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.

Keywords: 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 only male subjects and the 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 metabolism. Decreased circulating levels of 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.

![Figure 1](http://wikipedia.org)

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 http://wikipedia.org ... 

**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 (VO\textsubscript{2peak}) 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 myocardial triglycerides than males, making up 25% of total VO\textsubscript{2peak} for females and only 5% of total VO\textsubscript{2peak} 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 low-intensity 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 17-β-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 amenorrheic 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 carnitine-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
male. 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 gender-related 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 super-compensation.

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.

References

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