Gender Differences in Carbohydrate Metabolism and Carbohydrate Loading

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ABSTRACT

Prior to endurance competition, many endurance athletes participate in a carbohydrate loading regimen in order to help delay the onset of fatigue. The "classic" regimen generally includes an intense glycogen depleting training period of approximately two days followed by a glycogen loading period for 3-4 days, ingesting approximately 60-70% of total energy intake as carbohydrates, while the newer method does not consist of an intense glycogen depletion protocol. However, recent evidence has indicated that glycogen loading does not occur in the same manner for males and females, thus affecting performance. The scope of this literature review will include a brief description of the role of estradiol in relation to metabolism and gender differences seen in carbohydrate metabolism and loading. *Journal of the International Society of Sports Nutrition*. 3(1):28-35, 2006

Key words: glycogen loading, estradiol, eummenorrheic

INTRODUCTION

During bouts of endurance exercise lasting longer than 90 minutes, fatigue generally coincides with low muscle glycogen content, suggesting that simply ingesting carbohydrates during exercise and having glucose available in the blood is not enough to sustain exercise for an extended period of time. This notion led researchers to believe that it may be necessary to load one's body with glucose prior to the long exercise bout ¹. Carbohydrate loading (>6 g/kg/d) prior to participation in an endurance exercise competition has been shown to help delay the onset of fatigue by approximately 20% during endurance events lasting longer than 90 minutes 2-4. One exception to this rule is a study conducted by Burke et al.5, where seven trained cyclists ingesting 6-9 g/kg/d of carbohydrate showed no improvement in performance in a 100 kilometer timed trial, despite significantly increased muscle glycogen concentrations.

Nutritional recommendations for endurance athletes directly prior to competition have traditionally included an intense glycogen depleting training period of approximately two days followed by a glycogen loading period for 3-4 days, ingesting

approximately 60-70% of total energy intake as carbohydrates ⁶. These recommendations were constructed based on several studies conducted for performance enhancement for this type of athlete ⁷⁻⁹. However, most of these studies were conducted using male subjects and the onlv nutritional recommendations have since been used for populations including both males and females. This idea of normality across genders has recently proved to be incorrect as research has shown that there are many metabolic differences between genders that are stemmed from inherent hormonal differences. Specifically, the role of estradiol appears to be the mediator of these metabolic differences and could therefore affect the ability of a female to store, breakdown, and utilize carbohydrates in the same manner as a male ¹⁰⁻¹³. The scope of this literature review will include a brief description of the role of estradiol in relation to metabolism and gender differences seen in carbohydrate metabolism and loading.

THE ROLE OF ESTRADIOL IN METABOLISM

Estradiol primarily serves in development of female secondary sex characteristics. This steroid hormone is secreted cyclically by ovaries, peaking at the time of ovulation (see Figure 1) 14. In addition to assisting with development, estradiol has also been linked with various enzymes that play a role in energy Decreased circulating levels of metabolism. adipocyte lipoprotein lipase (LPL) has been correlated with high estradiol levels 15, which may result in enhanced triglyceride use in skeletal muscle at varying time points during the menstrual cycle ¹⁶-¹⁹. Some studies have also shown lipid utilization to be higher during the luteal phase of the menstrual cycle 20,21. In addition, there is no evidence that indicates variations in muscle glycogen concentrations throughout the menstrual cycle.

CARBOHYDRATE METABOLISM

Prior to examining gender related differences in carbohydrate loading, gender differences between carbohydrate metabolism must be examined. There appears to be no difference between genders in basal levels of muscle glycogen ^{13,22-24}, skeletal muscle GLUT-4 ²⁵, or hexokinase ¹³. However, females do appear to have an enhanced sensitivity to insulin in skeletal muscle ¹⁹, which would theoretically result in increased muscle glycogen storage, as well as enhanced fat storage, but the gender differences in insulin sensitivity are beyond the scope of this paper. In addition, there have yet to be any studies conducted assessing differences in glycogen synthase activity or branching enzyme ²⁶. Knowledge of changes of these enzymes could assist in the understanding of inherent metabolic differences that exist between genders.

DIFFERENCES IN SUBSTRATE UTILIZATION

While there appears to be no inherent difference at basal levels of muscle glycogen, there does appear to be a gender related difference in the actual breakdown and metabolism of carbohydrates (Table 1 provides a summary of specific studies). There is evidence that females tend to oxidize less total carbohydrate than men; however, the mechanism behind this phenomenon remains unclear ²⁶. One possible explanation could be that women have a lower rate of glucose appearance than that of men during endurance exercise ²⁷⁻²⁹. Roepstorff et al. ²⁹ assessed gender differences in substrate utilization during submaximal exercise. Males and females were matched according to peak oxygen consumption (VO₂peak) per kg lean body mass, training history, and physical activity level. All females were tested during mid-follicular phase of the menstrual cycle to avoid possible elevated lipid utilization that has been shown during the luteal phase ^{20,21}. Results of the study showed no gender differences for utilization of fatty acids, blood glucose, and glycogen, and that females oxidized more myocellular triglycerides than males, making up 25% of total VO₂peak for females and only 5% of total VO₂peak for males. This indicates that while there were no gender differences in the relative contribution of carbohydrates and lipids, there does seem to be a difference in the utilization of various lipid sources. This coincides with observations seen at rest, indicating greater utilization of fatty acids in the skeletal muscle rather than those derived from the adipose tissue ¹⁶⁻¹⁹.

Tarnopolsky et al. ^{22,23} conducted two similar studies evaluating glycogen depletion in the vastus lateralis during endurance exercise. The 1990 study ²² showed that women had significantly less glycogen depletion than men during treadmill running, but the 1995 study ²³ showed no gender difference in glycogen depletion during submaximal cycling. Despite no difference in glycogen depletion, the study did show that women oxidized significantly more lipid and less carbohydrate and protein compared to men during an exercise bout at 75% VO₂peak. These data concur with previous observations of greater lipid oxidation of females during submaximal endurance exercise ^{18,30,31}, but the source of fatty acids differ. It appears as though females tend to utilize more fatty acids from adipose tissue during submaximal exercise, whereas the main source of increased fatty acid utilization at rest is from skeletal muscle 16-19. Romijin and colleagues ^{32,33} also addressed intensity in relation to gender differences in substrate utilization in rats. In both studies, the participants exercised at intensities of 25, 65, and 85% of VO₂max. The 1993 study ³² showed that in males muscle triglyceride lipolysis was stimulated only at higher intensities and that at 65% VO₂max muscle glycogen and triglyceride oxidation decreased. The 2000 ³³ study showed that in females carbohydrate oxidation increased progressively with exercise intensity, and that the highest rate of fat oxidation was during exercise at 65% of VO₂max. When comparing the two studies, the authors concluded that after correction for differences in lean body mass, there were no differences between these results and previously reported data in endurance-trained men studied under the same conditions, except for slight differences in glucose metabolism during lowintensity exercise 33. It is important to note that not all of these studies controlled for variations of lipid metabolism during the menstrual cycle, thus the observed differences between rest and exercise may simply be due to measurement of fatty acid

utilization during different phases of the menstrual cycle.

Tarnopolsky also assessed glycogen use in the vastus lateralis via muscle biopsy over the course of a 31-day endurance cycling training protocol ¹³ and found no gender difference in glycogen sparing. A possible explanation of this contradiction with previous literature could be from different muscle recruitment between running and cycling. However, two other studies found that men use more glycogen than women during cycle exercise, but these two studies assessed glycogen use via a stable isotope method rather than muscle biopsy ^{28,34}.

Horton et al. ¹⁸ conducted a study to assess gender differences in fuel metabolism during long-duration exercise. Fuel oxidation was measured using indirect calorimetry and blood samples were drawn for circulating substrate and hormone levels. Results indicated that females expended more total energy from fat oxidation (50.9%) than that of men (43.7%), but less total energy from carbohydrates (45.7% for women and 53.1% for men). In addition to differences in fuel metabolism, males also had higher circulating levels of catecholamines. These results suggest that females may be more sensitive to the lipolytic actions of catecholamines than men.

EFFECTS OF ESTRADIOL ADMINISTRATION

With the knowledge that females tend to oxidize a greater amount of fatty acids than males, researchers then assessed the effects of estradiol administration to males. Results indicated that with the addition of 17β-estradiol to male rats, breakdown of muscle tissue was not diminished during endurance exercise ³⁵. In fact, administration of 17-β-estradiol to males and oophorectomized female rats resulted in hepatic and muscle glycogen sparing during endurance exercise ³⁶, increased intramuscular triglyceride content, and decreased adipocyte LPL ¹⁰. Similar results have been observed in human studies with 17-β-estradiol administration to males ³⁷ and ammenorrheic females ³⁸ resulting in a lower rate of glucose disappearance. The addition of 17-β-estradiol also appears to increase the activity of enzymes in fat oxidation pathways such as carnotine-palmitoyl transferase-1 (CPT-1) ³⁹. The role of CPT-1 is to transfer the fatty acyl group from CoA to carnitine on the cytosolic side of the inner membrane. Enhancement of this pathway allows for greater oxidation of fatty acids in skeletal muscle 40. Together, these findings suggest that the gender-related differences in carbohydrate metabolism and glycogen use in skeletal muscle may be due to both hepatic glycogen sparing ²⁶, as well as enhanced muscle triglyceride utilization ¹⁹.

CARBOHYDRATE LOADING

Increased dietary carbohydrate intake can result in enhanced endurance exercise performance by increasing muscle glycogen stores ²⁶, but may not in all instances as displayed by Burke et al. ⁵ Most of the early studies proving this performance enhancing strategy were conducted with predominantly male subjects ⁷⁻⁹. The need to assess gender differences with carbohydrate loading and glycogen storage stems from altered glycogen storing ability at different phases of the menstrual cycle 41 and the influence of estradiol on glycogen utilization 11,12,36. One of the first studies to evaluate a possible gender difference in glycogen storage after carbohydrate loading was conducted by Tarnopolsky et al. in 1995 ²³. In this study, male and female runners were asked to increase carbohydrate intake for four days, manipulating carbohydrate intake from 55% to 75% of total energy intake. The results of the study showed that men increased muscle glycogen content 41% and improved performance time 45% following a one-hour cycling bout, whereas women showed no increase in muscle glycogen and improved performance time by only 5%. The authors speculated that a possible reason for this genderrelated difference could be that the increase in dietary carbohydrate intake may not have been enough to elicit glycogen super-compensation. The female participants in this particular study ingested 6.4 g/kg body weight of carbohydrate, while the men ingested 8.2 g/kg body weight of carbohydrate. However, several studies suggest that there is a "carbohydrate loading threshold," of 8-10 g/kg that is necessary to achieve the ergogenic benefits of carbohydrate loading 7-9,42.

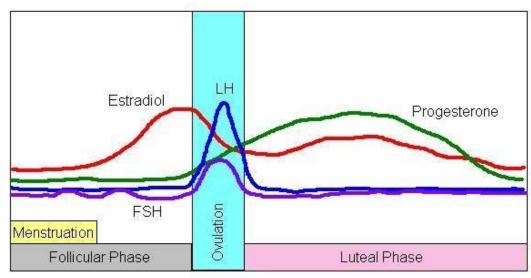
With this knowledge of a "carbohydrate loading threshold," James et al. ⁴³ also conducted a study to assess these gender differences, but rather than a moderate increase in dietary carbohydrate intake, participants ingested a carbohydrate level of 12 g/kg of fat free mass per day. James found that by regulating for fat free mass in conjunction with cessation of daily physical training, women and men were able to achieve similar levels of glycogen supercompensation.

After the "carbohydrate loading threshold" was determined, three other studies ^{13,43,44} assessed the loading ability of females at this level of dietary carbohydrate ingestion and found that in order to

achieve this intake, women would need to increase their total energy intake by 34% during the carbohydrate loading period. By increasing energy intake 34%, females were able to achieve similar concentrations of glycogen as males, and there were no gender differences in hexokinase activity 13. However, one study found that even with this increase in carbohydrate ingestion, the females were only able to achieve an increase in glycogen stores that was 50% of what was observed in males 44. Therefore, for a female to carbohydrate load and achieve benefits comparable to those of a male, the female must consume extra calories rather than simply increasing the percentage of dietary carbohydrate load. Specifically, a female needs to consume about 30% more daily energy for four days to ensure that carbohydrate intake achieves levels higher than 8 g/kg/d ¹³. For a 55 kg distance runner, this would be 440 g of carbohydrate, equaling about 1760 calories daily. If this runner is active and consuming 2500 calories per day, this would represent approximately 70% of the total daily energy intake from carbohydrate, which is in concurrence with current recommendations, and is only 5% higher than the 45-65% American Daily Recommendation for carbohydrate. One possible option that may assist with increased carbohydrate consumption and increased carbohydrate utilization is to employ both a loading method and carbohydrate supplementation prior to competition. Andrews et al. 1 showed that females used significantly more carbohydrates during submaximal performance following carbohydrate loading and supplementation compared to females who either only supplemented carbohydrates or ingested a placebo. However, the difference in performance time was negligible between three groups.

CONCLUSION AND FUTURE RECOMMENDATIONS

Despite many questions that remain to be answered in regards to gender differences in carbohydrate metabolism during endurance exercise, it appears as though female athletes do have the capacity for glycogen super-compensation at levels comparable to males when fed comparable amounts of carbohydrates relative to lean body mass ⁴³. In order to enhance glycogen-storing ability and obtain peak performance from female endurance athletes, it is necessary for future studies to control for menstrual cycle phase. In addition, future studies should assess the influence of estradiol on energy substrate utilization at rest and during various submaximal bouts of endurance exercise in relation to glycogen storage. With this research and knowledge, female athletes could not potentially erase physiological gender differences, but gender differences in performance as well.



1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 Days of Menstrual Cycle

Figure 1: Secretory cycle of female gonadal hormones during a 28-day menstrual cycle. Note the increase in estradiol during the follicular phase just before ovulation, and more even levels during the luteal phase after ovulation. Adapted from wikipedia.org

Author	Subject Population	er differences in substrate utiliza Dietary/Hormonal Protocol	Exercise Protocol	Results
Friedlander, 1998	17 healthy females	Glucose was infused during Two pretraining trials (45 and 65% of VO2 peak) and two posttraining trials [same absolute workload (65% of old VO2 peak) and same relative workload (65% of new VO2 peak)	5 days/wk, 1-h duration, 75% VO2peak	Glucose use is directly related to exercise intensity; training does reduce total carbohydrate oxidation
Carter, 2001	8 males	17 beta-estradiol at 3 mg/d was administered for 8 days	90 min cycling session	Short-term oral 17 beta-estradiol administration had no effect on substrate oxidation during exercise in men.
Roepstorff, 2002	7 males, 7 females; endurance trained	None	90 min of bicycle exercise at 58% VO2peak	In females, measured substrate oxidation accounted for 99% of the leg oxygen uptake, whereas in males 28% of leg oxygen uptake was unaccounted for in terms of measured oxidized lipid substrates
Galliven, 1997	7 women, 8 women	None	Study 1: high-intensity exercise at 90% VO2max; Study 2: moderate-intensity exercise at 70% VO2max in the AM and PM in the follicular (days 3-9), midcycle (days 10-16), and luteal (days 18-26) phases of the menstrual cycle	No significant in blood glucose levels; metabolic and hormonal responses to short-term, high-intensity exercise can be assessed with equal reliability in the AM and PM and that there are subtle differences in blood glucose responses to moderate-intensity exercise across menstrual cycle phase
Hackney, 1994	9 women	None	30-min treadmill run where intensity was increased every 10 min (35%, 60%, and 75% VO2peak); tests performed at midfollicular and the midfuteal phases of the menstrual cycle	The phase of the menstrual cycle in eumenorrheic women does influence metabolic substrate usage during low- to moderate-intensity submaximal exercise
Horton, 1998	14 men, 13 women	None	The interstitute of the control of the control of the cycling and 2 h of postexercise recovery	During exercise, women derived proportionally more of the total energy expended from fat oxidation, whereas men derived proportionally more energy from carbohydrate oxidation; Epinephrine and norepinephrine levels were greater during exercise in men than in women
Tarnopolsky, 1995	7 males and 8 females; endurance athletes	increase carbohydrate intake to75% of daily energy intake for a period of 4 days	Cycling at 75% VO2peak 60 min	Men increased muscle glycogen concentration 41% in response to dietary manipulation and showed an increase in performance time during an 85% VO2 peak trial (45%), whereas the women did not increase glycogen concentration (0%) or performance time (5%); The women oxidized significantly more lipid and less carbohydrate and protein compared with the men during exercise at 75% VO2-peak
Tarnopolsky, 1990	6 males, 6 females; endurance trained	None	Treadmill running at 65% VO2peak for 90- 101 min	Males showed greater muscle glycogen utilization (by 25%); during moderate-intensity long-duration exercise, females demonstrate greater lipid utilization and less carbohydrate and protein metabolism than equally trained and nourished males
Mittendorfer, 2002	5 males, 5 females	None	90 min of moderate- intensity at 50% VO2 peak on a cycle ergometer	Total fatty acid oxidation was similar in men and women, but the relative contribution of plasma FFA to total fatty acid oxidation was higher in women (76 +/- 5%) than in men (46 +/- 5%)
Tarnopolsky, 2001	6 males, 6 females; endurance trained	3 diets: habitual, high carbohydrate (75% total daily energy), and carbohydrate + extra energy (upward arrow~34% extra daily caloric intake)] for a 4-day period	None	Total glycogen concentration was higher for the men on the high carbohydrate and carbohydrate + extra energy trials compared with habitual, whereas women increased only on the carbohydrate + extra energy trial compared with habitual
Ruby, 2002	5 males, 6 females	None	Cycling for 25 min at 70 and 90% of O(2) uptake (VO(2)) at LT (70 and 90% LT	No differences between genders in the relative contribution of carbohydrate (CHO) to total energy expenditure; the relative contribution of blood glucose to total CHO oxidation was significantly higher in women

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