



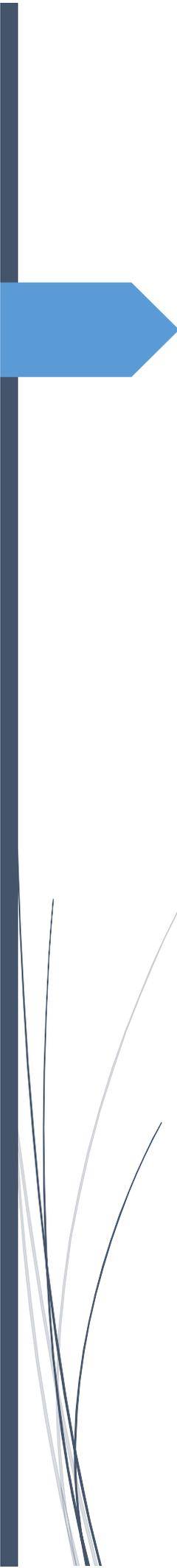
The Effect of Exercising in a Fasted State on Substrate Utilisation

Biomedical Sciences [Health, Exercise and Nutrition]

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1. Declaration

Statement 1

This work has not previously been accepted in substance for any degree and is not being concurrently submitted in candidature for any degree.

Signed: (Candidate)

Dated: 14/03/2018

Statement 2

This dissertation is the result of my own investigations, except where otherwise stated. Where corrections services have been used, the extent and nature of the correction is clearly marked in a footnote. Other sources are acknowledged by footnotes giving explicit references. A bibliography is appended.

Signed: (Candidate)

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Statement 3

I hereby give consent for my dissertation, if accepted to be available for photocopying and for inter library loan, and for the title and summary to be made available to outside organizations.

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Dated: 14/03/2018

2. Acknowledgements

This dissertation would not have been finished without my supervisor, [redacted]. I would like to thank him for his advice, support and encouragement throughout the completion of the dissertation.

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3. Abstract

3.1 Background

This crossover study was designed to establish if there was a difference in substrate utilisation when comparing exercise in the fed state with exercise in the fasted state. Previous studies have shown that exercising in the fasted state causes an increase in fat oxidation compared with exercise after a meal, particularly at lower exercise intensities. However, research into fasted exercise at higher intensities have elicited inconsistent results.

3.2 Methods

Three healthy males and three healthy females completed two identical exercise trials consisting of 10 minutes of constant cycling at 70% maximum heart rate. One trial took place after a 12 hr overnight fast and the other came after a standardised breakfast had been consumed. Participants cycled at between 50 and 60rpm, and load was added gradually until they reached 70% of their maximum heart rate. Ten minutes of continuous cycling then took place, and substrate utilisation was established by measuring the respiratory exchange ratio.

3.3 Results

Results show that there was no significant difference between substrate utilisation in the fed and fasted trials. This result was seen in both genders and the group as a whole.

3.4 Conclusion

Exercising in the fasted state did not elicit a significantly different substrate utilisation than exercising in the fed state.

4. Introduction

Carbohydrates and fats are the two main energy sources used by the body during exercise. Fats are generally the main energy substrate at lower intensities of exercise whilst carbohydrates are predominantly used at higher intensities. During low intensity, endurance events, fats are the major energy substrate and improving the body's ability to utilise fats as an energy source could be beneficial to performance. Despite this, the use of carbohydrate based drinks and gels remains prominent during training and competition during endurance events. Consuming carbohydrates pre-exercise increases carbohydrate availability and oxidation⁽¹⁾, but it inhibits the body's ability to oxidise fats⁽²⁾. The benefits of carbohydrate intake during exercise are well documented and irrefutable, the benefits of exercising in the fasted state have also been explored, with some suggestions that, whilst performance may be reduced initially, adaptations made long term could have serious positive effects on endurance capacity⁽³⁾.

Fasting is the absence of food intake lasting from a period of several hours up to 2-3 weeks, leading to a depletion of glucose in the blood⁽⁴⁾. This forces the body to rely on other energy substrates, namely fats, as an energy source. It is well known that exercise has positive effects on health; examples include a reduction in body weight, improved cardiovascular efficiency and improvements in insulin sensitivity⁽⁵⁾. Nevertheless, recent studies have found these improvements could be multiplied if exercise took place in the fasted state⁽³⁾. Insulin sensitivity is improved further when exercising in the fasted state as a result of reduced hepatic glycogen levels, prompting an increase in utilisation of fat as an energy source. From a performance perspective, fasted exercise has a number of potential benefits. Positive acute and chronic metabolic adaptations take place during fasted exercise that suggests a fasted training programme could have a number of long-term effects on performance⁽⁴⁾. Fasted exercise increases fat oxidation and lipolysis, increases free fatty acids (FFAs) in the blood and lowers the respiratory exchange ratio (RER) during exercise^(3, 6). Furthermore, regular fasted exercise can increase muscle glycogen levels and decrease the RER at set exercise intensities, as well as stimulate adaptations in muscle cells to facilitate energy production by fat oxidation and improving the oxidative capacity of mitochondria, ultimately leading to an increase in time to exhaustion⁽⁷⁾.

RER is determined by dividing the volume of CO₂ (VCO₂) produced during exercise by the volume of O₂ (VO₂) consumed. The RER value determines what substrate is being used to produce ATP, in that the amount of oxygen used during metabolism differs depending on what type of fuel is being oxidised: the more carbon present in the fuel, the more oxygen is required. If the RER is between 0.7 and 1.0, it indicates a mixture of fats and carbohydrates are being utilised for energy, an RER of >1.0 shows that the body is utilising solely carbohydrates.

A host of studies have examined substrate utilisation when exercising in a fasted state using markers other than RER. Studies measuring substrate oxidation and blood metabolite concentrations have produced conclusive results: in the fasted state, fat oxidation is increased⁽⁶⁻¹⁵⁾, blood FFA concentration is increased^(7-10, 12, 13, 15-19), as is the delivery of FFAs to the muscles, and intramyocellular triglycerides (IMTG) concentrations are increased^(3, 7, 8, 20). RER is an extremely good surrogate for measuring blood metabolite concentrations and is a valid technique of measuring substrate utilisation.

Whilst exercising in the fasted state has generally shown enhanced fat utilisation, a number of studies specifically measuring RER as a marker for substrate utilisation have produced contradicting results. Early studies showed exercising in a fasted state after a 23hr fast elicited a significantly lower RER than exercising in the fed state^(16, 21). The reliability of these studies could be called into question, the significantly lower RER found should not be disregarded. Nevertheless, later studies produced conflicting results when exercise took place at the same exercise intensity of 70% of VO₂ max. Numerous studies have backed up the early findings of Dohm et al and Neiman et al, in that RER was significantly lower in the fasted state⁽²²⁾. Others, however, showed that at 70% VO₂ max, nutritional state had no significant difference on RER^(17, 23). Despite there being no difference in RER, these studies still found that exercising in the fasted state at intensities of 70% brought about lower glycogen metabolism, increased blood FFA concentration and increased fat oxidation; suggesting fats were utilised more readily after a period of fasting.

At lower intensities, studies gave a clear view of how exercising in the fasted state affects substrate utilisation. Studies using exercise intensities of 50%-65% VO₂

max showed almost unanimously that RER was significantly lower in the fasted state^(3, 6, 7, 9, 10, 22-24). In these studies overweight, healthy and trained subjects were all used, and findings of a lower RER in the fasted state was consistent throughout, regardless of the characteristics of the participant. In addition to RER, aforementioned measurements of substrate utilisation consistently showed a shift towards fat utilisation as the main energy source.

The vast majority of studies in this area have studied men, with only two studies using women as part of the design. The aim of this study was to evaluate the relationship between nutritional status and substrate utilisation during a short exercise period at 70% of maximum heart rate (HR_{max}). The secondary aim was to investigate any differences in substrate utilisation between male and female participants.

5. Method

5.1 Subjects

Six healthy participants (three male and three female) between the ages of 18 and 30 were recruited by word of mouth at Cardiff Metropolitan University to take part in the study, which was approved by the Cardiff Metropolitan Ethics Committee. All participants were similar in age and took part in between three and six hours of physical activity a week. After they were informed in detail of all the procedures and potential risks associated with the experiment, subjects gave their written consent. Upon arrival in the physiology laboratory for their first visit, subjects had their height and weight measured, as well as their blood pressure, and filled out a physical activity readiness questionnaire, stating there was no medical reason they could not participate in the exercise component of the trial.

5.2 Standardised Breakfast

On the day of the fed trial each participant was asked to consume three pieces of toast with butter 1.5 hours before the time they were due at the lab.

5.3 Pre-exercise Period

On two separate occasions, separated by a period of at least seven days, subjects cycled for 10 minutes at 70% of their HR_{max} . In a crossover study design, trials were completed in random order in two different nutritional states: fasted or fed. There was a period of at least 1 week between the two trials. When partaking in the fasted trial, they arrived at the lab between 0900 hours and 1100 hours after a 12 hour overnight fast. In the fed trial, participants arrived at the same time, having consumed a standardised breakfast 1.5 hours before the commencement of the exercise. On both occasions subjects were instructed to abstain from alcohol and strenuous physical activity the day before the trial, and from caffeine in the 12 hour period prior to it. HR_{max} was established using the equation $220 - \text{age}$, and 70% was worked out using that figure. The lab temperature was maintained at 19° Celsius for every subject in both nutritional states. Participants were informed that a fan could be turned on during the exercise period if they required it.

After the anthropometric measurements had been taken, subjects were fitted with a heart rate monitor (Polar H1 Heart Rate Sensor) and had a five minute

familiarisation and warm up period on the cycle ergometer (Monark Ergomedic 894E), where the seat height and handle bar position could be adjusted. During this time the details of the individual participant was entered into the MetaSoft Studio software used to analyse the data collected and the Cortex Metalyzer (Cortex Metalyzer 3B) was calibrated, before being used to measure the VO_2 , VCO_2 and RER. Once familiarised, the subjects were fitted with a face mask, ensuring there was a seal to prevent air escaping and affecting the readings.

5.4 Exercise Period

Subjects initially pedalled at 55 rpm, and load was added in 0.2kg increments to increase their HR to 70% of their HR_{max} . Where more than 1.2kg of load was added, participants were asked to pedal at 60 rpm. Once 70% HR_{max} was reached, the mask was connected to the Cortex Metalyzer. It was at this point that the measurement of RER commenced and subjects cycled for a further 10 minutes. Load and RPM were continually adjusted to maintain HR throughout the 10 minute measurement period if required. VO_2 , VCO_2 , RER and HR were measured continuously, on a breath-by-breath basis, throughout the 10 minute measurement period. For each participant, load added and rpm was noted, and used for reference in the second visit, allowing 70% HR_{max} to be reached more efficiently. Load was added in 0.4kg increments until the load used from the first session was reached.

5.5 Statistical Analysis

On completion of the experimental procedure, data were analysed using software package Minitab. All data are presented as means \pm SD and statistical significance was accepted at $P < 0.05$. Paired sample t-tests were used to compare RER of all of the participants in the two experimental conditions, and to compare male and female subjects separately in each nutritional state. A paired t-test was used because all of the subjects undertook the same experiment twice under different conditions.

6. Results

Three male and three female participants completed the 10 minute cycle, cycling at 58.2 ± 2.71 RPM during both the fasted and fed exercise sessions. This brought about a VO_2 of 1.89 ± 0.65 L/min in the fed state and 1.83 ± 0.75 L/min in the fasted state, and a VCO_2 of 1.92 ± 0.73 L/min in the fed state and 1.82 ± 0.85 L/min in the fasted state. There was no significant difference in VO_2 or VCO_2 in the fed or fasted trails. After using a paired t-test to evaluate any differences in VO_2 and VCO_2 in the two nutritional states, no significant difference was found in either parameter between the two states.

Table 1: Descriptive characteristics of subjects ($n = 6$)

Variable	Mean
Age (years)	22.33 ± 2.50
Height (cm)	176.83 ± 13.39
Body Mass (kg)	77.07 ± 22.29
BMI (kg/m^2)	24.23 ± 3.61

Note: Values are means \pm SD ($n = 6$). BMI, body mass index.

6.1 Substrate Utilisation

A paired sample t-test was used to evaluate the RER data. When RER values were compared in the two nutritional states, mean fasting RER values were not significantly lower than fed values in the whole group, male participants, or female participants (figure 1, A-C respectively).

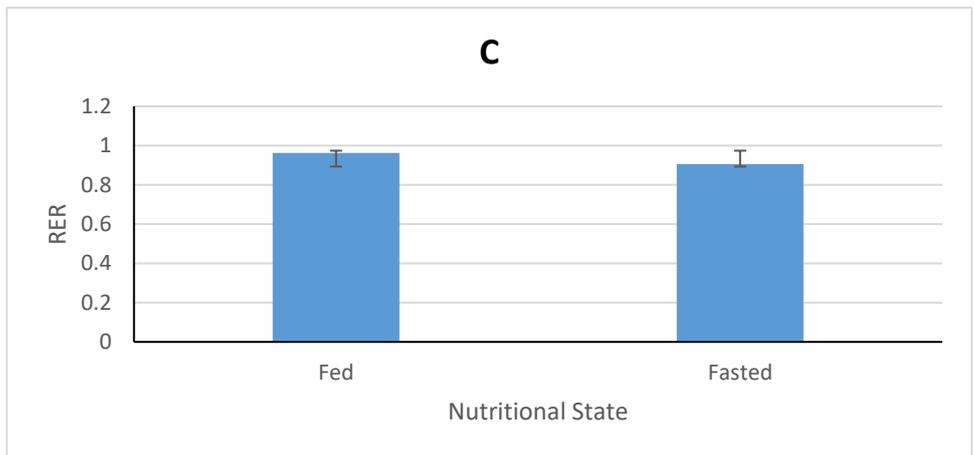
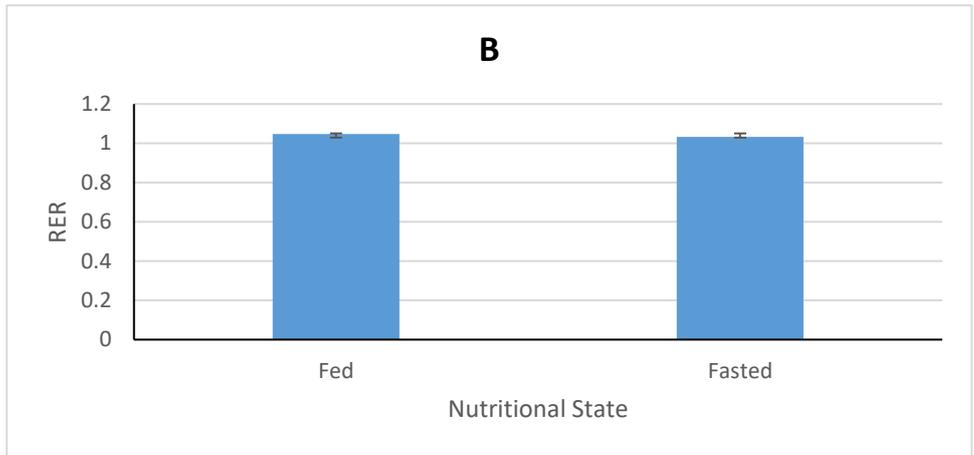
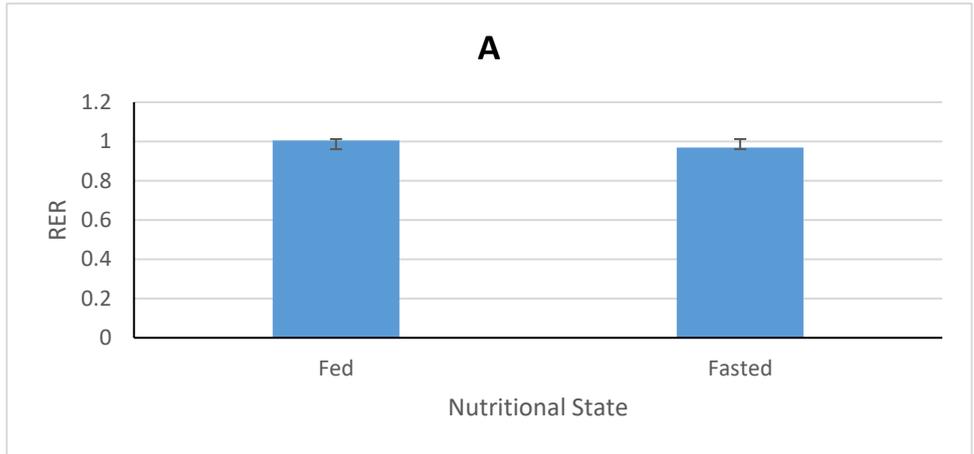


Figure 1: Effect of training in the fed state compared with the fasted state on RER during a 10 minute exercise at 70% HR_{max}. Data provided are means, the same number of participants was used in each nutritional state. Results shown are for the whole participant group (**A**: $n = 6$), the male participants (**B**: $n = 3$) and the female participants (**C**: $n = 3$). RER was not significantly different in any of the three groups, but was generally lower.

The results of a paired sample t-test on total RER data (figure 1, A) revealed no significant difference between nutritional state and RER ($P = 0.120$). However, the mean RER was generally lower when exercising in the fasted state (fed = 1.005; fasted = 0.969).

When using a paired t-test to analyse just the male participants, the results followed a similar trend (figure 1, B). Whilst RER was slightly lower during fasted exercise (fed = 1.047; fasted = 1.032), there was no statistical significance between the nutritional states ($P = 0.368$). This result was also seen when just the women's results were analysed by a paired sample t-test (figure 1, C). A lower RER was again observed but no significant difference was present ($P = 0.248$).

7. Discussion

The outcome of this study showed that there was no significant difference in substrate utilisation when exercising in the fasted state when compared with exercising in the fed state. When exercising in the fed state, mean RER of the group was 1.005, a clear indication that carbohydrates were the sole contributor to ATP production. RER was slightly lower in the fasted state, at 0.969, suggesting that some fats were being metabolised as well as carbohydrates, but the difference was not statistically significant, meaning the change in RER cannot be directly associated with the pre-exercise nutritional state of the participants (figure 1, A).

When the results were separated into genders, similar patterns were observed. Male participants had an average RER of 1.047 in the fed state, and 1.032 in the fasted state, with no significant difference between the two experimental conditions (figure 1, B). What is interesting about these findings is that even in the fasted state, all three male participants had an average RER of over 1.0, showing that carbohydrates were the sole source of energy. Two of the three participants had an RER greater than 1.0 throughout the whole 10 minute exercise period. The three women that participated in the trial also showed no significant difference between RER in the fasted and fed trials. When fed, average RER was 0.962, whilst in the fasted state it was 0.905 (figure 1, C). In contrast to the male participants, all three female subjects had an average RER lower than 1.0 throughout the entire ten minutes when exercising in the fasted state, indicating that they continued to utilise fats throughout the exercise period, something that male participants did not do.

The difference in substrate utilisation between the genders is intriguing. There was no significant difference between the RER when exercising in the fed state ($P = 0.091$), but in the fasted state, the difference was statistically significant ($P = 0.033$). This result suggests that the female population utilises fats more readily in the fasted state than men, though the fact that there is no difference in RER between fed and fasted exercise in the female participants suggests that this area needs more research to be conducted. It may be that there is in fact no significant difference, but appears to be one because of the low statistical power of the

experiment. What is clear is that the area requires further investigation to gain clarity.

The study performed had certain limitations. The main weakness of the study is the low number of participants recruited, leading to weak statistical power. Statistical power would be improved if more participants were recruited, although previous studies have also used relatively small subject groups^(8-10,23). Using HR_{max} as a marker for exercise intensity was also a limitation, albeit a more manageable one. Gold standard for exercise intensity would be using a VO₂ max test, but HR_{max} remains a viable measure of maximum exertion and has been used in studies previous to the current one⁽²⁵⁾; it acts as a good surrogate for VO₂ max, and ensures that participants are all working at the same relative exercise intensity. A VO₂ max test would have also required an additional visit to the lab for each participant and the time-scale of the project unfortunately did not allow for this.

Despite the limitations mentioned, as much as possible was done to improve the strength of the study. A cross over study was used because it is the best form of control in exercise studies. As part of the crossover study design, all of the participants were used in both of the nutritional states. Measuring the same participants in both states with a blow-out time in between the two trials guards against bias and confounding, improving the strength of the study compared with using two different participant groups. Using breath-by-breath analysis to measure RER increases the validity of the results, compared with other studies that measure RER non-continuously throughout the exercise. The main strength of RER over indirect calorimetry is that it does not require complicated stoichiometric equations, and is more reliable at higher intensities⁽²⁶⁾. All of the participants were of a similar age, in good health, non-smokers and all participated in at least 3 hours of physical activity a week. Moreover, all of the subjects refrained from strenuous activity and alcohol 24 hours prior to the trial, and didn't consume any caffeine in the 12 hours before arriving at the lab. Additionally, all participants consumed the same meal 1.5 hours before the commencement of the trial. Furthermore, very few previous studies have included

women as part of the research; using an equal number of male and female participants allows for improved understanding of any differences in results between the different gender groups.

The results of this study support those of similar studies conducted previously, in that there was no significant difference in substrate utilisation during fasted and fed exercise, when exercising at 70% of maximal exertion. In a number of studies, 70% maximal exertion is the exercise intensity where significant difference in substrate utilisation was not present^(17, 23, 25). In these studies, subjects cycled or ran at 70% of VO₂ max and RER was measured either throughout or pre- and post-test, although none of the previous studies measured RER breath by breath, as performed in the current study. Schabert et al⁽¹⁷⁾ tested participants to exhaustion at 70% VO₂ max, and found no significant difference in RER at any point throughout exercise. Bergman and Brooks⁽²³⁾, exercised trained and untrained cyclists at 20, 40, 60 and 80% VO₂ max. At 60 and 80% VO₂ max fasting did not bring about a difference in mean RER compared with the fed state, in either trained or untrained subjects. At these intensities, subjects cycled for 1.5 hours and for at least 30 minutes respectively. The reason for the difference in results of these studies with the current study is likely due to time spent exercising, as RER drops throughout a prolonged exercise period⁽²⁷⁾.

A more recent study⁽²²⁾ utilised a similar experimental protocol as Bergman and Brooks⁽²³⁾, in that substrate utilisation was measured across three different exercise intensities: 50%, 60% and 70% VO₂ max. The study by Kang et al⁽²²⁾ also utilised shorter exercise periods, as subjects exercised for just 10 minutes at each intensity. Results found RER to be significantly lower at all three intensities in the fasted state, indicating an increased rate of fat oxidation compared with the fed state.

These results differ from the current study, despite similar methodology and participant characteristics. Kang et al⁽²²⁾ recruited more subjects, 20 in all, 10 of each gender, and this improved statistical power may go some way to explaining the different results. On the other hand, that study did not continually measure RER, which may have caused a difference, but the most likely reason for the difference between the studies is that despite measuring RER at three different

intensities, subjects cycled continuously for 30 minutes, with exercise intensity being increased at each ten minute interval. This continuous, longer bout of exercise could have caused the RER to be lower at 70% $\text{VO}_2 \text{ max}$ ⁽²⁷⁾.

In addition to the findings of Kang et al⁽²²⁾, a study by another research group⁽⁷⁾ assessing RER at 70% $\text{VO}_2 \text{ max}$ also found a significant difference between RER in fasted and fed exercise. Participants cycled for 2 hours, and RER was significantly lower at the start of the exercise period and after 60 and 120 minutes. Once again, the difference in the results to the current study are likely due to the difference in time spent exercising, and because de Bock et al⁽⁷⁾ also used $\text{VO}_2 \text{ max}$, as opposed to HR_{max} .

At lower exercise intensities fats are the predominant energy source regardless of nutritional state⁽²⁸⁾. At 70% of maximal exertion, fat cannot provide enough energy to maintain muscle function. Increasing exercise intensities during normal, fed exercise doesn't reduce the amount of fat oxidation, but the oxidation of carbohydrates is greatly increased, providing ATP much more rapidly, as is required at greater exercise intensities⁽²⁹⁾. Studies conducted at intensities lower than 70% of maximal exertion have found that there is an increase in fat utilisation when exercise takes place in the fasted state compared with exercising in the fed state, and that carbohydrate intake prior to exercise actually inhibits the utilisation of fats as an energy source^(6-15, 22-24).

Numerous studies found that exercise intensities lower than 70% $\text{VO}_2 \text{ max}$ elicited lower RER^(3, 6, 7, 9, 10, 22-24), increased fat oxidation and lower carbohydrate oxidation⁽⁶⁻¹⁵⁾. Studies found that RER in the fasted state was consistently lower than when participants were not fasted, indicating an increased reliance on fats as an energy source.

The findings of this study suggest that women utilise fat better than men when exercising in the fasted state. One area of potential future study would be to investigate this finding, using a larger participant group to ratify these results. It is well documented that when exercise intensity is greater than 70%, nutritional state has no significant effect on RER. However, there is minimal data when it comes to high intensity exercise in women. If the results of this study were to be confirmed, it could lead to women being advised to exercise in the fasted state

for improved sporting performance, to improve general health, and as an aid to weight loss regimes.

This study, and others of a similar scope, also lead to potential studies of a more significant impact than whether women utilise fats better than their male counterparts. The acute effects of fasted exercise have been well covered, particularly in men. An area that does need further clarification, however, is how a fasted training programme could induce long-term benefits to health, and performance. Van Proeyen et al⁽³⁾ and De Bock et al⁽³⁰⁾ both ran studies assessing the use of fasted training programmes. Van Proeyen et al⁽³⁾ found that a number of adaptations seen as a result of the training programme were enhanced in the cohort that trained in the fasted state. After both training regimes VO₂ max and time to exhaustion had both increased at a similar rate in both groups, but maximal rate of fat oxidation was improved considerably more in the fasted cohort than maximal carbohydrate oxidation in the fed participants.

On the other hand, De Bok et al⁽³⁰⁾ found that short-term endurance training whilst fasted produced largely similar adaptations to training in the fed state. They did, however, find that upregulation of fat transporter protein was totally inhibited in the fed state. Furthermore, they found that glycogen breakdown was significantly lower when training took place when fed, but the reason for this glycogen sparing is currently unclear. This could have major implications on both public health and athletic performance. From a performance stand point, if fasted training regimes do bring about positive adaptations, that remain present even when carbohydrates are consumed for competition, it has the potential to give endurance athletes the edge over their opponents. Future studies should investigate whether the glycogen sparing seen when training in the fasted state, along with other adaptations, allow one to work aerobically for longer, rely on fat stores for energy for longer at higher intensities and increase time to exhaustion. If it became clear this was the case, it could revolutionise training techniques and see improved performance in many athletic events.

From a public health perspective, the benefits of fasted exercise could hold even more importance. The scope could be broadened to study the effect of fasted exercise on weight loss: it is known that fasted exercise induces a change in

substrate utilisation, but no research has been carried out along these lines. If a study with a similar design to that of van Proeyen et al⁽³⁾ and De Bock et al⁽³⁰⁾ was to be carried out on individuals who are obese, it may lead to results showing fasted exercise induces more rapid weight loss than fed exercise. These potential findings would be beneficial for the application of weight loss programs to combat obesity. Increased fat utilisation would add to an already large number of benefits of obese individuals partaking in low-intensity exercise⁽³¹⁾. If exercising in the fasted state does lead to more rapid weight loss, it could lead to more people implementing it as part of a weight loss regime.

The reason this needs further research is because few studies have focussed on the effect fasted exercise has on weight loss, and those that have done so, have produced conflicting results. Paoli et al⁽²⁵⁾ found that resting energy expenditure was higher after exercising in the fed state, and that RER was in fact higher in the hours after exercising when fasted than after fed exercise. That study concluded that fasting before exercise does not enhance lipid utilisation, but that a light meal pre-exercise is advisable if fat loss is the main goal of the exercise. On the contrary, in a similar study conducted by Deighton et al⁽³²⁾, there was found to be no difference in RER between exercise trials, whilst resting energy expenditure was actually higher after exercising in the fasted state, rather than fed. If further research into this area produces clearer results suggesting fasted exercise is more effective for weight loss, the impact on health could be significant.

8. Conclusion

The major purpose of the study was to examine the interaction between nutritional status and substrate utilisation during a short bout of exercise. The study showed there was no significant difference between RER, and therefore substrate utilisation, when exercising in the fed or fasted state in either gender group, or the group as whole. These results are in line with previous studies that observed substrate utilisation during the fasted and fed states at 70% maximal exercise intensity. The results did show that women had a significantly lower RER when exercising in the fasted state than men did, suggesting that women utilise fat more readily than men. Due to the low number of people recruited for this study, more data should be collected to clarify this finding.

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10. Appendix

10.1 Ethical Approval Form



Monday, 13 November 2017
chs/ethics /approved

Brown, Christopher
BSc Biomedical Sciences [Health, Exercise & Nutrition]
Cardiff School of Health Sciences

Dear Applicant

Re: Application for Ethical Approval: The effect of exercising in a fasted state on substrate utilisation

Project Reference Number : 9521

Your ethics application, as shown above, was considered by the Biomedical Sciences Ethics Panel on 01-11-17.

I am pleased to inform you that your application for ethical approval was **APPROVED**.

Minor issues may still need addressing before you commence any work – if so these will be listed below.

1. Add BSc to form
2. Indicate "no" to human samples
3. Please include more information in part B2 of application
4. PIL section needs reference number

Where changes to the information sheet, consent form and/or procedures are deemed necessary you must submit revised versions to the relevant ethics inbox. If you are a student – your supervisor must do this on your behalf.

Note: Failure to comply with any issues listed above will nullify this approval.

Standard Conditions of Approval

1. Your Ethics Application has been given a Project Reference number as above. This **MUST** be quoted on all documentation relating to the project (e.g. consent forms, information sheets), together with the full project title.
2. All documents must also have the approved University Logo and the Version number in addition to the reference and project title as above.
3. A full Risk Assessment must be undertaken for this proposal, as appropriate, and be made available to the Committee if requested.
4. Any changes in connection to the proposal as approved, must be referred to the Panel/Committee for consideration **without delay quoting your Project Reference Number**. Changes to the proposed project may have ethical implications so must be approved.
5. Any untoward incident which occurs in connection with this proposal must be reported back to the Panel **without delay**.

Cardiff School of Health Sciences Western Avenue, Cardiff, CF5 2ED Ysgol Gwyddoniaethydd Caerdydd Khadarn Gwyddoniaeth, Caerdydd, CF5 2ED	Telephone/Ffôn +44 (0)117 2311 6070 Fax/Ffôn +44 (0)117 2311 6480 www.cardiffmet.ac.uk
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6. If your project involves the use of human samples, your approval is given on the condition that you or your supervisor notify the HTA Designated Individual of your intention to work with such material by completing the form entitled "Notification of Intention to Work with Human Samples". The form must be submitted to the PD (Sean Duggan), BEFORE any activity on this project is undertaken.

This approval expires on 01-11-18. It is your responsibility to reapply/request extension if necessary.

Yours sincerely



Dr Rachel Adams
Chair of BMS Ethics Panel
Cardiff School of Health Sciences

Tel : 029 20416855
E-mail : radams@cardiffmet.ac.uk
Cc:

PLEASE RETAIN THIS LETTER FOR REFERENCE