REVIEW ARTICLE

ROLE OF SKELETAL MUSCLE GLYCOGEN IN EXERCISE

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INTRODUCTION

Glucose, the primary fuel for all body cells, is derived primarily from carbohydrates. If needed, glucose can also be metabolized from protein. After a meal, some of the glucose, which is not used immediately for fuel, travels to the liver and skeletal muscles, where it is converted to glycogen through the process of glycogenesis [1].

Glycogen is the major reservoir of carbohydrate in the body. It comprises of long chain polymers of glucose molecules containing 120,000 glucose units in each molecule. The body stores approximately 450-550 grams of glycogen within the muscles and liver that is used during exercise. Skeletal muscles are the largest reservoir of glycogen as three fourth of the total glycogen in body is stored in skeletal muscles. Although liver cells store glycogen up to 8-10% of their weight while muscle cells can store glycogen up to 1-3% of the muscle mass but muscle is much greater in quantity due to its greater mass [2]. When body's glucose level drops, the liver releases glucose into the blood stream by converting some of its glycogen back into glucose through glycogenolysis. Muscle cells, on the other hand, are unable to reconvert glycogen into glucose. Instead, they convert glycogen directly to fuel through a process called glycolysis [3].

This present article summarizes our understanding regarding the role of glycogen in enhancing the capability of skeletal muscles during exercise.

GLYCOGEN AS FUEL DURING EXERCISE

Glycolysis is a cellular anaerobic process in which muscle glycogen is broken down into pyruvic acid during exercise and rapidly produces a small amount of adenosine triphosphate (ATP); the necessary fuel for body cells. However, excessive accumulation of pyruvic acid in muscles can substantially slow down or even stop the process of ATP formation. It has been demonstrated that glycogen is stored in proximity to the site of contraction and sustains high rates of adenosine diphosphate (ADP) phosphorylation. Therefore, glycogen is viewed as the primary fuel for the maintenance of moderate to intense exercise [4].

During high intensity exercise, glycogen becomes the main fuel utilized by the skeletal muscles and there is depletion of muscle glycogen up to 65-85%. Christensen and Hansen established in 1939 that high pre-exercise glycogen levels exert a positive influence on time for exhaustion. The concentration of muscle and liver glycogen prior to the exercise plays an important role in endurance exercise capacity and to ensure optimal exercise performance [5]. The endurance athletes are encouraged to maximise the availability of muscle glycogen through ingestion of a high carbohydrate diet prior to the competition [6].

Muscle fiber type is another important factor implicated in the depletion of glycogen. Due to greater enzymatic capacity of the type II (red) muscle fibers, their glycogen is subjected to rapid depletion during exercise. However, their glycogen replenishment occurs at significantly greater rate than type I (white) muscle fibers [7, 8]

In aerobic exercise, glycogen has been associated with the increased work output and duration. Moreover, glycogen is the preferred substrate during endurance exercise with a consequential depletion of muscle glycogen stores [5, 9].

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Receive 31 July 2008: Accepted 10 Feb 2009

A linear relationship exists between the pre-exercise muscle glycogen levels in the range of 50–120 mmol/kg wet mass and its subsequent utilization during exercise [10, 11]. It is known that glycogen can bind glycogen phosphorylase and increases its activity, a process that suggests the enhanced glycogenolysis during exercise [12]. Muscle glucose uptake during exercise may also be influenced by pre-exercise muscle glycogen. The divergent results are related to the confounding effects of pre-trial exercise and dietary manipulations which have been used to produce differences in muscle glycogen [13, 14]. Alterations in plasma glucose, insulin (14) and catecholamine concentrations [15], secondary to high dietary carbohydrate or fat intake, can modulate the effects of muscle glycogen availability on glucose uptake [16]. These effects are largely eliminated in the perfused rat hind limb model, in which an inverse relationship between muscle glycogen and glucose uptake and transport during contractions has been clearly demonstrated [11]. Translocation of GLUT4 [17] and increase in AMP-activated protein kinase (AMPK) activity [18, 19] are enhanced in low muscle glycogen states and these mechanisms potentially mediate glycogen effects on glucose uptake. Whether GLUT4 is associated with glycogen, has not been definitively proved [20]. In relation to AMPK, it has recently been demonstrated that b subunit of AMPK has a glycogen-binding domain that targets AMPK to glycogen [14]. An inverse relationship between leg glucose uptake during exercise and the intramuscular glucose-6-phosphate concentration has been demonstrated, implying that elevated muscle glycogen may also inhibit glucose uptake via effects on hexokinase and glucose metabolism [20]. Depletion of muscle glycogen during exercise activates glycogen synthase, resulting in a faster rate of glycogen resynthesis in the early post-exercise period [21, 22]. The absence of glycogen degradation during exercise in patients with McArdle's disease is associated with a decrease in glycogen synthase activity [23]. The link between glycogen and glycogen synthase may be mediated by protein phosphatase 1, which is targeted to the glycogen molecule. The regulatory or glycogen targeting subunit of protein phosphatase 1 is essential for the exercise-induced activation of glycogen synthase in skeletal muscle [24].

EFFECT OF GLYCOGEN ON EXERCISE COMPLIANCE

Endurance exercise at intensities up to 70-80% of maximal oxygen consumption (VO2 max) substantially lowers muscle glycogen concentration and subsequently leads to the inability of muscles to maintain exercise intensity at 70-80% VO2 max [25]. Therefore, it has been recommended that muscle glycogen must be restored between daily training sessions to facilitate optimal training capabilities [26]. Even if energy intake matches energy expenditure, but reduced muscle glycogen has been associated to the complaints of local muscular fatigue, difficulty in completing the performance sessions, increased ratings of perceived exertion and slightly higher oxygen because of its efficient energy yield per liter of oxygen consumed. Some of the studies suggest that weight training is associated consumption [27, 28]. The reduction in muscle glycogen by 20% due to inadequate energy intake declines the training compliance significantly [28].

EFFECT OF GLYCOGEN ON SKELETAL MUSCLE FATIGUE

Low skeletal muscle glycogen is known to promote skeletal muscle fatigue. In athletes working at 65-85% VO2max, fatigue occurs concurrently with the depletion of muscle glycogen. Furthermore, the time to fatigue is directly proportional to the initial muscle glycogen concentration [29, 30]. The glycogenolysis occurs most rapidily during the first 20-30 minutes of exercise at 75% VO2max which is followed by a slower decline in muscle glycogen until fatigue occurs that is related to muscle glycogen depletion after about 60 minutes in untrained subjects [31]. Barnes et al conducted a study in three different types of rat strains, Tg-Prkag3225Q (increased muscle glycogen), wild type (normal muscle glycogen) and Prkag 3225Q (decreased muscle glycogen). Extensor digitorum longus (EDL) muscles of Tg-Prkag 3225Q mice were found fatigue resistant manifested by the increased ability to sustain work compared with wild-type mice. In contrast, EDL muscles of Prkag 3225Q mice were found fatigue prone and manifested the decreased time to fatigue. These findings provide direct evidence of higher skeletal muscle glycogen content leading to delay in muscle fatigue [32]. Although not scientifically tested, athletes with low muscle glycogen concentrations have been proposed to be more susceptible to muscle injury [33].

EFFECT OF GLYCOGEN ON MAXIMAL MUSCULAR STRENGTH

Skeletal muscle glycogen is regarded as essential to promote skeletal muscle strength. In various studies the effect of different exercise protocols on muscle strength has been observed and increased muscle glycogen content was found to be associated with better performance. In a study, the glycogen exhaustion of fast twitch fiber type lead to impaired maximal muscular strength produced during a single dynamic contraction while muscle fatigue was increased in slow fibers [34]. In a study, consumption of a moderate (5 g/ kg of body mass per day) carbohydrate diet maintained muscle glycogen concentrations at120mmol/ kg wet weight while athletes consuming the high-carbohydrate diet (10 g/ kg of body mass per day) had a progressive (65%) increase in glycogen stores to 155mmol /kg wet weight. While all participants were able to successfully complete the prescribed training sessions, athletes consuming the high-carbohydrate diet showed improvement of up to 11% in muscle strength as compared to only 2% in those consuming the moderate-carbohydrate diet [35]. Similar results were found in studies [36-41] using different exercise and diet protocols. These results demonstrate that high muscle glycogen stores lead to significantly improved muscle strength.

EFFECT OF GLYCOGEN ON LIPID AND PROTEINS UTILIZATION DURING EXERCISE

Glucose is needed by the central nervous system to keep the body functioning. Therefore, during periods of moderate exercise longer than 20 minutes, the body works to conserve stored muscle and liver glycogen. It does so by reducing the percentage of fuel derived from glycogen to 40% or 50%, with the remainder supplied by fat [41].

During exercise periods lasting longer than 4 or five hours, as much as 60% to 85% of fuel produced by oxidation may be derived from fat. Fats need carbohydrates in order to burn efficiently. The breakdown of carbohydrates generates oxaloacetic acid, which is needed for the breakdown of fats into fuel. If insufficient carbohydrate levels exist, the concentration of oxaloacetic acid may also drop, making it difficult for the body to continue producing a high level of fuel from fat. Although body can break down fats in the absence of carbohydrates but it does so at a slower rate [42]. Lipid oxidation during exercise is increased when pre-exercise muscle glycogen is low consequently leading to increased plasma non-esterified fatty acid (NEFA) uptake that is secondary to the higher plasma levels. Because NEFA clearance during exercise does not differ between low and high glycogen conditions. Presumably the higher plasma NEFA levels are a result of increased adipose tissue lipolysis as a consequence of lower plasma insulin levels and increased sympathetic activity, as reflected by higher catecholamine levels. Increased b acetyl-CoA carboxylase phosphorylation, mediated via increased AMPK activity, may contribute to the enhanced fat oxidation. The influence of muscle glycogen on intramuscular triacylglycerol utilisation has not been studied to date [43].

Low glycogen availability has also been shown to increase net protein degradation, measured by tyrosine and phenylalanine release and is associated with greater activation of the branched-chain oxoacid dehydrogenase in skeletal muscle implying increased amino acid oxidation [44].

POST - EXERCISE GLYCOGEN RESYNTHESIS

Following exhaustive exercise, the body needs to replenish the depleted glycogen reserves. Increasing the intake of carbohydrates promotes the storage of glycogen in the liver and muscles. Therefore, a diet consisting of approximately 60% or more of complex carbohydrates (starch) is recommended after strenuous exercise in order to promote glycogen replenishment. With adequate consumption of complex carbohydrates, coupled with extra rest, most of the glycogen replenishment occurs within 24 hours. If a diet high in protein and fat is consumed, glycogen replenishment may take longer than one week [45].

The time for glycogen replenishment after exercise-induced depletion had been demonstrated 48 hours or more, while recent data have controverted this thought. The carbohydrate intake up to 550-625 grams per day has been documented to restore muscle glycogen to the pre-exercise level within 22 hours between exercise sessions [27]. These findings were supported by another study in which carbohydrate intake of 3100 kcal resulted in complete resynthesis of glycogen within 24 hours. There also appears to be a two-hour optimal window immediately after the cessation of exercise for the administration of carbohydrate [29]. Simple carbohydrates are the preferred replacement during this replenishment period [46].

Normally, 2% of glycogen is resynthesized per hour immediately after the initial 2 hours of exercise. With administration of 50 grams of carbohydrate for every 2 hours after the completion of exercise, the rate of resynthesis rises to 5% per hour, but does not rise further when additional carbohydrates are administered [24]. Administration of 0.7grams carbohydrates per kg body weight every two hours is another strategy that appears to maximize the rate of glycogen resynthesis [25]. There is also some evidence that even smaller amounts of carbohydrates (28 grams every 15 minutes) may induce even greater repletion rates [27]. However, at least 20 hours are required to recover muscle glycogen stores, even when the diet is optimal. So, athletes working out two times per day should complete one workout at a diminished workload to decrease the reliance on glycogen reserves and allow their replenishment [26].

CONCLUSION

The skeletal muscle glycogen content has important functional implications, not only in athletes, but also within industry workers who consistently undergo depletion of glycogen stores due to prolonged bouts of exertion, or extended lifting tasks which are glycolytic in nature or induce the myofibrillar ischemia due to static contractions.

Athletes participating in weight training satisfactorily maintained muscle glycogen stores by a balanced and calorifically sufficient diet. It is important that an excess carbohydrate intake, exceeding the energy expenditure, will result in weight gain. However, individuals undergoing concurrent aerobic exercise with high-intensity resistance training and/or completing multiple training sessions per day, should be concerned about the maintenance of glycogen stores, because glycogen depletion reduces work output and duration. The larger the stores of glycogen in liver and muscles, the longer and effectively an athlete can perform during prolonged strenuous exercise. Therefore, carbohydrates should make at least 60% to 70% of an athlete's diet.

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