditions of participation in this study and that you have had the opportunity to have your questions answered by the researchers.

Initial interview and testing session:

Name of Participant	*Signature*	*Date*

Confirmatory testing session:

Name of Participant	*Signature*	*Date*

Physical endurance test #1:

Name of Participant	*Signature*	*Date*

Physical endurance test #2:

Name of Participant	*Signature*	*Date*

A copy of this consent will be left with you, and a copy will be taken by the researcher.

APPENDIX C: MODIFIED BORG SCALE OF PERCEIVED EXERTION

SCALE	SEVERITY
0	Nothing At All
0.5	Very Very Slight (Just Noticeable)
1	Very Slight
2	Slight
3	Moderate
4	Some What Severe
5	Severe
6	
7	Very Severe
8	
9	Very Very Severe (Almost Maximum)
10	Maximum

Modified Borg scale, From Burdon JGW,Juniper EF,Killian KJ,Hargrave FE,Campbell EJM. The perception of breathlessness in asthma. Am Rev Respir Dis 1982;126:825-8. (Official Journal of the American Thoracic Society. © American Lung Association.)

APPENDIX D: DATA COLLECTION INSTRUMENTS

1. Initial Interview Form

The effect of caffeine on endurance performance in trained female cyclists

Meghan MacLeod, University of Victoria
meghanm@uvic.ca

Initial Interview

Subject _____ Date _____

Menstrual Status

First day of last period _____

Approx length of cycle _____ (Days)

Consistent _____ (Yes / No)

Oral contraceptive use _____ (Yes / No) Type _____

Caffeine Habits

Typical consumption _____ (Daily, 2-3 days, weekly, etc)

Typical form _____ (Coffee, tea, stimulant, etc)

Amount _____

Training Status

Number of years cycling _____

Current avg km / week _____

Typical intensity _____

40km time trial _____ (If known)

Anthropometric Measurements

Height _____

Weight _____

Skinfolds

	Trial 1	Trial 2	Trial 3	Final
Triceps	_____	_____	_____	_____
Biceps	_____	_____	_____	_____
Subscapular	_____	_____	_____	_____
Iliac crest	_____	_____	_____	_____
Calf	_____	_____	_____	_____

Sum of 5 Skinfolds _____

2. VO_2max Form

The effect of caffeine on endurance performance in trained female cyclists

Meghan MacLeod, University of Victoria
meghanm@uvic.ca

VO_2max Test

Subject _____ Date _____

Weight _____ Time _____

Cycle Ergometer Settings

Seat height _____ Bar height _____

Seat position _____ Bar position _____

Time	Watts	HR	RPM	VO_2	V_E
0:00					
1:00					
2:00					
3:00					
4:00					
5:00					
6:00					
7:00					
8:00					
9:00					
10:00					
11:00					
12:00					
13:00					
14:00					
15:00					
16:00					
17:00					

VO_2max _____ **80% VO_2max** _____

Power Output at 80% VO_2max _____

3. Confirmatory Test Form

The effect of caffeine on endurance performance in trained female cyclists

Meghan MacLeod, University of Victoria
meghanm@uvic.ca

Confirmatory Test

Subject _____ Date _____

Weight _____ Time _____

Cycle Ergometer Settings

Seat height _____ Bar height _____

Seat position _____ Bar position _____

Target VO_2 _____ Target HR _____

Power Output _____

Time	RPM	HR	VO_2	V_E
0:00				
1:00				
2:00				
3:00				
4:00				
5:00				
6:00				
7:00				
8:00				
9:00				
10:00				

Accurate Reflection of 80% VO_2max?

Yes / No

LT Estimation

Computer _____

VCO_2 vs VO_2 _____

V_E vs PO _____

Relationship of 80% VO_2max to LT _____

4. Endurance Exercise Trial Form

Page 1

The effect of caffeine on endurance performance in trained female cyclists

Meghan MacLeod, University of Victoria
meghanm@uvic.ca

Trial _____ Date _____ ____
Subject _____ Time _____

Weight _____

Day 1 _____

Recent Activity

Recent Caffeine

Resting HR _____

Lemonade Ingestion __

HR 20 min __ 40 min _____ 60 min __

Cycle Ergometer Settings
Seat height _____ Bar height _____
Seat pos'n _____ Bar pos'n _____

Warm-up _____ **HR** _____

Time between warm-up and trial _____

Power Output _____ Target VO_2 _____ Target HR __

Comments

Page 2

The effect of caffeine on endurance performance in trained female cyclists

Meghan MacLeod, University of Victoria
meghanm@uvic.ca

	HR	RPM	RPE	VO_2	V_E
0:00					
1:00					
2:00					
3:00					
4:00					
5:00					
6:00					
7:00					
8:00					
9:00					
10:00					
11:00					
12:00					
13:00					
14:00					
15:00					
16:00					
17:00					
18:00					
19:00					
20:00					
21:00					
22:00					

Page 3

	HR	RPM	RPE	VO_2	V_E
23:00					
24:00					
25:00					
26:00					
27:00					
28:00					
29:00					
30:00					
31:00					
32:00					
33:00					
34:00					
35:00					
36:00					
37:00					
38:00					
39:00					
40:00					
41:00					
42:00					
43:00					
44:00					
45:00					
46:00					
47:00					
48:00					

Page 4

	HR	RPM	RPE	VO_2	V_E
49:00					
50:00					
51:00					
52:00					
53:00					
54:00					
55:00					
56:00					
57:00					
58:00					
59:00					
60:00					
61:00					
62:00					
63:00					
64:00					
65:00					
66:00					
67:00					
68:00					
69:00					
70:00					
71:00					
72:00					
73:00					
74:00					
75:00					

Page 5

	HR	RPM	RPE	VO_2	V_E
76:00					
77:00					
78:00					
79:00					
80:00					
81:00					
82:00					
83:00					
84:00					
85:00					
86:00					
87:00					
88:00					
89:00					
90:00					
91:00					
92:00					
93:00					
94:00					
95:00					
96:00					
97:00					
98:00					
99:00					
100:00					
101:00					
102:00					

5. Pre-Test Diary for Participants

Page 1

The effect of caffeine on endurance performance in trained female cyclists

Meghan MacLeod, University of Victoria
meghanm@uvic.ca

Pre-test Diary of Food, Liquid, Caffeine and Physical Activity

Subject _____ Exercise Test _____

Please provide as much information as possible, including meal times.
For example, when detailing food, include the **name, the amount, and the brand.**

When detailing activity, please include what **type, duration, and intensity**.

Day 1 Date _____

Food

Liquid

Caffeine

Physical Activity

The effect of caffeine on endurance performance in trained female cyclists

Pre-test Diary of Food, Liquid, Caffeine and Physical Activity

Subject _____ Exercise Test _____

Day 2 Date _____

Food

Liquid

Caffeine

Physical Activity

Pre-test Diary of Food, Liquid, Caffeine and Physical Activity

Subject _____ Exercise Test _____

Day 3 (Day of Exercise Test) Date _____

Food

Liquid

Caffeine

Physical Activity

6. Subject Master List

The effect of caffeine on endurance performance in trained female cyclists

Meghan MacLeod
University of Victoria
meghanm@uvic.ca

Subject Master List

Subject Number	Name	Telephone Number	Email
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12			
13			
14			
15			

7. Subject Trial Log

The effect of caffeine on endurance performance in trained female cyclists

Meghan MacLeod
MSc Thesis Data
meghanm@uvic.ca

SUBJECT TRIAL LOG

Subject Number	Caffeine (mg)	Trial 1 Date *To be added upon completion of experiment*	Caffeine / Placebo	Trial 2 Date *To be added upon completion of experiment*	Caffeine / Placebo
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					

APPENDIX E: STANDARDIZED PHYSIOLOGICAL DATA

Caffeine naïve = subjects 4-6, caffeine habituated = subjects 1-3, 7-8.
Oral contraceptive non-users = subjects 1-4, oral contraceptive users = subjects 5-8.

Individual heart rate data at % blocks of total time to exhaustion (Exh).

Subject	Onset	10%	20%	30%	40%	50%	60%	70%	80%	90%	99%	Exh
1	170.33	176.00	179.33	178.67	178.67	179.33	180.33	181.00	180.67	181.00	182.67	181.50
	173.00	179.50	183.00	184.67	188.33	188.33	189.67	190.67	189.67	190.33	190.00	191.00
2	155.33	167.33	172.33	176.67	178.00	180.33	181.00	180.67	179.33	178.00	177.33	176.00
	160.00	170.00	174.33	177.33	178.83	181.33	182.00	182.00	181.83	185.00	185.00	183.00
3	142.33	152.33	156.67	158.33	158.67	161.00	162.00	161.33	161.00	163.00	163.33	163.50
	141.67	149.00	152.67	155.33	157.00	156.67	156.67	157.33	157.67	158.00	160.00	161.00
4	169.00	177.00	178.67	180.33	181.67	183.33	183.00	182.17	180.33	181.67	184.00	187.50
	161.67	173.67	176.67	180.67	181.17	180.33	179.33	179.67	179.33	177.67	180.33	181.00
5	156.33	164.33	168.00	170.00	168.00	171.33	172.00	173.00	171.33	174.67	176.00	175.50
	158.67	166.00	166.67	169.67	172.00	173.17	175.33	177.33	177.67	179.67	181.00	182.50
6	162.33	170.33	174.83	177.67	178.33	179.33	180.17	180.00	179.50	180.67	181.67	183.50
	167.33	173.33	177.00	179.83	182.33	185.50	187.33	188.50	189.67	188.67	190.67	193.00
7	139.67	149.00	151.33	152.67	153.00	154.00	154.67	155.67	156.67	157.33	159.00	157.00
	140.33	149.00	151.33	155.67	156.67	157.33	158.83	160.33	161.33	162.33	162.33	162.00
8	163.67	168.50	172.33	176.33	177.67	177.00	178.33	178.67	178.59	178.00	180.33	182.00
	162.00	168.50	172.33	176.67	179.33	180.33	180.59	180.33	180.00	179.33	178.50	182.18
Mean	**157.38**	**165.60**	**169.19**	**171.33**	**171.75**	**173.21**	**173.94**	**174.06**	**173.43**	**174.29**	**175.54**	**175.81**
	158.08	**166.13**	**169.25**	**172.48**	**174.46**	**175.37**	**176.22**	**177.02**	**177.23**	**177.63**	**178.48**	**179.46**

Placebo trial, caffeine trial

Individual VO_2 data at % blocks of total time to exhaustion (Exh).

Subject	Onset	10%	20%	30%	40%	50%	60%	70%	80%	90%	99%	Exh
1	42.98	44.77	46.15	46.80	47.10	47.00	#	48.00	47.57	47.50	#	45.90
	45.88	48.88	50.37	50.18	50.70	50.88	51.73	51.10	#	51.33	50.43	48.90
2	48.88	49.05	51.20	51.10	51.08	51.18	51.48	47.85	49.33	#	#	49.40
	46.03	49.50	50.35	51.43	50.68	51.68	51.55	51.65	50.23	50.62	50.15	48.17
3	#	#	#	#	#	#	#	#	#	#	#	#
	#	#	#	#	#	#	#	#	#	#	#	#
4	33.63	36.60	37.28	38.42	38.49	37.83	37.68	37.62	37.46	38.16	38.13	38.40
	33.30	37.43	37.95	38.33	38.21	37.78	38.09	38.03	38.30	38.24	38.32	38.33
5	42.95	45.80	44.78	45.53	45.85	44.20	45.28	43.55	43.43	45.42	44.78	45.32
	43.13	44.34	44.76	43.15	43.86	42.98	43.15	42.95	42.63	43.70	43.66	45.93
6	45.85	48.13	48.61	47.53	48.33	48.45	48.85	48.38	48.47	48.64	48.22	47.62
	45.83	48.53	47.73	46.83	46.95	47.26	47.88	48.08	47.52	47.88	48.27	46.18
7	41.73	44.62	43.96	42.58	42.83	44.80	43.95	45.08	45.88	45.55	46.70	44.98
	45.33	46.85	46.93	47.03	47.24	47.04	47.55	48.58	48.00	47.63	48.58	48.25
8	40.60	#	43.05	44.00	42.33	42.55	42.13	41.90	42.78	41.63	40.68	41.93
	40.08	#	44.90	43.65	44.60	44.83	44.38	43.35	43.30	43.12	41.40	44.33
Mean	**42.37**	**44.83**	**45.00**	**45.14**	**45.14**	**45.14**	**44.89**	**44.63**	**44.99**	**44.48**	**43.70**	**44.79**
	42.79	**45.92**	**46.14**	**45.80**	**46.03**	**46.06**	**46.33**	**46.25**	**45.90**	**46.07**	**45.83**	**45.73**

Placebo trial, caffeine trial, # = missing data

Individual V_E data at % blocks of total time to exhaustion (Exh).

Subject	Onset	10%	20%	30%	40%	50%	60%	70%	80%	90%	99%	Exh
1	69.33	78.04	85.12	86.24	85.88	88.23	#	91.58	88.33	87.90	#	87.15
	70.13	83.80	91.12	94.80	98.90	105.08	103.35	103.20	#	104.90	102.13	103.50
2	68.28	69.80	75.28	78.82	78.98	83.18	85.32	79.40	79.83	#	#	75.95
	67.03	76.46	75.80	84.05	81.90	82.28	85.05	83.95	83.89	85.12	84.88	77.45
3	63.45	77.03	81.30	80.20	79.83	84.67	88.75	89.15	87.97	93.08	92.78	97.15
	67.85	75.23	75.88	80.83	82.23	79.79	83.70	85.83	90.00	88.95	90.77	92.58
4	67.15	84.68	85.80	89.50	88.08	88.05	86.08	88.32	83.84	87.94	89.92	99.00
	67.60	86.88	89.79	94.35	95.36	91.35	87.79	85.93	84.53	85.71	88.40	88.42
5	90.40	92.80	96.70	102.38	100.75	102.28	105.08	101.50	105.70	106.58	106.28	103.75
	98.90	96.04	98.28	102.80	101.90	103.28	110.43	107.28	114.63	114.45	110.34	117.12
6	70.75	69.88	82.50	79.83	83.56	86.60	84.90	84.14	84.26	86.68	85.15	86.28
	70.83	73.15	78.23	77.73	75.55	80.38	86.15	90.45	92.50	93.24	93.35	92.95
7	51.36	72.42	71.22	68.05	67.05	73.23	77.80	83.88	82.33	89.25	102.00	88.73
	66.70	71.33	74.15	75.30	77.26	79.36	81.10	83.18	79.83	86.97	92.65	105.10
8	70.90	#	80.35	78.58	84.80	84.83	85.48	87.55	88.10	81.55	84.70	87.17
	65.75	#	79.60	89.80	93.08	97.68	98.38	96.73	97.60	96.77	94.70	99.77
Mean	**68.95**	**77.81**	**82.28**	**82.95**	**83.62**	**86.38**	**87.63**	**88.19**	**87.54**	**90.43**	**93.47**	**90.65**
	71.85	**80.41**	**82.85**	**87.46**	**88.27**	**89.90**	**91.99**	**92.07**	**91.85**	**94.51**	**94.65**	**97.11**

Placebo trial, caffeine trial, # = missing data