REVIEW ARTICLE

Sports Med 2003; 33 (2): 117-144
0112-1642/03/0002-0117/$30.00/0

Determinants of Post-Exercise Glycogen Synthesis During Short-Term Recovery

Roy Jentjens and *Asker E. Jeukendrup*

Human Performance Laboratory, School of Sport and Exercise Sciences, University of Birmingham, Edgbaston, Birmingham, UK

Contents

Abstract

The pattern of muscle glycogen synthesis following glycogen-depleting exercise occurs in two phases. Initially, there is a period of rapid synthesis of muscle glycogen that does not require the presence of insulin and lasts about 30–60 minutes. This rapid phase of muscle glycogen synthesis is characterised by an exercise-induced translocation of glucose transporter carrier protein-4 to the cell surface, leading to an increased permeability of the muscle membrane to glucose. Following this rapid phase of glycogen synthesis, muscle glycogen synthesis occurs at a much slower rate and this phase can last for several hours. Both muscle contraction and insulin have been shown to increase the activity of glycogen synthase, the rate-limiting enzyme in glycogen synthesis. Furthermore, it has been shown that muscle glycogen concentration is a potent regulator of glycogen

synthase. Low muscle glycogen concentrations following exercise are associated with an increased rate of glucose transport and an increased capacity to convert glucose into glycogen.

The highest muscle glycogen synthesis rates have been reported when large amounts of carbohydrate (1.0–1.85 g/kg/h) are consumed immediately post--exercise and at 15–60 minute intervals thereafter, for up to 5 hours post-exercise. When carbohydrate ingestion is delayed by several hours, this may lead to ~50% lower rates of muscle glycogen synthesis. The addition of certain amino acids and/or proteins to a carbohydrate supplement can increase muscle glycogen synthesis rates, most probably because of an enhanced insulin response. However, when carbohydrate intake is high (≥1.2 g/kg/h) and provided at regular intervals, a further increase in insulin concentrations by additional supplementation of protein and/or amino acids does not further increase the rate of muscle glycogen synthesis. Thus, when carbohydrate intake is insufficient (<1.2 g/kg/h), the addition of certain amino acids and/or proteins may be beneficial for muscle glycogen synthesis. Furthermore, ingestion of insulinotropic protein and/or amino acid mixtures might stimulate post-exercise net muscle protein anabolism. Suggestions have been made that carbohydrate availability is the main limiting factor for glycogen synthesis. A large part of the ingested glucose that enters the bloodstream appears to be extracted by tissues other than the exercise muscle (i.e. liver, other muscle groups or fat tissue) and may therefore limit the amount of glucose available to maximise muscle glycogen synthesis rates. Furthermore, intestinal glucose absorption may also be a rate-limiting factor for muscle glycogen synthesis when large quantities (>1 g/min) of glucose are ingested following exercise.

Muscle glycogen is the primary fuel source during prolonged moderate-to-high intensity exercise.[1] Fatigue during prolonged exercise is often associated with muscle glycogen depletion[2,3] and therefore high pre-exercise muscle glycogen levels are believed to be essential for optimal performance.[4-7] The restoration of muscle glycogen stores following exhaustive exercise is probably the most important factor determining the time needed to recover. It appears that muscle glycogen synthesis in the post-exercise recovery period has such high metabolic priority that intramuscular triglycerides are broken down at an increased rate to supply lipid fuel for oxidative muscle metabolism.[8] Depending on the extent of glycogen depletion and provided that sufficient carbohydrate (CHO) is consumed, the complete restoration of muscle glycogen can occur within 24 hours.[2,9-11] Furthermore, it has been shown that when a high-CHO diet is consumed for at least 3 days after exercise, muscle glycogen concentrations can increase to above 'normal' levels in the previously exercised muscle, a process often referred to as glycogen supercompensation.[12]

While dietary interventions to achieve supercompensated muscle glycogen concentrations in preparation for competition have been well defined,[13-16] these procedures do not address the problem of athletic events that require rapid synthesis of muscle glycogen within a short period of time (<8 hours). Athletes may train or compete more than once per day, and some events require qualification <8 hours before the actual event. Although it is unlikely that muscle glycogen stores can be completely resynthesised within hours, it would be of benefit to the athlete to define nutrition guidelines that would maximise the rate of glycogen storage in the early hours post-exercise.

In this review a detailed summary of the literature on post-exercise muscle glycogen synthesis during short-term recovery (<8 hours) will be presented.

The main questions that will be addressed are: what are the best nutritional strategies to obtain maximal muscle glycogen synthesis rates following exercise and which factors limit the ability of skeletal muscle to synthesise glycogen. The purpose of this review is to give a comprehensive overview and critical discussion of the research that has addressed the factors affecting post-exercise muscle glycogen synthesis. This review will conclude with guidelines for CHO ingestion post-exercise to achieve high rates of muscle glycogen synthesis and to maintain high muscle glycogen concentrations for daily training or competition. It should be noted that results of different studies are sometimes difficult to compare because of differences in experimental designs, such as variations in biopsy methods, site of biopsy taking, timing of biopsy taking, pre- and post-exercise muscle glycogen concentrations and training status of participants. The reader should keep this in mind when interpreting the results of various studies. In order to facilitate comparison of data between studies, muscle glycogen synthesis rates in this review are all expressed as mmol/kg dry weight (dw)/h, unless otherwise stated. Therefore, muscle glycogen concentrations reported in the literature as mmol/kg wet weight (ww), were multiplied by 4.28 to account for water weight.[17]

1. Regulation of Muscle Glycogen Synthesis

1.1 Glucose Transport

Replenishment of muscle or liver glycogen stores requires glucose derived from the diet or glucose resulting from gluconeogenesis. In the postabsorbtive state, the majority of glucose for glycogen synthesis comes from orally ingested CHO. The first step in the pathway of muscle glycogen synthesis is the transport of glucose across the muscle cell membrane (figure 1). Glucose transport in the skeletal muscle occurs primarily by facilitated diffusion, utilising glucose transporter carrier proteins (GLUT).[18] Two isoforms of the facilitative glucose transporter family, GLUT-4 and GLUT-1, are expressed in the skeletal muscle.[19] GLUT-1 is present in very low abundance in skeletal muscle and is suggested to play a role in basal glucose uptake by the muscle.[20] In the unstimulated state, the GLUT-4 isoform is located intracellularly and is translocated to the plasma membrane when insulin binds to its receptor. Muscle contractions stimulate glucose transport directly, independent of insulin action, by inducing the GLUT-4 transporter to the cell surface (figure 1).[21,22] The observation that maximal insulin stimulation and contraction have additive effects on translocation of GLUT-4 in muscle may suggest the presence of two different pools of glucose transporters.[18,21] However, the exact intracellular locations of the putative exercise- and insulin-stimulated GLUT-4 pools (pools A and B, respectively in figure 1) have not yet been elucidated. The maximal rate of muscle glucose transport is determined by both the total GLUT-4 concentration and the proportion that is translocated to the cell membrane in response to insulin and/or muscle contraction.[23] Furthermore, the intracellular signalling pathways that lead to insulin- and exercise-stimulated GLUT-4 translocation are also different. Insulin activates a phosphatidylinositol-3-kinase-dependent mechanism, whereas the contraction signal may be initiated by calcium (Ca^{2+}) release from the sarcoplasmic reticulum, leading to the activation of other signalling intermediaries (e.g. protein kinase C). Other possible signals that trigger exercise-induced GLUT-4 translocation are: increased concentrations of nitric oxide and adenosine, increased activity of AMPK and low muscle glycogen concentrations. The importance of the GLUT-4 transporters for muscle glycogen synthesis will be further discussed in section 2.1. In addition, for more detailed information on this topic the reader is referred to reviews by Ivy and Kuo[24] and by Richter et al.[25]

1.2 Conversion of Glucose to Glycogen

Upon entering the muscle cell, glucose is rapidly phosphorylated to glucose-6-phosphate (G6P) by the enzyme hexokinase (figure 1).[26] G6P is then converted to glucose-1-phospate (G1P) by the action of phosphoglucomutase. Thereafter, uridine diphosphate glucose (UDP-glucose) is synthesised

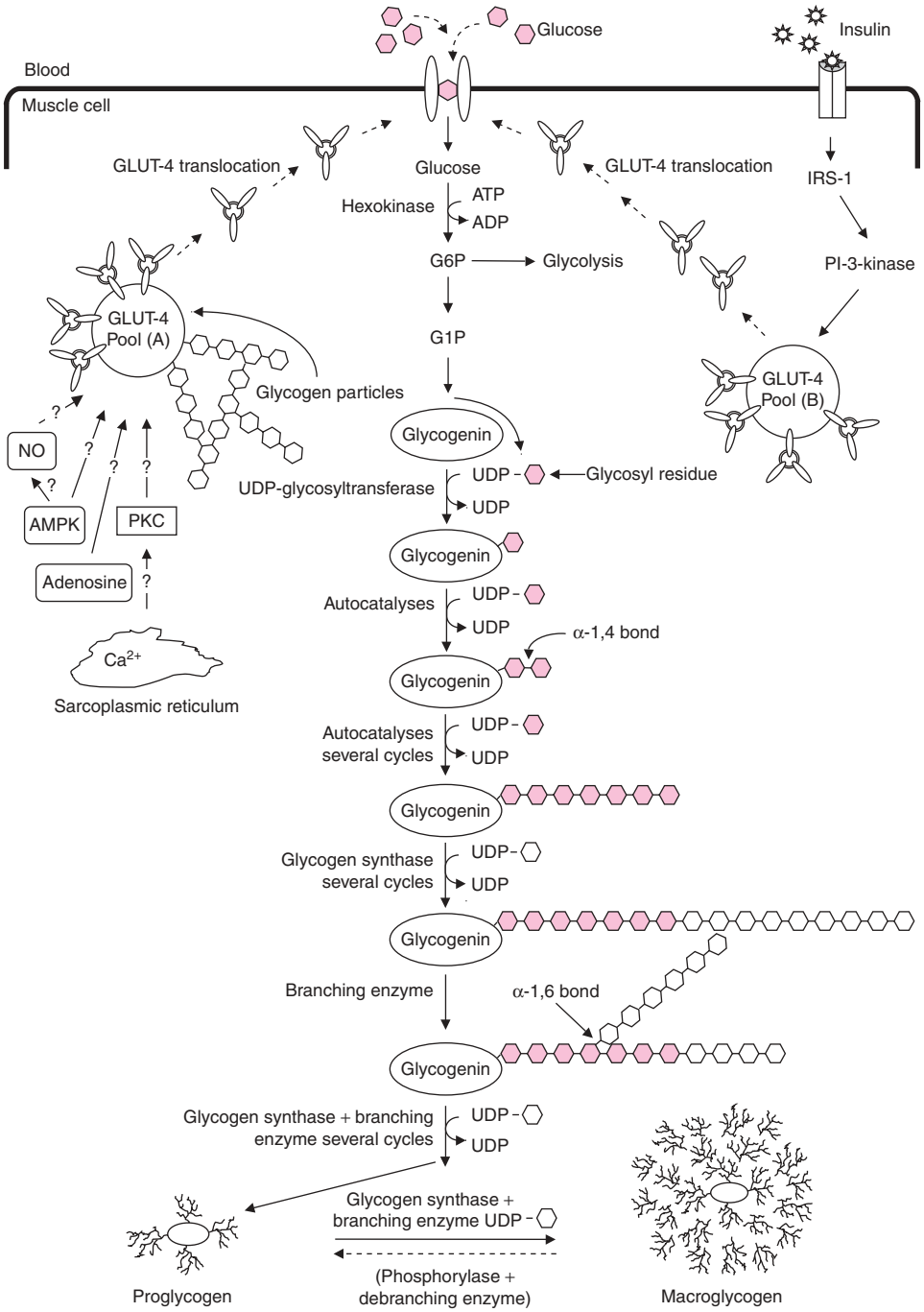

Fig. 1. Schematic representation of muscle glycogen synthesis in skeletal muscle (see sections 1.1 and 1.2 for details). **AMPK** = AMP-activated protein kinase; **G1P** = glucose-1-phosphate; **G6P** = glucose-6-phosphate; **GLUT-4** = glucose transporter-4; **IRS-1** = insulin receptor substrate-1; **NO** = nitric oxide; **PI-3-kinase** = phosphatidylinositol-3-kinase; **PKC** = protein kinase C; **UDP** = uridine diphosphate.

from G1P and uridine triphosphate (UTP), catalysed by G1P uridyltransferase.

The glucose residue is then attached by an α-1,4 glycosidic bond to the free end of a pre-existing glycogen molecule and UDP is subsequently released from the enzyme. The incorporation of the glycosyl residue from UDP-glucose into glycogen is catalysed by glycogen synthase.[27] Of note, glycogen contains many branches, with branching points formed by α-1,6 bonds after every 8–12 glucose units (figure 1). These glycogen branches provide numerous free ends that are readily accessible for glycogen synthesis or degradation. The branch points are introduced into the glycogen structure by the activity of amylo-(1,4-1,6)-transglycosylase, also termed the branching enzyme. This enzyme transfers a fragment of 6–7 glucose residues (detached from a polymer of at least 11 glucose residues long) to a neighbouring chain, where it is reattached by an α-1,6 bond (figure 1).

Until recently, the source of the first glycogen molecule that might act as a primer in glycogen synthesis was unknown. It has been demonstrated that a protein called glycogenin is located at the core of the glycogen molecules.[28-30] Glycogenin is characterised by autocatalytic activity that enables it to transfer glucose residues from UDP-glucose to itself. Before glycogenin is able to synthesise a glycogen molecule, it is considered that glycogenin and glycogen synthase must first form a tight 1:1 complex.[30,31] Glycogenin subsequently generates an oligosaccharide primer of 7–11 glycosyl residues, which serves as a substrate for glycogen synthase (figure 1). The branching enzyme and glycogen synthase then act to catalyse the formation of two physiologically distinct pools of glycogen: proglycogen and macroglycogen.[28] The formation of proglycogen occurs first and as more glycosyl units are added, proglycogen expands to the macroglycogen form (figure 1). The two glycogen pools have identical protein contents but differ in the number of glycogen units, with proglycogen being the smaller glycogen entity with a molecular mass of up to 4×10^5 Da, whereas macroglycogen can reach a molecular mass of 10^7 kDa.[32,33] Furthermore, proglycogen and macroglycogen appear to differ in their rates of degradation and synthesis and in their sensitivity to dietary manipulation.[32-34] It has been reported that proglycogen is more sensitive to dietary CHO and is synthesised more rapidly following post-exercise glycogen depletion, reaching a plateau after 24 hours. On the other hand, the synthesis of macroglycogen is relatively slow and more constant and can last for at least 48 hours post-exercise.[32] The macroglycogen pool is also responsible for glycogen supercompensation, observed when a high-CHO diet is consumed in the days following glycogen-depleting exercise.[32] At present, the exact regulatory mechanisms of the two glycogen pools and the role of nutrition on the synthesis of these glycogen pools are largely unknown. Most studies in this review have reported 'total' muscle glycogen concentrations and have not distinguished between sub glycogen pools. More research is needed to better understand the factors that regulate the balance between glycogenin, proglycogen and macroglycogen.

2. The Rapid and Slow Phases of Glycogen Synthesis

Several studies have demonstrated that the pattern of muscle glycogen synthesis following exercise-induced glycogen depletion occurs in a biphasic manner.[35-41] When the results from a large number of studies are combined and graphed, an exponential relationship has been found between the rate of muscle glycogen synthesis and post-exercise recovery time.[42] Initially, there is a rapid phase of glycogen synthesis, which generally lasts between 30–60 minutes. This phase can proceed without the presence of insulin[38,39] and is therefore also called the insulin-independent phase. It has been suggested that the rapid phase only occurs when post-exercise muscle glycogen concentrations are lower than 128–150 mmol/kg dw[38,41] and CHO is provided immediately after exercise.[43] Following this rapid phase of glycogen synthesis, muscle glycogen synthesis occurs at a much slower rate (slow phase or insulin-dependent phase) and, in the presence of CHO availability and high insulin levels, this phase can last for several hours.[7] In sections 2.1 and 2.2

the mechanisms and regulating factors responsible for the two phases of muscle glycogen synthesis will be discussed.

2.1 The Rapid Phase of Muscle Glycogen Synthesis

A potential mechanism that may contribute to the rapid phase of muscle glycogen synthesis is an increased glycogen synthase activity immediately following exercise. Like many other enzymes, this enzyme exists in an inactive non-phosphorylated (D) form and a more active phosphorylated (I) form.[27] The conversion of glycogen synthase D into the more active I form involves the dephosphorylation of glycogen synthase D by a glycogen synthase phosphatase-I enzyme. Both muscle contraction and insulin have been shown to increase glycogen synthase activity.[11,27,44-46] Several studies have demonstrated a negative correlation between post-exercise muscle glycogen concentration and the activity of glycogen synthase following exercise.[47-49] It has recently been demonstrated that muscle glycogen concentration is a far more potent regulator of glycogen synthase activity than insulin or muscle contraction.[46] The reason for the inverse relationship between muscle glycogen content and glycogen synthase I activity may be related to binding of both glycogen synthase and glycogen synthase phosphatase to glycogen as part of a glycogen protein complex that also includes glycogen phosphorylase.[24] When the glycogen concentration decreases, both glycogen synthase phosphatase and glycogen synthase are released. The active phosphatase then catalyses dephosphorylation of glycogen synthase converting it to its I form,[24] which may lead to increased glycogen synthesis rates.[50] It is therefore likely that an increased glycogen synthase activity induced by low post-exercise muscle glycogen concentrations is partly responsible for the rapid phase of muscle glycogen synthesis.

Although glycogen synthase is suggested to be the rate-limiting enzyme for muscle glycogen synthesis, a fast glycogen synthesis rate can only proceed when adequate glucose is available in the muscle. Thus, another important mechanism responsible for the rapid increase in muscle glycogen after exercise might be a protracted increase in the permeability of the muscle cell membrane to glucose.[51-53] The relative importance of glycogen synthase and glucose transport in controlling the rate of glycogen synthesis has been debated over the years. Recently, much attention has focused on the importance of glucose transporters in determining the rate of glycogen synthesis,[54,55] and a widely held view is that most of the control is at the level of the glucose transporter.[56,57]

Several studies in animals[21,54,58-60] and in humans[22,50,61] have shown that an acute exercise session can initiate an increase in muscle GLUT-4 protein expression, which can be further enhanced when a CHO supplement is provided following exercise.[54] More importantly, a positive correlation ($r = 0.63$) has been found between muscle GLUT-4 protein concentration and glycogen storage in human skeletal muscle during a 6-hour post-exercise period.[50] This finding is further supported by the results of a study in genetically modified mice that were GLUT-4 deficient.[62] Muscle glycogen levels were completely restored 5 hours post-exercise in muscles that contained GLUT-4, whereas no significant glycogen accumulation was observed in skeletal muscle lacking GLUT-4 protein.[62] It has been suggested that the increase in glucose transport immediately after exercise is the result of an increased number of GLUT-4 transporters at the plasma membrane rather than increased transport capacity of GLUT-4 transporters (intrinsic activity).[24,63]

The mechanism(s) responsible for the contraction-induced GLUT-4 translocation in skeletal muscle is/are largely unknown. Possible signals that trigger GLUT-4 translocation in contracting muscle are increased concentrations of intracellular Ca^{2+}, nitric oxide and adenosine, increased activity of AMP-activated protein kinase (AMPK) and low muscle glycogen concentrations (figure 1).[25,63] It is unlikely that contraction-induced muscle glucose transport is regulated by the action of one signalling pathway. Exercise-stimulated glucose transport is most probably regulated by several intracellular signalling mechanisms that are activated to different

extents according to the metabolic needs of the muscle. Of note, muscle glycogen content has been suggested as an important modulator of signalling events in glucose metabolism during and after exercise.[25,63] Fell et al.[64] provided indirect evidence suggesting that a low muscle glycogen content following exercise is associated with an increased rate of glucose transport into the muscle and an increased capacity to convert glucose into glycogen. An inverse relationship has been found between muscle glycogen concentration and insulin- and contraction-induced glucose transport.[24,51,65,66] This raises the possibility that glycogen may have some control over the number of GLUT-4 transporters that can be actively associated with the plasma membrane.[24] The mechanism by which glycogen might control the plasma membrane GLUT-4 protein concentration is not completely understood. One possible mechanism by which glycogen levels could influence glucose transport is the binding of GLUT-4 protein or GLUT-4-containing vesicles to the glycogen particles (figure 1). Coderre et al.[67] postulated that a large portion of the GLUT-4-containing vesicles in skeletal muscle might be bound to glycogen. This suggests that the number of GLUT-4-containing vesicles available for translocation in response to insulin or contraction may increase when the muscle glycogen concentration is low, and decrease when the muscle glycogen concentration is high. One may question whether glycogen depletion itself, or another metabolite or signal, is the promoting factor of increased GLUT-4 transporters at the cell membrane after glycogen-depleting exercise.[65]

In conclusion, post-exercise glycogen depletion may induce an increase in the number of GLUT-4 transporters at the plasma membrane and in glycogen synthase activity, both likely to be responsible for the rapid phase of muscle glycogen synthesis.

2.2 The Slow Phase of Muscle Glycogen Synthesis

The slow phase of muscle glycogen synthesis is characterised by a marked increase in the sensitivity of muscle glucose uptake and glycogen synthesis to insulin.[51] Insulin sensitivity is defined as the insulin concentration that elicits 50% of the maximal response.[68,69] The increased muscle insulin sensitivity after exercise can persist for a very long period of time (>48 hours) depending on CHO intake and the magnitude of glycogen concentration.[51]

Increased insulin sensitivity of skeletal muscle glucose uptake is usually observed after a single bout of exercise.[63,68,70] Hansen et al.[69] have shown that the increase in glucose transport, resulting from increased insulin sensitivity 3.5 hours after a single bout of exercise, was mediated by translocation of more GLUT-4 transporters to the cell surface. The magnitude of the increase in GLUT-4 translocation closely matched the increase in glucose transport activity, indicating that an increase in GLUT-4 intrinsic activity does not play a role in the exercise-induced increase in insulin sensitivity.

Recently, it has been demonstrated that prior exercise also increases the insulin sensitivity of glycogen synthase activation.[70] The mechanism for this increased insulin sensitivity is poorly understood but could possibly be ascribed to low glycogen levels caused by exercise.[46,70] In support of this hypothesis, Derave et al.[71] demonstrated that insulin-stimulated glucose transport in fast-twitch muscle of rats was significantly higher when muscle glycogen concentrations were low compared with high muscle glycogen concentrations. The enhanced insulin-stimulated glucose uptake in muscle with low glycogen content has been associated with an increased activity of protein kinase B (PKB; also called Akt). Interestingly, the effect of muscle glycogen content on insulin-stimulated glucose transport was less pronounced in mixed-fibre type muscle and was absent in slow-twitch muscle. These findings suggest that the effect of muscle glycogen content on insulin-stimulated glucose transport is fibre type-specific or, more likely, muscle glycogen is not the only factor responsible for the enhanced insulin sensitivity after exercise.

Gao et al.[72] have shown that the exercise-induced increase in insulin sensitivity depends on a serum factor present during the contraction period. Furthermore, it has been recently suggested that the

enhanced insulin sensitivity of muscle glucose transport following exercise is mediated by activation of AMPK and involves a step beyond PKB.[73] It was speculated that AMPK phosphorylates a protein that is involved in the translocation of GLUT-4 to the cell surface in response to a given submaximal insulin level. In addition, several studies have suggested that the exercise-induced increase in muscle insulin sensitivity is partly a result of enhanced activation of insulin-signalling molecules.[18,69-71] However, it is currently not known at which level of the insulin-signalling pathway this enhancement would occur.[63,70] From the above studies is seems reasonable to conclude that increased muscle insulin sensitivity following exercise is regulated by a combination of factors, including muscle glycogen concentration, serum factor(s), AMPK and insulin-signalling molecules.

3. Timing of Carbohydrate (CHO) Intake

A study by Ivy et al.[43] demonstrated 45% lower muscle glycogen synthesis rates when CHO ingestion post-exercise was delayed by 2 hours compared with the ingestion of CHO immediately post-exercise (table I). The authors suggested that the reduced rate of muscle glycogen storage was a result of reduced muscle glucose uptake. An exercise-induced increase in post-exercise glucose transport has been shown to reverse rapidly in the absence of CHO.[51,58] Goodyear et al.[58] demonstrated that 2 hours post-exercise, the number of glucose transporters associated with the plasma membrane from rat skeletal muscle had returned to pre-exercise concentrations. It is therefore not unlikely that the delayed post-exercise CHO feeding in the study of Ivy et al.[43] was accompanied by a reduced number of glucose transporters, which may have contributed to the lower muscle glycogen synthesis rates. In a study by Parkin et al.,[74] delayed ingestion of a high glycemic index meal by 2 hours did not affect the rate of muscle glycogen synthesis during an 8-hour post-exercise period. These results seem in contrast with the previous results of Ivy et al.[43] However, in the study of Ivy et al.[43] muscle glycogen synthesis rates were determined over a 4-hour post-exercise period, while Parkin et al.[74] calculated muscle glycogen synthesis rates over an 8-hour period. Muscle glycogen has been found to inhibit its own synthesis.[75] It is not unlikely that muscle glycogen synthesis rates in the study of Parkin et al.[74] were higher in the initial post-exercise period (the first 4–6 hours post-exercise) with immediate CHO feeding compared with delayed CHO feeding. It should be noted that in the 'immediate CHO feeding condition' participants ingested 0.8 g/kg/h during the first 4 hours post-exercise and no CHO was ingested thereafter. It cannot be ruled out that if CHO feeding was continued for a second 4-hour period, this might have resulted in a higher muscle glycogen storage 8 hours post-exercise.

Although it may be beyond the scope of this review, it is interesting to note that recently it was shown that whole body and leg protein synthesis, as well as net protein deposition, is enhanced when nutrients are consumed immediately after exercise as opposed to 3 hours later.[97] These data and those of Ivy et al.[43] indicate that the timing of post-exercise nutrient intake may affect the rate of muscle glycogen synthesis, as well the rate of whole body and leg protein synthesis.

Thus, it can be concluded that athletes should consume CHO immediately after strenuous exercise as this may increase the rate of muscle glycogen storage. This CHO feeding strategy may be especially important when there is less than 8 hours between two exercise bouts.

4. Amount of CHO

When no CHO is ingested after exercise, muscle glycogen synthesis rates have been found to be low (7–12 mmol/kg dw/h).[17,43,87,92] The rate of muscle glycogen storage with CHO supplementation immediately after exercise has generally been reported to be in a range of 20–50 mmol/kg dw/h (table I).[35,38,40,43,48,77,88,89,92] Only a few studies have directly investigated the effect of different rates of CHO ingestion on muscle glycogen synthesis rates.[35,37] Blom et al.[35] demonstrated that increasing the CHO consumption from 0.18 to 0.35 g/kg/h increased the rate of glycogen storage by more than

Table I. Overview of the literature investigating post-exercise muscle glycogen synthesis during short-term recovery (<8h)[a]

Participants	$\dot{V}O_{2max}$ (mL/kg)	Exercise protocol	CHO intake (g/h)	CHO intake (g/kg/h)	Timing (h)[b]	Intake of other nutrients	Glycogen post-exercise (mmol/kg dw)	Period (h)[c]	Glycogen synthesis rate (mmol/kg dw/h)	Reference
8 male		Glycogen-depleting exercise	70 (infusion)	1	0–4		33.3	0–4	85	Bergström & Hultman[76]
		No exercise	70 (infusion)	1	0–4		325	0–4	11.5	
5 male	51.5	Cycling to exhaustion, int. 20 min 75% $\dot{V}O_{2max}$	14 (glucose)	0.18	0, 2 and 4		137	0–5	9.0	Blom et al.[35]
5	53.4		26 (glucose)	0.35	0, 2 and 4		64	0–5	24.8	
5	58.0		52 (glucose)	0.70	0, 2 and 4		98	0–5	24.4	
5	58.0		26 (sucrose)	0.35	0, 2 and 4		34	0–5	26.5	
7	57.8		25 (fructose)	0.35	0, 2 and 4		98	0–5	13.7	
5 male	51.6	Cycling to exhaustion, int. 20 min 75% $\dot{V}O_{2max}$	80.6	1.4/0.7/0.7	0, 1 and 2		94	0–3	40.0	Blom[77]
			32 (infusion)	0.37	0–3		60	0–3	35.6	
4 male		Cycling 70% $\dot{V}O_{2max}$ to exhaustion		0.35	0, 2, 4 and 6			0–8	8.4	Blom et al.[78]
4				0.7					18.9	
4				1.0					23.0	
7 male	42.3	Cycling 30 min 70% $\dot{V}O_{2max}$, 6 × 1-min 140% $\dot{V}O_{2max}$ and 45 min 70% $\dot{V}O_{2max}$	30.5 (glucose)	0.4	0		50	0–2	22.7	Bowtell et al.[79]
			30.5 (sucrose)	0.4	0		34	0–2	17.4	
			20.6 (sucrose)	0.27	0		21	0–2	14.7	
7 male	38.9	Cycling 30 min 70% $\dot{V}O_{2max}$, 6 × 1 min 140% $\dot{V}O_{2max}$	30.5	0.4	0–0.33			0–2	21.6	Bowtell et al.[80]
			30.5	0.4	0–0.33	8g glutamine		0–2	19.3	
8 male	55.7	Cycling 75 min 70% $\dot{V}O_{2max}$, 6 × 1-min 125% $\dot{V}O_{2max}$	75.4	1	0, 0.5h until 3.5h		107	0–4	31	Carrithers et al.[81]
			53.4	0.71		Protein + fat	118	0–4	28	
			64.8	0.86		Amino acids	87	0–4	29	

Continued next page

Table I. Contd

Participants	$\dot{V}O_{2max}$ (mL/kg)	Exercise protocol	CHO intake (g/h)	CHO intake (g/kg/h)	Timing (h)[b]	Intake of other nutrients	Glycogen post-exercise (mmol/kg dw)	Period (h)[c]	Glycogen synthesis rate (mmol/kg dw/h)	Reference
8 male		1 leg cycling exhaustion	76	1.4/0.8/0.8	0, 1 and 2		25 18 (I) 33 (II)	0–3 0–3 0–3	40 40.6 30.3	Casey et al.[9]
10 male		Cycling 75 min 70% $\dot{V}O_{2max}$, 5 × 1-min 100% $\dot{V}O_{2max}$, 10 sets of 10 concentric, one-legged contractions	126	1.6	0.25, 0.5h until 4h		144	0–4	42.5	Doyle et al.[82]
4 male + 2 female	34.9	Cycling, 4 × 30 min 70% $\dot{V}O_{2max}$	88	1.4	0.25, 2 and 4	Protein + fat		0–6	19.26	Greiwe et al.[83]
	43.8	5 × 1-min 100% $\dot{V}O_{2max}$	88	1.4	0.25, 2 and 4	Protein + fat		0–6	44.9	
2 male		60 min knee extensions at 70% $\dot{V}O_{2max}$	160 (infusion)	2.1	0–6		220	0–6	130	Hansen et al.[84]
		No exercise	160 (infusion)	2.1	0–6		540	0–6	70.0	
6 male	59.6	Cycling: 2h 75% $\dot{V}O_{2max}$, 5 × 1 min 100% $\dot{V}O_{2max}$	103	1.4	0, 2 and 4	Protein + fat	55	0–6	50.5	Hickner et al.[85]
6 male	38.3		96	1.4	0, 2 and 4	Protein + fat	25	0–6	21.8	
8 male	52.3	15-min int. at 62% and 75% $\dot{V}O_{2max}$, cycling	57	0.75	0 and 2		153	0–2 2–4	22.3 16.9	Ivy et al.[37]
			113	1.5	0 and 2		137	0–2 2–4	24.8 19.3	
12 male	59.6	70 min of cycling, int. 68–88% $\dot{V}O_{2max}$	70.2 70.2 0	1.0 1.0 0	0 2		153 132 132	0–2 2–4 0–2	33.0 17.5 10.7	Ivy et al.[43]
8 male		Cycling to exhaustion: 2-min int. at intensities between 50 and 90% $\dot{V}O_{2max}$	83.5	1.2	0.5, 1.0, until 2.5		106	0–3	40.0	Jentjens et al.[86]

Continued next page

Table I. Contd

Participants	$\dot{V}O_{2max}$ (mL/kg)	Exercise protocol	CHO intake (g/h)	CHO intake (g/kg/h)	Timing (h)[b]	Intake of other nutrients	Glycogen post-exercise (mmol/kg dw)	Period (h)[c]	Glycogen synthesis rate (mmol/kg dw/h)	Reference
			83.5	1.2		Amino acids + wheat hydr.	176	0–3	25.0	
8 male	59.5	Cycling to exhaustion: 2-min int. at intensities between 50 and 90% $\dot{V}O_{2max}$	55 (liquid)	0.75	0.5, 1.5, 2.5, 3.5, 4.5	Protein + fat	72	0–5	24.8	Keizer et al.[10]
			62 (solid)	0.84		Protein + fat	69	0–5	24.6	
5 male	47	Cycling to exhaustion, 70% $\dot{V}O_{2max}$	0	0			92.5	0–4	7	Maehlum & Hermansen[87]
6 male	43.4	Cycling to exhaustion, 70% $\dot{V}O_{2max}$	40	0.55	0.25		68	0–2.5	27.6	Maehlum et al.[88]
11 male		2h cycling, int. 70–100% $\dot{V}O_{2max}$	77	1.0	0, 2 and 4		116	0–6	37.4	McCoy et al.[50]
6 male	60.5	Cycling 70% $\dot{V}O_{2max}$, 2h + 4 × 30s sprints	31 31	0.4 0.4	0, 2 and 4 2, 4 and 6	Protein + fat Protein + fat	80 90	0–8 0–8	28.0 28.8	Parkin et al.[74]
4 male	55.0	Swimming/running/ cycling, exhaustion	36	0.51	2	Protein + fat	98	0–5	35.1	Piehl[39]
13 male		60-min run on treadmill + 60 min of submax cycling + short sprints to exhaustion	150	1.8	0, 0.5, 1 and 1.5					Piehl Aulin et al.[40]
			84 mosmol/L 350 mosmol/L 84 mosmol/L 350 mosmol/L				53 58	0–2 0–2 2–4 2–4	50.2 29.9 18.8 23.2	
8 male	51.0	2h cycling, 15-min int. at 60–65% and 70–75% $\dot{V}O_{2max}$	55.9 (liquid) 55.9 (solid) 55.9 (infusion)	0.75 0.75 0.75	0 and 2 0 and 2 0–4		119 105 131	0–4 0–4 0–4	21.8 23.5 24.0	Reed et al.[89]
8 male		One-legged exercise prolonged		2.0	0–4			0–4	85	Roch-Norlund et al.[90]

Continued next page

Table I. Contd

Participants	$\dot{V}O_{2max}$ (mL/kg)	Exercise protocol	CHO intake (g/h)	CHO intake (g/kg/h)	Timing (h)[b]	Intake of other nutrients	Glycogen post-exercise (mmol/kg dw)	Period (h)[c]	Glycogen synthesis rate (mmol/kg dw/h)	Reference
10 male		Approx. 1h and 20 min of exercise which consisted of a full body workout	87 57 0	1 0.66 0	0 and 1 0 and 1 0 and 1	Protein + fat	235 220 247	0–4 0–4 0–4	19.3 23.0 2.0	Roy & Tarnopolsky[91]
8 male	56.9	Cycle exercise, 90 min 65% $\dot{V}O_{2max}$	55 73	0.75 1.0	0 and 1 0 and 1	Protein + fat	142 163	0–4 0–4	25.5 40.0	Tarnopolsky et al.[92]
8 female	51.7	Cycle exercise, 90 min 65% $\dot{V}O_{2max}$	46 61	0.75 1.0	0 and 1 0 and 1	Protein + fat	142 163	0–4 0–4	23.5 34.5	
16 (male/female)			0	0.0	0 and 1		210	0–4	6.8	
5 male	61	Cycling to exhaustion: 2-min int. at intensities between 50 and 90% $\dot{V}O_{2max}$	88 (sucrose)	1.2	0, 0.25, 0.5 until 4h		90	0–4	40.5	van Hall et al.[17]
			88 (sucrose)	1.2		Whey protein hydr.	69	0–4	38.3	
			0	0.0			78	0–4	12.0	
8 male		Cycling to exhaustion: 2-min int. at intensities between 50 and 90% $\dot{V}O_{2max}$	57.6 57.6 57.6 57.6	0.8 0.8 0.8 0.8	0, 1 and 2 0, 1 and 2 0, 1 and 2 0, 1 and 2	Glutamine Wheat hydr. Whey hydr.		0–3 0–3 0–3 0–3	28.0 26.0 33.0 34.0	van Hall et al.[93]
8 male		Cycling to exhaustion: 2-min int. at intensities between 50 and 90% $\dot{V}O_{2max}$	56	0.80	0, 0.5, 1.0 until 4.5		190	0–5	16.6	van Loon et al.[94]
			56	0.80		Amino acids + wheat hydr.	174	0–5	35.4	
			84	1.20			138	0–5	44.8	
12 male	67.2	Alternating workloads between 60 and 80% $\dot{V}O_{2max}$ for 2h	72	1.0	1, 2 and 3	Arginine	143 131	0–4 0–4	25.6 34.9	Yaspelkis & Ivy[95]

Continued next page

Table I. Contd

Participants	$\dot{V}O_{2max}$ (mL/kg)	Exercise protocol	CHO intake (g/h)	CHO intake (g/kg/h)	Timing (h)[b]	Intake of other nutrients	Glycogen post-exercise (mmol/kg dw)	Period (h)[c]	Glycogen synthesis rate (mmol/kg dw/h)	Reference
6 male	58.7	1 and 2 leg cycling, 1h 75% $\dot{V}O_{2max}$	52.5	0.7	0.33, 0.66 until 6h			0–6	37.6	Zachwieja et al.[48]
								0–6	14.1	
9 male	66.6	10 × 1-min max. sprints, 2h cycling, int. 60–85% $\dot{V}O_{2max}$	56	0.77	0 and 2		223	0–4	28.3	Zawadzki et al.[96]
			56	0.77	0 and 2	Protein	217	0–4	39.0	

a Muscle glycogen concentration immediately post-exercise. Data reported as mmol/kg ww in the literature were multiplied by 4.28 to account for water weight.

b Timing of CHO ingestion post-exercise.

c Post-exercise glycogen synthesis period.

CHO = carbohydrate; **hydr.** = hydrolysate; **I and II** = type I and type II fibres; **int.** = interval(s); $\dot{V}O_{2max}$ = maximal oxygen consumption.

150% (from 9.0 to 24.8 mmol/kg dw/h). However, increasing the CHO intake further from 0.35 to 0.7 g/kg/h did not result in an increased muscle glycogen storage rate. The authors suggested that a 'glycogen synthesis threshold' occurs at a CHO intake of 0.35 g/kg/h. However, this is most unlikely since several other studies[9,17,40,50,92,94] have found glycogen synthesis rates that were higher than the maximal glycogen synthesis rates observed in the study of Blom et al.[35] It should be noted that Blom et al.[35] reported a remarkably high glycogen synthesis rate when 0.35 g/kg/h CHO was ingested, which may explain why no further increase in muscle glycogen synthesis was found at a higher rate of CHO intake (0.7 g/kg/h).

In a study by Ivy et al.[37] the effect of moderate and high amounts of CHO ingestion on muscle glycogen synthesis was investigated during a 4-hour post-exercise period. No difference was found in muscle glycogen synthesis rates when either 0.75 or 1.5 g/kg/h of CHO was provided (19.6 vs 22.0 mmol/kg dw/h, respectively). This study supports the findings of Blom et al.[35] However, recently a study by van Loon et al.[94] showed that when the rate of CHO ingestion was increased from 0.8 to 1.2 g/kg/h this resulted in higher muscle glycogen synthesis rates (16.6 vs 35.4 mmol/kg dw/h, respectively). In this study, CHO supplements were provided at 30-minute intervals, while studies in which no differences in muscle glycogen synthesis rates were found with increasing CHO intake, have supplemented CHO at 2-hour intervals.[35,37] It has been suggested that CHO supplements provided at 2-hour intervals may not adequately increase and maintain blood glucose and insulin levels for 2 hours,[56] which could explain the discrepancy between the results of van Loon et al.[94] and those of others.[35,37] It might be postulated that frequent small CHO feedings result in different gastric emptying rates than one large CHO feeding and this might increase the availability of glucose for muscle glycogen synthesis. However, it has been shown that a large bolus empties faster from the stomach than a small bolus and the rate of gastric emptying follows an exponential pattern.[98] It is therefore likely that

the total volume emptied from the stomach over a certain period of time (i.e. a 3-hour period) is not different when small frequent feedings are provided compared with one or two larger feedings and hence it is unlikely that differences in gastric emptying are responsible for the higher glycogen synthesis rates.

Several studies have reported very high glycogen synthesis rates (between 40 and 43 mmol/kg dw/h) when 1.0–1.85 g/kg/h of CHO was consumed at frequent intervals (15- to 60-minute intervals) during a 3- to 4-hour recovery period,[9,40,82,86,94] which supports the findings of van Loon et al.[94] Although the amount of CHO intake seems to be an important factor determining the rate of muscle glycogen synthesis, it is currently not known how much CHO needs to be consumed post-exercise to maximise the rate of muscle glycogen synthesis. Figure 2 illustrates maximal muscle glycogen synthesis rates found in studies after ingestion of different rates of CHO in the early hours post-exercise. This graph shows a trend towards a higher glycogen synthesis rate when more CHO is ingested with no obvious levelling off.

Furthermore, it can be seen that at a given rate of CHO intake large variability exists in the rate of glycogen synthesis. This might be because of differences in experimental protocols, including the time interval of CHO supplementation, type of CHO ingested, training status of the participants and the duration of time over which muscle glycogen synthesis rates are calculated. Considering the limitations when comparing results of different studies, it seems reasonable to conclude that maximal glycogen synthesis rates occur at a CHO intake of ~1.2 g/kg/h. It is clear that the rate of CHO intake to obtain maximal glycogen synthesis rates is higher than previously suggested by some authors.[35,56] More research is required to quantify the exact amount of CHO that needs to be ingested to elicit maximal rates of muscle glycogen synthesis.

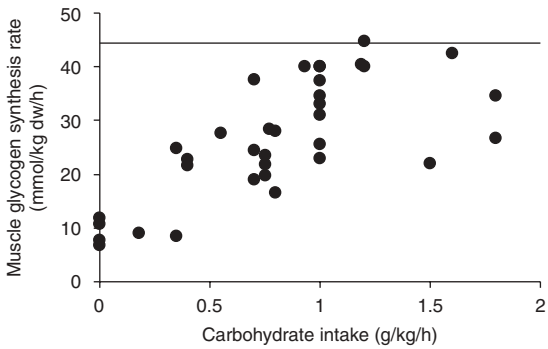

Fig. 2. Muscle glycogen synthesis rates are depicted against the rate of carbohydrate ingestion. The horizontal line depicts the absolute maximum for muscle glycogen synthesis.

5. Presence of Other Nutrients

As discussed earlier, insulin stimulates both muscle glucose uptake and activation of glycogen synthase,[56] the rate-limiting enzyme for glycogen synthesis. Several studies have therefore attempted to increase post-exercise insulin levels to optimise the rate of muscle glycogen synthesis.[17,86,94,96,99] The most important physiological stimulus for pancreatic insulin secretion is an increased blood glucose concentration. In addition, certain amino acids[93,100-102] and proteins[17,94,96,99,103,104] have been shown to exert a synergistic effect on the insulin release when administered separately or in combination with a CHO load. The mechanism responsible for this effect has not been completely elucidated yet. It has been shown that leucine can activate glutamate dehydrogenase activity in pancreatic β-cells *in vitro*.[105] This subsequently leads to an increase in tricarboxylic acid cycle activity and oxygen consumption of the pancreatic β-cells and is accompanied by increased pancreatic insulin secretion.[105]

In 1970, Floyd et al.[100,101] examined which combination of amino acids with glucose when administered intravenously would lead to the highest plasma insulin levels. It was found that combined intravenous administration of arginine-leucine and arginine-phenylalanine together with glucose resulted in the largest increase in plasma insulin levels. However, oral ingestion of arginine in combination with CHO is not effective in increasing plasma insulin levels[95,102] and muscle glycogen synthesis rates[95] compared with ingestion of CHO alone. Recently, van Loon et al.[102,106] investigated which type, combination and quantity of free amino acids or protein

sources would maximise the insulin response when added to a CHO beverage. It was demonstrated that the ingestion of a beverage containing a mixture of wheat protein hydrolysate, free leucine and free phenylalanine (0.4 g/kg/h) in combination with CHO (0.8 g/kg/h) resulted in very high insulin levels without causing gastrointestinal discomfort. Of note, some mixtures containing large quantities of free amino acids (arginine, leucine, phenylalanine and glutamine) resulted in similar or even higher insulin levels but these mixtures were not palatable and caused more gastrointestinal distress.[102] In another study by van Loon et al.,[94] it was shown that ingestion of this highly insulinotropic protein hydrolysate amino acid mixture, in combination with a moderate CHO intake (0.8 g/kg/h), resulted in increased muscle glycogen synthesis rates compared with the ingestion of CHO only (35.4 vs 16.6 mmol/kg dw/h, respectively). The increased rate of muscle glycogen synthesis was attributed to an increased clearance of glucose into the muscle as a result of higher insulin levels.[94,96]

A previous study by Zawadzki et al.[96] reported higher glycogen synthesis rates during a 4-hour post-exercise period with a combined CHO-whey protein supplement compared with a CHO supplement only. This study has been criticised by many investigators[81,91,92,99] because it did not include a control trial (isoenergetic amount of CHO). The higher rate of muscle glycogen storage observed in the CHO-protein trial may have been caused by an increased availability of substrate for gluconeogenesis as a result of the ingested protein. Several studies have found similar muscle glycogen synthesis rates for both CHO and isoenergetic CHO + protein (+ fat) supplements.[81,91,92,99] However, it is unlikely that increased gluconeogenesis has contributed to increased glycogen synthesis rates observed in the CHO-protein trials by Zawadzki et al.[96] and others.[102] The high insulin levels observed in the CHO-protein trials would have inhibited rather than stimulated gluconeogenesis. Furthermore, Zawadzki et al.[96] found that the rate of muscle glycogen storage following protein ingestion only was very low and not different from glycogen synthesis rates observed in studies where no supplement was provided after exercise.[2,43,88,107,108]

It is clear from the studies described above[94,96] that ingestion of some protein and/or amino acids in combination with a moderate CHO intake (~0.8 g/kg/h) leads to higher muscle glycogen synthesis rates compared with ingestion of the same amount of CHO without protein and/or amino acids. However, as discussed previously, van Loon et al.[94] showed that when the rate of CHO intake was increased from 0.8 to 1.2 g/kg/h this also resulted in higher muscle glycogen synthesis rates (table I). These findings suggest that maximal muscle glycogen synthesis rates were not reached when 0.8g/kg/h of CHO was ingested. Recently, we investigated whether the addition of an insulinotropic protein-amino acid mixture to a larger amount of CHO (1.2g/kg/h) would further increase muscle glycogen synthesis rates.[86] This study demonstrated that when the total CHO intake is very high (1.2 g/kg/h), the presence of a protein-amino acid mixture does not further increase the rate of muscle glycogen synthesis, despite a much higher insulin response. The results of this study,[86] and those of others,[17,94] suggest that insulin is not the limiting factor for muscle glycogen synthesis when total CHO intake is high (1.0–1.2 g/kg/h). The availability of CHO post-exercise, on the other hand, seems to play a more important role when maximal rates of muscle glycogen synthesis are required. It should be noted that although protein and/or amino acid ingestion may not always have an effect on muscle glycogen synthesis, there is evidence that amino acid ingestion in combination with,[109] and without, CHO[110] may increase post-exercise protein synthesis and net muscle protein balance (protein synthesis minus protein degradation). Furthermore, studies have shown that an increase in insulin levels when plasma amino acid concentrations are high may further increase net protein balance.[111,112] The insulinotropic protein and amino acid mixtures used in studies to optimise muscle glycogen synthesis may therefore also have some implications for stimulating post-exercise net muscle protein anabolism.[106] The importance of amino acid and/or protein inges-

tion following exercise to stimulate net muscle protein anabolism and the mechanisms involved remain to be elucidated.

6. Type of CHO Ingested

CHOs and CHO foods can be functionally classified according to the extent to which they increase blood glucose levels. This has lead to the concept of the Glycemic Index (GI), which is a measure for the blood glucose response observed after a certain food product is ingested with a certain amount of glucose (mostly 50g), compared with the blood glucose response observed when an equal amount of pure glucose or white bread (with an equal amount of glucose) is ingested.[113,114] The GI reflects the rate of digestion and absorption of a CHO-rich food (or a single CHO feeding) and is influenced by varying factors including: type of CHO and the content of dietary fat, protein and fibre present in the food.[114] A number of studies, discussed below, have compared the effect of single CHO feedings and CHO meals that differ in GI on muscle glycogen synthesis.

Several studies have reported lower rates of muscle glycogen synthesis when fructose (low GI) compared with glucose (high GI) was ingested.[35,115,116] This is possibly because of a slower absorption rate of fructose from the intestine[117,118] and the fact that fructose requires conversion to glucose by the liver before it can be metabolised in the skeletal muscle.[118-120] The latter is usually a relatively slow process.[121] Thus, when high muscle glycogen synthesis rates are required, the ingestion of glucose is preferred above fructose. However, fructose may be more of benefit in the restoration of liver glycogen.[115,122] It has been shown that fructose infusion results in higher liver glycogen synthesis compared with glucose infusion.[115,122] It remains to be investigated whether fructose ingestion leads to higher liver glycogen synthesis rates than the ingestion of glucose. With the advanced research techniques presently available (i.e. nuclear magnetic resonance spectroscopy), it should be possible to accurately determine the effect of fructose ingestion on post-exercise liver glycogen synthesis.

It is interesting to note that some studies have found similar rates of muscle glycogen synthesis when either glucose or sucrose (moderate GI) was ingested.[35,123] This is remarkable since sucrose contains equimolar amounts of glucose and fructose and hence only half the amount of glucose is directly available for muscle glycogen synthesis. It has been suggested that fructose, by virtue of its predominant metabolism in the liver compared with glucose, may inhibit post-exercise hepatic glucose uptake and because of this more glucose may escape from the liver and be available for muscle glycogen synthesis.[35] However, in a study by Bowtell et al.,[79] muscle glycogen storage was higher after consumption of a glucose polymer beverage (containing 61g CHO) than a sucrose beverage.[79] The discrepancy between these findings and those of Blom et al.[35] may be attributed to differences in the duration of the supplementation period and/or the total amount of CHO provided (2 vs 5 hours and 61 vs 130g, respectively). In a study by van Hall et al.,[17] high muscle glycogen synthesis rates (~40.5 mmol/kg dw/h) were observed when large amounts of sucrose (~1.2 g/kg/h) were ingested during a 4-hour post-exercise period. The glycogen synthesis rates found after sucrose ingestion were fairly similar to those reported in other studies after glucose ingestion.[86,94] Thus, when moderate to large quantities of sucrose are ingested after exercise this can result in similar glycogen synthesis rates compared with corresponding amounts of glucose.

Since glycogen storage is influenced by both insulin and a rapid supply of glucose to skeletal muscle, it has been proposed that high-GI foods may enhance post-exercise glycogen synthesis above moderate- and low-GI foods.[124] Kiens et al.[125] investigated post-exercise muscle glycogen synthesis rates following ingesting of high-CHO diets that differed in GI. After glycogen-depleting exercise, participants were provided with either a high- or low-GI isocaloric diet, each of which provided 70% of energy from CHO. Plasma insulin levels were on average 98% higher during the first 6 hours post-exercise when the high-GI diet was consumed and plasma glucose concentrations were similar between

the two diets. The high-GI CHO diet resulted in ~61% higher muscle glycogen synthesis rates compared with the low-GI CHO diet (40 vs 24 mmol/kg dw/h). The muscle glycogen synthesis rates observed after consumption of the high-GI CHO diet were almost similar to the glycogen synthesis rates found in studies in which participants ingested large amounts of CHO (~1.2 g/kg/h).[17,86,94] Unfortunately, the exact quantity of CHO present in the diets was not reported in the study of Kiens et al.,[125] which makes comparisons with other studies difficult. However, the data clearly indicate high muscle glycogen synthesis rates during the initial hours after exercise can occur when a high-GI CHO diet is ingested.

7. Form of CHO Intake

Only two studies have investigated the effect of liquid versus solid CHO foods (with a high GI) on glycogen synthesis in the early hours post-exercise (table I).[10,89] Keizer et al.[10] demonstrated that glycogen synthesis rates were similar after consumption of either a liquid or solid CHO meal (24.8 vs 24.6 mmol/kg dw/h, respectively). It should be noted that the solid meal in this study contained ~10% more CHO (35g in 5 hours) compared with the liquid meal and there were substantial differences in fat and protein content between the two meals. This may have confounded the results. Reed et al.[89] also investigated the effect of liquid and solid CHO supplements on muscle glycogen synthesis. No difference was found in the rate of muscle glycogen storage between liquid and solid CHO feedings when supplemented immediately and 2 hours post-exercise (21.8 and 23.5 mmol/kg dw/h, respectively). It can therefore be concluded that both liquid and solid CHO foods (with a high GI) are equally effective in providing CHO for muscle glycogen synthesis post-exercise.[10,89,126] This is somewhat surprising as liquid CHO supplements empty more rapidly from the stomach and are more easily digested than solid CHO foods.[98] However, it should be noted that in the studies described above the rate of CHO intake was relatively low (0.75–0.85 g/kg/h). It can not be ruled out that when large amounts of CHO are consumed, liquid CHO feedings may result in higher muscle glycogen synthesis rates than solid CHO feedings. Of note, liquid forms of CHO are often recommended to athletes because fluid absorption and delivery is faster from a solution compared with solid food and hence rehydration will be improved. One may question whether the intake of water together with solid food will increase gastric emptying because of an increased volume. Although the combined ingestion of water and solid food may enhance the rate of gastric emptying, the delivery rate of CHO into the intestine is probably the same since a less concentrated solution is emptied from the stomach.[98] The intake of water together with solid food will therefore most likely not affect the rate of muscle glycogen synthesis.

8. Factors Related to Post-Exercise Glycogen Synthesis

8.1 Training Status

Exercise training induces several adaptations at the muscular level that may contribute to increased insulin sensitivity,[18,68,127,128] including: increased GLUT-4 content,[129-131] improved insulin signalling[132,133] and increased blood flow.[127,128] All these adaptations would favour glucose uptake and could possible lead to increased muscle glycogen synthesis. It is therefore likely that trained athletes have higher glycogen synthesis rates than individuals who are sedentary.

Hickner et al.[85] examined the effect of training status on muscle glycogen synthesis. Following glycogen-depleting exercise, six trained cyclists and six untrained volunteers were provided with high-CHO meals supplying 1.4 g/kg/h CHO during the first 6 hours post-exercise. The rate of muscle glycogen storage was more than 2-fold higher in the trained cyclists than in untrained individuals (51 vs 22 mmol/kg dw/h) [table I]. In addition, muscle GLUT-4 content immediately post-exercise was 3-fold higher in the trained cyclists than in untrained participants and correlated with glycogen synthesis rates. The same research group also investigated the

effect of endurance training on muscle glycogen synthesis.[83] Participants conducted a 10-week training program which consisted of high-intensity cycling exercise 3 days/week and submaximal running 3 days/week. Muscle glycogen synthesis was measured before and after the training program. The rate of muscle glycogen synthesis was markedly increased after 10 weeks of endurance exercise training. This finding is in agreement with the results of training studies in rats[60,134] and supports the data of Hickner et al.[85] Furthermore, a higher GLUT-4 content was found after exercise training, and GLUT-4 content post-exercise was correlated with muscle glycogen concentrations 6 hours after exercise. This relationship is in agreement with findings of McCoy et al.[50] and Hickner et al.[85]

A rapid increase in GLUT-4 transporters has been observed following 2, 5 and 7 days of training,[60,129-131,135,136] and this may be accompanied by an increase in insulin-stimulated glucose uptake.[60,130,135] Furthermore, exercise training has been shown to enhance insulin signal transduction, which has been associated with increased glucose disposal.[132,133] Because trained individuals have higher GLUT-4 concentrations[83,85,127,129,131] and a higher insulin signal activity,[133] they may be able to synthesise muscle glycogen at a faster rate than untrained individuals.[83,127,131] Interestingly, Host et al.[130] demonstrated that the increase in GLUT-4 content and in insulin-stimulated glucose transport were completely reversed within 40 hours after the last exercise bout, after both 5 days and 5 weeks of training. This suggests a short half-life of the GLUT-4 protein.[60,130] Therefore, to maintain a training-induced increase in GLUT-4, it is necessary to exercise at least every other day.

It is also possible that the higher post-exercise glycogen synthesis rates in trained compared with untrained individuals is a result of higher glycogen synthase activity.[85,127,137] Glycogen synthase I activity in the study of Hickner et al.[85] was indeed 2-fold higher in trained than in untrained individuals immediately after exercise. However, no correlation was found between glycogen synthase I activity and glycogen accumulation rates over the initial 6 hours post-exercise. In addition, studies have shown 2-fold higher glycogen synthesis rates in trained rats compared with sedentary rats despite similar glycogen synthase I activity.[60,134] It is therefore unlikely that glycogen synthase plays an important role in the higher glycogen synthesis rates observed in trained athletes.

It should be noted that in both the study of Greiwe et al.[83] and of Hickner et al.[85] muscle glycogen concentrations immediately post-exercise were significantly different between the trained and untrained state. As discussed below (in section 8.3), the magnitude of muscle glycogen depletion seems to affect the rate of muscle glycogen synthesis. However, it is unlikely that the higher muscle glycogen synthesis rate in the trained compared with the untrained individuals was a result of a difference in post-exercise muscle glycogen content between the two conditions, since muscle glycogen content after exercise was higher in the trained individuals and this would have slowed down rather than increased muscle glycogen synthesis.

It has been suggested that enhanced insulin sensitivity in athletes is partly a result of a training-induced increase in blood flow.[127,133] A positive correlation has been found between basal limb blood flow and insulin-mediated glucose disposal in athletes.[127] Although speculative, it is possible that a higher basal blood flow in trained athletes may increase glucose delivery to the muscle and this may lead to higher glycogen synthesis rates compared with untrained individuals. Future studies are needed to investigate if blood flow is a limiting factor for glycogen synthesis in untrained individuals.

8.2 Feeding Schedule

It has been suggested that the ingestion of CHO supplements at frequent intervals maintains high plasma glucose and insulin concentrations and may contribute to high muscle glycogen synthesis rates.[56,82,94] This hypothesis is supported by studies which found high muscle glycogen synthesis rates (40–45 mmol/kg dw/h) when large amounts of CHO (1.2–1.6 g/kg/h) were provided at regular intervals

(≤30 minutes).[82,94] As mentioned earlier, the rate of gastric emptying will increase with increasing volume of ingested content.[98] It is likely that gastric emptying rates are similar when a CHO beverage is ingested as small repetitive feedings, as opposed to one large bolus since the total volume of fluid consumed is the same. Therefore, the rate of gastric emptying can not explain the higher muscle glycogen synthesis rates observed when CHO supplements are provided at frequent intervals.

At present, no studies have directly investigated the effect of different feeding schedules on the rate of glycogen synthesis. There seems to be moderate evidence that serial feedings are more beneficial for high muscle glycogen synthesis rates than bolus feedings, which is best described in a study by van Loon et al.[94] In addition, ingestion of small CHO feedings at frequent intervals may reduce the risk of gastrointestinal discomfort (i.e. bloated feeling).

8.3 Magnitude of Muscle Glycogen Depletion

The extent of glycogen depletion has been suggested to be an important factor in the regulation of muscle glycogen synthesis. Bonen et al.[138] investigated post-exercise muscle glycogen synthesis in two groups of participants who had depleted muscle glycogen concentrations in the vastus lateralis of both legs by either 80 or 35%, referred to as LG (low post-exercise glycogen concentrations) and MG (moderate post-exercise glycogen concentrations), respectively. Immediately and 2 hours after cycle exercise, participants consumed a glucose drink (0.75 g/kg/h). Glycogen synthesis rates were higher for the LG condition compared with the MG condition. However, the results may be confounded because experimental group sizes were different (7 vs 3) and glycogen-depleting exercise in the LG condition finished with intermittent intense exercise (the effect of the latter on glycogen synthesis will be discussed in section 8.4). Zachwieja et al.[48] conducted a more controlled study, in which they attempted to determine the effect of muscle glycogen depletion on the rate of glycogen synthesis. In order to generate different amounts of glycogen depletion in the vastus lateralis muscle of each leg, participants performed three separate cycling tasks in one trial. Initially, participants performed 30 minutes of one-legged cycling at 75% of the one-legged maximal oxygen uptake, ($\dot{V}O_{2max}$) which was followed by ten 1-minute maximal sprints with the same leg (LG). The final task involved riding with two legs for 30 minutes at a workload of 75% of the two-legged $\dot{V}O_{2max}$ (MG). Following the exercise, participants ingested a 24% CHO solution every 20 minutes in order to achieve a CHO intake of 0.7 g/kg/h during a 6-hour period. Both the glycogen synthesis rate and the glycogen synthase activity were significantly higher in the LG leg than in the MG leg. These results imply that a higher degree of glycogen depletion results in a higher rate of muscle glycogen synthesis during the early hours post-exercise.

In the studies described above, it was not possible to determine whether the increased glycogen synthesis rate was a result of a higher magnitude of glycogen degradation or because of a lower post-exercise muscle glycogen concentration that remains in the muscle after exercise-induced glycogen depletion. Recently, Price et al.[139] investigated the effect of different post-exercise muscle glycogen concentrations on glycogen synthesis, when the magnitude of glycogen degradation during the initial glycogen-depleting exercise bout was kept the same. Thus, muscle glycogen utilisation and the exercise duration and intensity performed were similar between conditions, and therefore the concentration of muscle glycogen remaining after exercise was the sole variable that was different. Price et al.[139] showed that the rate of muscle glycogen synthesis was higher in the 'low post-exercise glycogen condition' compared with the 'high post-exercise glycogen condition'. The results of this study clearly indicate that the rate of muscle glycogen storage is more strongly influenced by the actual glycogen concentration remaining in the muscle after exercise than by a large decline in muscle glycogen as a result of previous exercise.[139] These findings and those of others,[75] support a key role for post-exercise glycogen concentration in regulating

the rate of glycogen synthesis during the initial hours after exercise. As mentioned earlier (in section 2.1), the higher rate of glycogen synthesis in more depleted muscles might be attributed to either higher glycogen synthase activity[27,44,46,48] or increased glucose transport into the muscle,[64] because of a higher number of GLUT-4 transporters[65,71] at the cell membrane, or possibly a combination of these factors.[140]

8.4 Muscle Fibre Types

Most studies have examined muscle glycogen synthesis in biopsy samples of mixed-fibre muscle. Only a few studies have attempted to determine glycogen synthesis rates in single human muscle fibres. While some studies have reported higher muscle glycogen synthesis rates in type II fibres compared with type I fibres,[39,141] other studies have found higher rates of glycogen storage in type I fibres.[9,142] The contradictory findings between studies may be partly the result of the different methods used to quantify muscle glycogen. Studies that have found higher muscle glycogen synthesis rates in type II fibres have used histochemical methods (e.g. periodic acid-Schiff stain intensity) to determine muscle glycogen concentrations, whereas studies that have reported higher glycogen synthesis rates in type I fibres have used biochemical methods.

In a study by Casey et al.,[9] glycogen synthesis rates in type I and type II skeletal muscle fibres were investigated using biochemical analysis. Seven participants performed one-legged cycling exercise to exhaustion. Following exercise, participants were provided with glucose beverages at 0 hours (1.4 g/kg/h), 1 hour (0.8 g/kg/h) and 2 hours (0.8 g/kg/h) post-exercise. During the initial 3-hour post-exercise period a 25% higher rate of muscle glycogen synthesis was found in type I compared with type II fibres (41 vs 31 mmol/kg dw/h). However, post-exercise muscle glycogen concentrations were 46% lower (not significant) in type I compared with type II muscle fibres and this may have slightly confounded the results. It should be noted that between 3 and 10 hours post-exercise, the rate of glycogen synthesis in type I fibres declined by 60%, whereas the glycogen synthesis rate in type II fibres was maintained. Muscle glycogen synthesis rates during this period were significantly lower in type I compared with type II fibres. The pattern of glycogen synthesis in both fibre types appeared to be closely related to the muscle glycogen concentration of the fibre, which supports the findings in mixed muscle biopsy samples.[38,48,50] The initial higher glycogen synthesis rates in type I fibres might be a result of an increased glucose uptake in this fibre type. In humans, whole body glucose uptake after insulin stimulation has been found to positively correlate with the percentage of type I fibres and negatively correlate with the percentage of type IIb fibres.[143] Since skeletal muscle is responsible for the major part of insulin-stimulated plasma glucose disposal,[144] a higher glucose uptake in type I fibres might be expected. Gaster et al.[145] showed direct evidence that GLUT-4 was more abundantly expressed in type I compared with type II fibres. Furthermore, it has been shown that the rate of glycogen synthesis and the GLUT-4 content are both positively correlated with the percentage of type I fibre.[85] Thus, a higher GLUT-4 expression in type I fibres might explain the higher glycogen synthesis rates in type I fibres. It should be noted here that although the density of GLUT-4 is higher in type I compared with type II fibres, the magnitude of the difference is relatively small (15–20%).[145,146] Suggestions have been made that the GLUT-4 content of an individual muscle fibre is related more to the activity level of the fibre than to its actual fibre type.[145,146]

In a study by Phiel,[39] a histochemical method was used to examine muscle glycogen synthesis in different fibre types. The glycogen synthesis rates tended to be higher in type II muscle fibres than type I muscle fibres, which is in contrast with the result of Casey et al.[9] Although the discrepancy between the two studies might be because of the different methods used to quantify muscle glycogen, it might also be a result of differences in the experimental exercise protocols used to deplete muscle glycogen stores (i.e. differences in fibre type recruitment pattern). In the study by Casey et al.,[9] participants

exercised at a predetermined submaximal workload to exhaustion, while participants in the study of Phiel[39] performed 2 hours of prolonged submaximal exercise immediately followed by repeated bouts of brief maximal exercise. During short-term, high-intensity exercise the rate of glycogenolysis is higher in type II fibres than type I fibres.[147] The high rate of glycogen utilisation in type II fibres is likely to be accompanied by high muscle and blood lactate concentrations immediately post-exercise, which can both be used as substrates for glycogen synthesis.[74,148,149] It has been estimated that between 13 and 27% of the lactate present in the muscle after short-term, high-intensity exercise is converted into glycogen.[148] Therefore, the higher glycogen synthesis rates in type II fibres observed in the study of Phiel[39] could be accounted for by a greater availability of lactate for glycogen synthesis in this fibre type. Clearly, the majority of muscle glycogen synthesis derived from lactate must occur during the early post-exercise period when high lactate concentrations are present in muscle and blood.

In conclusion, studies that have investigated glycogen synthesis in human muscle fibre types have shown conflicting results, which may partly be because of differences in methods used to quantify muscle glycogen concentrations (histochemical vs biochemical methods). Some studies have reported higher glycogen synthesis rates in type I fibres than type II fibres when using biochemical methods, while others have found lower glycogen synthesis rates in type I fibres when using histochemical methods to determine muscle glycogen concentrations.

8.5 Mode of Exercise

Prolonged eccentric exercise, is known to induce severe muscle damage and this has been suggested to impair muscle glycogen synthesis.[150,151] To our knowledge, only one study[82] has investigated the effect of concentric and eccentric exercise on muscle glycogen synthesis during the early hours post-exercise. In a study by Doyle et al.,[82] participants cycled for 70 minutes at 70% $\dot{V}O_{2max}$ immediately followed by high-intensity interval exercise to deplete glycogen stores in both fast-twitch and slow-twitch muscle fibres. After glycogen-depleting exercise, participants performed ten sets of ten repetitions of either concentric or eccentric contractions in opposite legs. During the first 4 hours after exercise, participants ingested 1.6 g/kg/h of CHO, which was provided at 15-minute intervals. The authors concluded that muscle glycogen synthesis rates during the first 4 hours post-exercise were not different after eccentric compared with concentric exercise. Interestingly, muscle glycogen synthesis rates 48 hours post-exercise were 25% lower after eccentric compared with concentric exercise. These findings are supported by a study by Widrick et al.,[152] which showed that muscle glycogen synthesis was impaired 24–72 hours after eccentric exercise, while no impairment was found during the first 6 hours post-exercise.

The mechanism(s) for the impaired glycogen synthesis following eccentric exercise remain(s) largely unknown. Studies have shown a decreased GLUT-4 content[153] and a period of insulin resistance[154] 1–2 days after unaccustomed eccentric exercise. It is not unlikely that a decreased GLUT-4 content and/or insulin resistance is/are responsible for the impaired muscle glycogen synthesis following eccentric exercise. In addition, muscle damage, often observed after eccentric exercise, is followed by the infiltration of inflammatory cells (i.e. leucocytes, lymphocytes and macrophages) in the damaged muscle and these cells are known to increase glucose utilisation and lactate production.[155,156] Suggestions have been made that the impaired muscle glycogen synthesis following eccentric exercise results from increased glucose uptake by inflammatory cells and hence less glucose is available for glycogen synthesis in previously exercised muscle.[157] It should be noted that there is generally a delay of several hours up to several days between the occurrence of muscle fibre damage and accumulation of most inflammatory cells.[158] Although speculative, the time course of muscle glycogen synthesis after eccentric exercise might be related to the inflammatory cell response to muscle damage.

Based on the limited amount of data available in the literature, it can be concluded that muscle glycogen synthesis during the first 4–6 hours post-exercise is not different after eccentric compared with concentric exercise. However, muscle glycogen synthesis after eccentric exercise seems to be impaired during the next 18–72 hours post-exercise or possibly even longer.

9. Limitations of Muscle Glycogen Synthesis

In a recent study we have suggested that insulin is not a limiting factor for glycogen synthesis when CHO intake is sufficient (≥1.2 g/kg/h) and provided at regular intervals.[86] CHO availability, on the other hand, is more likely a rate-limiting factor for muscle glycogen synthesis. The availability of CHO is dependent on the rate of gastric emptying and intestinal absorption of the ingested CHO, glucose output by the liver and glucose entry into the muscle. Studies which have examined gastric emptying in relation to exogenous CHO oxidation have shown that the rate of gastric emptying is not the limiting step in the oxidation of the oral ingested glucose.[159,160] It is therefore unlikely that the rate of gastric emptying will limit the rate of glycogen synthesis.

Several studies have reported extremely high muscle glycogen synthesis rates up to 130 mmol/kg dw/h when large amounts of glucose (up to 2.1 g/kg/h) were infused following glycogen-depleting exercise.[76,84,90] These glycogen synthesis rates were far above the maximal glycogen synthesis rates of 40–50 mmol/kg dw/h often found in studies where glucose was ingested orally after exercise (table I).[9,77,82,85,94] It is therefore likely that the rate of muscle glycogen synthesis is at least in part limited by the rate of digestion and absorption of CHO by the intestine and subsequent transport of glucose into the bloodstream regulated by the liver.

It has been suggested that the upper limit for glucose absorption in humans is approximately 1.0–1.7 g/min,[161,162] which may be slightly higher in the post-exercise state.[163,164] Assuming an active muscle mass of 10kg during cycling,[165] the maximal rate of muscle glycogen storage following oral glucose consumption should be in the range of 0.28–0.32 g/min (figure 3). Thus, the maximal glycogen synthesis rate in the leg seems to be 65–85% lower than the maximal absorption rate by the gut, which indicates that part of the absorbed glucose is either oxidised, extracted by other tissues (i.e. liver,[123] other muscle groups and/or fat tissue) or is synthesised to fat in the previously exercised muscle. Therefore, the transport capacity of the intestine for glucose cannot be the only factor that determines the maximal rate of muscle glycogen synthesis.

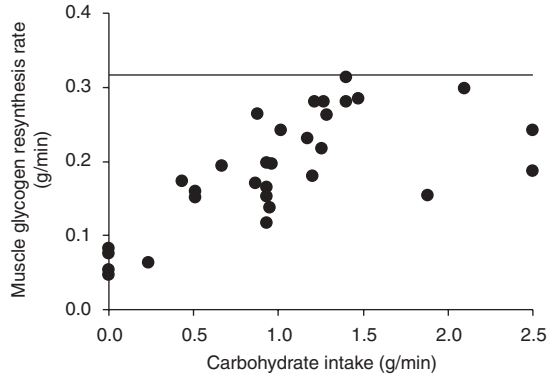

Fig. 3. Muscle glycogen synthesis rates are depicted against the rate of carbohydrate ingestion. Muscle glycogen concentrations reported in the literature as mmol/kg dry weight were divided by 4.28 to account for water weight in wet muscle mass. Furthermore, it was assumed that 10kg of leg muscle was engaged in cycle exercise and that the rate of glycogen synthesis in the total leg muscle was the same as in the vastus lateralis. The horizontal line depicts the absolute maximum for muscle glycogen synthesis.

Studies by Bowtell et al.[79,80] have shown that when a low dose of glucose was ingested after exercise (61g of CHO within a 2-hour period), ~26% of the glucose disappearing from the blood was used for glycogen synthesis within the previously exercised leg muscle. This suggests that muscle glycogen synthesis is not the predominant route of the ingested glucose in the early hours after exercise. This is further supported by a study of Hansen et al.,[84] where a hyperglycaemic hyperinsulinaemic clamp was performed in two participants during an 8-hour post-exercise period. Glucose infusion rates averaged ~3 g/min and plasma glucose concentrations were maintained around 21 mmol/L throughout the 8-hour infusion period. Interestingly,

the rate of glucose uptake in the exercised leg (one-leg exercise) did not exceed 0.9 g/min. In theory, the rate of glucose uptake in the previously exercised muscle could be a limiting factor for muscle glycogen synthesis. Although the mechanisms are not known, these results clearly indicate that most of the glucose that enters the systemic circulation following exercise is used by tissues other than the previously exercised muscles. The fate of the glucose that is not used for glycogen synthesis in glycogen-depleted muscles remains to be determined.

In conclusion, intestinal glucose absorption may be a rate-limiting factor for muscle glycogen synthesis when large quantities (>1 g/min) of glucose are ingested following exercise. Furthermore, a large part of the absorbed glucose appears to be extracted by tissues other than the exercised muscle and may therefore limit the amount of glucose available to maximise muscle glycogen synthesis rates. Alternatively, the glucose transport capacity of the previously exercised muscle may limit glycogen synthesis. Most likely, muscle glycogen synthesis is limited by a combination of factors (i.e. glucose absorption and/or delivery in the bloodstream, extraction of glucose by other tissues and the glucose transport capacity of the muscle).

10. Directions for Future Research

Although considerable research has addressed the factors and underlying mechanisms that determine (maximal) post-exercise glycogen synthesis rates, several questions remain to be answered. One of the questions is the minimal amount of CHO that needs to be ingested to obtain maximal glycogen synthesis rates. It has recently been shown that glycogen synthesis rates can be increased when the rate of CHO intake is increased from 0.8 to 1.2 g/kg/h and provided at 30-minute intervals.[94] The provision of CHO supplements at frequent intervals has been suggested to be an important factor when high muscle glycogen synthesis rates are required. The effects of serial or bolus CHO feedings on muscle glycogen synthesis are currently not known. Future studies should investigate whether muscle glycogen synthesis rates can be further increased when CHO intake is very high (>1.2 g/kg/h) and supplemented at regular intervals of 30 minutes or less.

Another question that should be addressed is the fate of the ingested CHO, which is not used for muscle glycogen synthesis. Although part of the ingested CHO may be (temporarily) trapped in the gastrointestinal tract or stored as glycogen in the liver, this does not explain why studies have found relatively low muscle glycogen synthesis rates (0.60–0.91 g/min) when fairly large amounts of glucose were infused into the systemic circulation (1.2–2.7 g/min) for up to 6 hours post-exercise.[76,84,90] In this respect, it may also be important to know which factors eventually determine the maximal muscle glycogen synthesis rate.

11. Practical Implications, Guidelines and Conclusions

For a rapid restoration of muscle glycogen, it is recommended that 75–90g of CHO (1.2 g/kg) are ingested immediately after exercise. Consuming this much every hour or as multiple small meals will maintain a maximal rate of muscle glycogen storage for as many as 4–6 hours after exercise. Ingestion of glucose and sucrose results in a faster replenishment of muscle glycogen stores than ingestion of fructose. When sufficient CHO is consumed (1.2. g/kg/h), there is no need for protein and/or amino acid ingestion in order to enhance the insulin levels. Higher insulin concentrations do not further increase the rate of muscle glycogen synthesis when CHO intake is sufficient. However, it should be noted that from a practical point of view, it might not be possible for an athlete to consume such large amounts of CHO. Alternatively, athletes may want to consume a moderate CHO intake (0.8 g/kg/h) in combination with some protein and/or amino acids, because this practice has been shown to result in similar muscle glycogen synthesis rates to the ingestion of a large amount of CHO only (1.2 g/kg/h). Furthermore, ingestion of insulinotropic protein and/or amino acid mixtures might stimulate post-exercise net muscle protein anabolism, and this might contribute to faster tissue growth and repair. Consumption of CHO foods with a moderate to high GI is recom-

mended because this might result in higher glycogen synthesis rates than ingestion of low-GI CHO foods. Whether the CHO supplement is in solid or liquid form does not seem to affect the rate of muscle glycogen synthesis. When appetite is suppressed immediately after exercise, there is a preference for drinking fluids rather than eating solid foods. Therefore, CHO beverages are recommended in the first few hours after exercise since it also provides fluid for rapid rehydration.

Acknowledgements

This work was supported by a grant from SmithKline Beecham Consumer Healthcare (UK).

References

1. Romijn JA, Coyle EF, Sidossis LS, et al. Regulation of endogenous fat in carbohydrate metabolism in relation to exercise intensity and duration. Am J Physiol 1993; 265: E380-91
2. Bergström J, Hermansen L, Hultman E, et al. Diet, muscle glycogen and physical performance. Acta Physiol Scand 1967; 71: 140-50
3. Hultman E. Physiological role of muscle glycogen in man, with special reference to exercise. Circ Res 1967; 20-21 (1): I99-I114
4. Burke L, Collier GR, Beasley SK, et al. Effect of coingestion of fat and protein with carbohydrate feedings on muscle glycogen storage. J Appl Physiol 1995; 78: 2187-92
5. Coggan AR, Mendenhall LA. Effect of diet on substrate metabolism during exercise. In: Lamb DR, Gisolfi CV, editors. Perspectives in exercise science and sports medicine: energy metabolism in exercise and sport. Traverse City (MI): Cooper Publishing group, 1992: 435-71
6. Costill DL. Carbohydrates for exercise: dietary demands for optimal performance. Int J Sports Med 1988; 9: 1-18
7. Ivy JL. Muscle glycogen synthesis before and after exercise. Sports Med 1991; 11: 6-19
8. Kiens B, Richter EA. Utilization of skeletal muscle triacylglycerol during postexercise recovery in humans. Am J Physiol 1998; 275: E332-7
9. Casey A, Short AH, Hultman E, et al. Glycogen resynthesis in human muscle fibre types following exercise-induced glycogen depletion. J Physiol 1995; 483 (1): 265-71
10. Keizer H, Kuipers H, van Kranenburg G. Influence of liquid and solid meals on muscle glycogen resynthesis, plasma fuel hormone response, and maximal physical working capacity. Int J Sports Med 1987; 8: 99-104
11. Kochan RG, Lamb DR, Lutz SA, et al. Glycogen synthase activation in human skeletal muscle: effects of diet and exercise. Am J Physiol 1979; 236 (6): E660-6
12. Bergström J, Hultman E. Muscle glycogen synthesis after exercise: an enhancing factor localized to the muscle cells in man. Nature 1966; 1210: 309-10
13. Madsen K, Pedersen PK, Rose P, et al. Carbohydrate supercompensation and muscle glycogen utilization during exhaustive running in highly trained athletes. Eur J Appl Physiol 1990; 61: 467-72
14. Sherman WM, Costill DL, Fink WJ, et al. Effect of exercise-diet manipulation on muscle glycogen and its subsequent utilisation during performance. Int J Sports Med 1981; 2: 114-8
15. Sherman WM, Doyle MA, Lamb DR, et al. Dietary carbohydrate, muscle glycogen and exercise performance during 7 d of training. Am J Clin Nutr 1993; 57: 27-31
16. Tarnopolsky MA, Atkinson SA, Phillips SM, et al. Carbohydrate loading and metabolism during exercise in men and women. J Appl Physiol 1995; 75: 2134-41
17. van Hall G, Shirreffs SM, Calbet JA. Muscle glycogen resynthesis during recovery from cycle exercise: no effect of additional protein ingestion. J Appl Physiol 2000; 88 (5): 1631-6
18. Goodyear LJ, Kahn BB. Exercise, glucose transport, and insulin sensitivity. Annu Rev Med 1998; 49: 235-61
19. Mueckler M. Facilitative glucose transporters. Eur J Appl Physiol 1994; 219: 713-25
20. Gaster M, Nandberg A, Beck-Nielsen H, et al. Glucose transporter expression in human skeletal muscle fibers. J Appl Physiol 2000; 279: E529-38
21. Lund S, Holman GD, Schmitz O, et al. Contraction stimulates translocation of glucose transporter GLUT-4 in skeletal muscle through a mechanism distinct from that of insulin. Proc Natl Acad Sci U S A 1995; 92: 5817-21
22. Thorell A, Hirshman MF, Nygren J, et al. Exercise and insulin cause GLUT-4 translocation in human skeletal muscle. Am J Physiol 1999; 277 (4 Pt 1): E733-41
23. MacLean PS, Zheng D, Dohm GL. Muscle glucose transporter (GLUT 4) gene expression during exercise. Exerc Sport Sci Rev 2000; 28 (4): 148-52
24. Ivy JL, Kuo CH. Regulation of GLUT4 protein and glycogen synthase during muscle glycogen synthesis after exercise. Acta Physiol Scand 1998; 162: 295-304
25. Richter EA, Derave W, Wojtaszewski JFP. Glucose, exercise and insulin: emerging concepts. J Physiol 2001; 535 (2): 313-22
26. Maughan R, Gleeson M, Greenhaff PL. Biochemistry of exercise and training. New York: Oxford University Press, 1997
27. Danforth WJ. Glycogen synthase activity in skeletal muscle. J Biol Chem 1965; 240: 588-93
28. Alonso MD, Lomako J, Lomako WM, et al. A new look at the biogenesis of glycogen. FASEB J 1995; 9 (12): 1126-37
29. Lomako J, Lomako WM, Whelan WJ. The nature of the primer for glycogen synthesis in muscle. FEBS Lett 1990; 268 (1): 8-12
30. Smythe C, Cohen P. The discovery of glycogenin and the priming mechanism for glycogen biogenesis. Eur J Biochem 1991; 200 (3): 625-31
31. Smythe C, Watt P, Cohen P. Further studies on the role of glycogenin in glycogen biosynthesis. Eur J Biochem 1990; 189 (1): 199-204
32. Adamo KB, Tarnopolsky MA, Graham TE. Dietary carbohydrate and postexercise synthesis of proglycogen and macroglycogen in human skeletal muscle. Am J Physiol 1998; 275: E229-34
33. Adamo KB, Graham TE. Comparison of traditional measurements with macroglycogen and proglycogen analysis of muscle glycogen. J Appl Physiol 1998; 84 (3): 908-13
34. Asp S, Daugaard JR, Rohde T, et al. Muscle glycogen accumulation after a marathon: roles of fiber type and pro- and macroglycogen. J Appl Physiol 1999; 86 (2): 474-8

35. Blom PCS, Hostmark AT, Vaage O, et al. Effect of different post-exercise sugar diets on the rate of glycogen synthesis. Med Sci Sports Exerc 1987; 19 (5): 491-6
36. Garetto LP, Richter EA, Goodman MN, et al. Enhanced muscle glucose metabolism after exercise in the rat: the two phases. Am J Physiol 1984; 246 (6 Pt 1): E471-5
37. Ivy JL, Lee MC, Brozinick JT, et al. Muscle glycogen storage after different amounts of carbohydrate ingestion. J Appl Physiol 1988; 65 (5): 2018-23
38. Maehlum S, Hostmark AT, Hermansen L. Synthesis of muscle glycogen during recovery after prolonged severe exercise in diabetic and non-diabetic subjects. Scand J Clin Lab Invest 1977; 37: 309-16
39. Piehl K. Time course for refilling of glycogen stores in human muscle fibres following exercise-induced glycogen depletion. Acta Physiol Scand 1974; 90: 297-302
40. Piehl Aulin K, Soderlund K, Hultman E. Muscle glycogen resynthesis rate in humans after supplementation of drinks containing carbohydrates with low and high molecular masses. Eur J Appl Physiol 2000; 81 (4): 346-51
41. Price TB, Rothman DL, Taylor R, et al. Human muscle glycogen resynthesis after exercise: insulin-dependent and -independent phases. J Appl Physiol 1994; 76: 104-11
42. Robergs RA. Nutrition and exercise determinants of post-exercise glycogen synthesis. Int J Sport Nutr 1991; 1: 307-37
43. Ivy JL, Katz AL, Cutler CL, et al. Muscle glycogen synthesis after exercise: effect of time of carbohydrate ingestion. J Appl Physiol 1988; 64 (4): 1480-5
44. Cohen P. Muscle glycogen synthase. In: Boyer P, Krebs EG, editors. The enzymes. Orlando (FL): Academic Press Incorporation, 1986: 461-97
45. Friedman JE, Neufer PD, Dohm GL. Regulation of glycogen resynthesis following exercise. Sports Med 1991; 11 (4): 232-43
46. Nielsen JN, Derave W, Kristiansen S, et al. Glycogen synthase localization and activity in rat skeletal muscle is strongly dependent on glycogen content. J Physiol 2001; 531 (Pt 3): 757-69
47. Montell E, Arias A, Gómez-Foix AM. Glycogen depletion rather than glucose 6-P increments controls early glycogen recovery in human cultured muscle. Am J Physiol 1999; 276: R1489-95
48. Zachwieja JJ, Costill DL, Pascoe DD. Influence of muscle glycogen depletion on the rate of resynthesis. Med Sci Sports Exerc 1991; 23 (1): 44-8
49. Yan Z, Spencer MK, Katz A. Effect of low glycogen on glycogen synthase in human muscle during and after exercise. Acta Physiol Scand 1992; 145: 345-52
50. McCoy M, Proieto J, Hargreaves M. Skeletal muscle GLUT-4 and postexercise muscle glycogen storage in humans. J Appl Physiol 1996; 80 (2): 411-5
51. Cartee GD, Young DA, Slepper MD, et al. Prolonged increase in insulin-stimulated glucose transport in muscle after exercise. Am J Physiol 1989; 256: E494-9
52. Holloszy JO, Narahara HT. Changes in permeability of 3-methylglucose associated with contraction of isolated frog muscles. J Biol Chem 1965; 240: 3493-500
53. Ivy JL, Holloszy JO. Persistent increase in glucose uptake by rat skeletal muscle following exercise. Am J Physiol 1981; 241 (5): C200-3
54. Kuo CH, Hunt DG, Ding Z, et al. Effect of carbohydrate supplementation on postexercise GLUT-4 protein expression in skeletal muscle. J Appl Physiol 1999; 87 (6): 2290-5
55. Ren JM, Marshall BA, Gulve EA, et al. Evidence from transgenic mice that glucose transport is rate-limiting for glycogen deposition and glycolysis in skeletal muscle. J Biol Chem 1993; 268 (22): 16113-5
56. Ivy JL. Glycogen resynthesis after exercise: effect of carbohydrate intake. Int J Sports Med 1998; 19: S142-5
57. Fisher JS, Nolte LA, Kawanaka K, et al. Glucose transport rate and glycogen synthase activity both limit skeletal muscle glycogen accumulation. Am J Physiol Endocrinol Metab 2002; 282 (6): E1214-21
58. Goodyear LJ, Hirshman MF, King PA, et al. Skeletal muscle plasma membrane glucose transport and glucose transporters after exercise. J Appl Physiol 1990; 68: 193-8
59. Kuo CH, Browning KS, Ivy JL. Regulation of GLUT-4 protein expression and glycogen storage after prolonged exercise. Acta Physiol Scand 1999; 165: 193-201
60. Ren JM, Semenkovich CF, Gulve EA, et al. Exercise induces rapid increases in GLUT-4 expression, glucose transport capacity, and insulin-stimulated glycogen storage in muscle. J Biol Chem 1994; 269 (20): 14396-401
61. Kraniou Y, Cameron-Smith D, Misso M, et al. Effects of exercise on GLUT-4 and glycogenin gene expression in human skeletal muscle. J Appl Physiol 2000; 88 (2): 794-6
62. Ryder JW, Kawano Y, Galuska D, et al. Postexercise glucose uptake and glycogen synthesis in skeletal muscle from GLUT4-deficient mice. FASEB J 1999; 13 (15): 2246-56
63. Hayashi T, Wojtaszewski JPP, Goodyear LJ. Exercise regulation of glucose transport in skeletal muscle. Am J Physiol 1997; 273: E1039-51
64. Fell RD, Terblanche SE, Ivy JL, et al. Effect of muscle glycogen content on glucose uptake following exercise. J Appl Physiol 1982; 52 (2): 434-7
65. Derave W, Lund S, Holman GD, et al. Contraction-stimulated muscle glucose transport and GLUT-4 surface content are dependent on glycogen content. Am J Physiol 1999; 277 (6 Pt 1): E1103-10
66. Kawanaka K, Han DH, Nolte LA, et al. Decreased insulin-stimulated GLUT-4 translocation in glycogen-supercompensated muscles of exercised rats. Am J Physiol 1999; 276: E907-12
67. Coderre L, Kandor KV, Vallega G, et al. Identification and characterization of an exercise-sensitive pool of glucose transporters in skeletal muscle. J Biol Chem 1995; 270 (46): 27584-8
68. Borghouts LB, Keizer HA. Exercise and insulin sensitivity: a review. Int J Sports Med 2000; 21 (1): 1-12
69. Hansen PA, Nolte LA, Chen MM, et al. Increased GLUT-4 translocation mediates enhanced insulin sensitivity of muscle glucose transport after exercise. J Appl Physiol 1998; 85 (4): 1218-22
70. Wojtaszewski JF, Hansen BF, Gade J, et al. Insulin signalling and insulin sensitivity after exercise in human skeletal muscle. Diabetes 2000; 49 (3): 325-31
71. Derave W, Hansen BF, Lund S, et al. Muscle glycogen content affects insulin-stimulated glucose transport and protein kinase B activity. Am J Physiol Endocrinol Metab 2000; 279 (5): E947-55
72. Gao J, Gulve EA, Holloszy JO. Contraction-induced increase in muscle insulin sensitivity: requirement for a serum factor. Am J Physiol 1994; 266 (2 Pt 1): E186-92
73. Fisher JS, Gao J, Han DH, et al. Activation of AMP kinase enhances sensitivity of muscle glucose transport to insulin. Am J Physiol Endocrinol Metab 2002; 282 (1): E18-23

74. Parkin JA, Carey MF, Martin IK, et al. Muscle glycogen storage following prolonged exercise: effect of timing of ingestion of high glycemic index food. Med Sci Sports Exerc 1997; 29 (2): 220-4
75. Laurent D, Hundal RS, Dresner A, et al. Mechanism of muscle glycogen autoregulation in humans. Am J Physiol Endocrinol Metab 2000; 278 (4): E663-8
76. Bergström J, Hultman E. Synthesis of muscle glycogen in man after glucose and fructose infusion. Acta Med Scand 1967; 182 (1): 93-107
77. Blom PCS. Post-exercise glucose uptake and glycogen synthesis in human muscle during oral or IV glucose intake. Eur J Appl Physiol 1989; 59: 327-33
78. Blom P, Vaage O, Kardel K, et al. Effect of increasing glucose loads on the rate of muscle glycogen resynthesis after prolonged exercise [abstract]. Acta Physiol Scand 1980; 108: C12
79. Bowtell JL, Gelly K, Jackman ML, et al. Effect of different carbohydrate drinks on whole body carbohydrate storage after exhaustive exercise. J Appl Physiol 2000; 88 (5): 1529-36
80. Bowtell JL, Gelly K, Jackman ML, et al. Effect of oral glutamine on whole body carbohydrate storage during recovery from exhaustive exercise. J Appl Physiol 1999; 86 (6): 1770-7
81. Carrithers JA, Williamson DL, Galagher PM, et al. Effects of postexercise carbohydrate-protein feedings on muscle glycogen restoration. J Appl Physiol 2000; 88: 1976-82
82. Doyle JA, Sherman WM, Strauss RL. Effects of eccentric and concentric exercise on muscle glycogen replenishment. J Appl Physiol 1993; 74 (4): 1848-55
83. Greiwe JS, Hickner RC, Hansen PA, et al. Effects of endurance exercise training on muscle glycogen accumulation in humans. J Appl Physiol 1999; 87 (1): 222-6
84. Hansen BF, Asp S, Kiens B, et al. Glycogen concentration in human skeletal muscle: effect of prolonged insulin and glucose infusion. Scand J Med Sci Sports 1999; 9 (4): 209-13
85. Hickner RC, Fisher JS, Hansen PA, et al. Muscle glycogen accumulation after endurance exercise in trained and untrained individuals. J Appl Physiol 1997; 83 (3): 897-903
86. Jentjens RL, van Loon LJ, Mann CH, et al. Addition of protein and amino acids to carbohydrates does not enhance postexercise muscle glycogen synthesis. J Appl Physiol 2001; 91 (2): 839-46
87. Maehlum S, Hermansen L. Muscle glycogen concentration during recovery after prolonged severe exercise in fasting subjects. Scand J Clin Lab Invest 1978; 38 (6): 557-60
88. Maehlum S, Felig P, Wahren J. Splanchic glucose and muscle glycogen metabolism after glucose feeding during postexercise recovery. Am J Physiol 1978; 4 (3): E255-60
89. Reed JM, Brozinick JT, Lee MC, et al. Muscle glycogen storage postexercise: effect of mode of carbohydrate administration. J Appl Physiol 1989; 66 (2): 720-6
90. Roch-Norlund AE, Bergstrom J, Hultman E. Muscle glycogen and glycogen synthetase in normal subjects and in patients with diabetes mellitus: effect of intravenous glucose and insulin administration. Scand J Clin Lab Invest 1972; 30 (1): 77-84
91. Roy BD, Tarnopolsky MA. Influence of differing macronutrient intakes on muscle glycogen resynthesis after resistance exercise. J Appl Physiol 1998; 84 (3): 890-6
92. Tarnopolsky MA, Bosman M, MacDonald JR, et al. Postexercise protein-carbohydrate and carbohydrate supplements increase muscle glycogen in men and women. J Appl Physiol 1997; 83 (6): 1877-33
93. van Hall G, Saris WH, van de Schoor PA, et al. The effect of free glutamine and peptide ingestion on the rate of muscle glycogen resynthesis in man. Int J Sports Med 2000; 21 (1): 25-30
94. van Loon LJC, Saris WHM, Kruijshoop M, et al. Maximizing postexercise muscle glycogen synthesis: carbohydrate supplementation and the application of amino acid or protein hydrolysate mixtures. Am J Clin Nutr 2000; 72 (1): 106-11
95. Yaspelkis IBB, Ivy JL. The effect of a carbohydrate-arginine supplement on postexercise carbohydrate metabolism. Int J Sport Nutr 1999; 9 (3): 241-50
96. Zawadzki KM, Yaspelkis III BB, Ivy JL. Carbohydrate-protein complex increased the rate of muscle glycogen storage after exercise. J Appl Physiol 1992; 72 (5): 1854-9
97. Levenhagen DK, Gresham JD, Carlson MG, et al. Postexercise nutrient intake timing in humans is critical to recovery of leg glucose and protein homeostasis. Am J Physiol Endocrinol Metab 2001; 280 (6): E982-93
98. Rehrer NJ, Brouns F, Beckers EJ, et al. The influence of beverage composition and gastrointestinal function on fluid and nutrient availability during exercise. Scand J Med Sci Sports 1994; 4: 159-72
99. Rotman S, Slotboom J, Kreis R, et al. Muscle glycogen recovery after exercise measured by 13C-magnetic resonance spectroscopy in humans: effect of nutritional solutions. MAGMA 2000; 11 (3): 114-21
100. Floyd Jr JC, Fajans SS, Pek S, et al. Synergistic effect of essential amino acids and glucose upon insulin secretion in man. Diabetes 1970; 19: 109-15
101. Floyd Jr JC, Fajans SS, Pek S, et al. Synergistic effect of certain amino acid pairs upon insulin secretion in man. Diabetes 1970; 19: 102-8
102. van Loon LJC, Saris WHM, Verhagen H, et al. Plasma insulin responses after ingestion of different amino acid or protein mixtures with carbohydrate. Am J Clin Nutr 2000; 72 (1): 96-105
103. Nuttall FQ, Mooradian AD, Gannon MC, et al. Effect of protein ingestion on the glucose and insulin response to a standardized oral glucose load. Diabetes Care 1984; 7 (5): 465-70
104. Rabinowitz D, Merimee TJ, Maffezolli R, et al. Patterns of hormonal release after glucose, protein, and glucose plus protein. Lancet 1966; II: 454-6
105. Sener A, Malaisse WJ. L-leucine and a nonmetabolized analogue activate pancreatic islet glutamate dehydrogenase. Nature 1980; 288 (5787): 187-9
106. van Loon LJC, Kruijshoop M, Verhagen H, et al. Ingestion of protein hydrolysate and amino acid-carbohydrate mixtures increases postexercise plasma insulin responses in men. J Nutr 2000; 130 (10): 2508-13
107. Costill DL, Sherman WM, Fink WJ, et al. The role of dietary carbohydrates in muscle glycogen resynthesis after strenuous running. Am J Clin Nutr 1981; 34: 1831-6
108. Hultman E, Bergström J, Roch-Norlund AE. Glycogen storage in human skeletal muscle. In: Pernow B, Saltin B, editors. Muscle metabolism during exercise. New York: Plenum Press, 1971: 273-87
109. Rasmussen BB, Tipton KD, Miller SL, et al. An oral essential amino acid-carbohydrate supplement enhances muscle protein anabolism after resistance exercise. J Appl Physiol 2000; 88 (2): 386-92
110. Tipton KD, Ferrando AA, Phillips SM, et al. Postexercise net protein synthesis in human muscle from orally administered amino acids. Am J Physiol 1999; 276 (4 Pt 1): E628-34

111. Gelfand RA, Barrett EJ. Effect of physiologic hyperinsulinemia on skeletal muscle protein synthesis and breakdown in man. J Clin Invest 1987; 80: 1-6
112. Hillier TA, Fryburg DA, Jahn LA, et al. Extreme hyperinsulinemia unmasks insulin's effect to stimulate protein synthesis in the human forearm. Am J Physiol 1998; 274: E1067-74
113. Jenkins DJA, Wolever TM, Taylor RH, et al. Glycemic index of foods: a physiological basis for carbohydrate exchange. Am J Clin Nutr 1981; 34: 362-6
114. Wolever TMS, Jenkins DJA, Jenkins AL, et al. The glycemic index: methodology and clinical implications. Am J Clin Nutr 1991; 54: 846-54
115. Conlee RK, Lawler RM, Ross PE. Effects of glucose or fructose feeding on glycogen repletion in muscle and liver after exercise or fasting. Ann Nutr Metab 1987; 31: 126-32
116. van den Bergh AJ, Houtman S, Heerschap A, et al. Muscle glycogen recovery after exercise during glucose and fructose intake monitored by 13C-NMR. J Appl Physiol 1996; 81 (4): 1495-500
117. Fujisawa T, Mulligan K, Wada L, et al. The effect of exercise on fructose absorption. Am J Clin Nutr 1993; 58 (1): 75-9
118. Henry RR, Crapo PA, Thorburn AW. Current issues in fructose metabolism. Annu Rev Nutr 1991; 11: 21-39
119. Chen M, Whistler RL. Metabolism of D-fructose. Adv Carbohydr Chem Biochem 1977; 34: 265-343
120. Mayes PA. Intermediary metabolism of fructose. Am J Clin Nutr 1993; 58: 754S-65S
121. Mendolff AI, Weichselbaum TE. Role of the human liver in the assimilation of intravenously administered fructose. Metabolism 1953; 2: 450-8
122. Nilsson LH, Hultman E. Liver and muscle glycogen in man after glucose and fructose infusion. Scand J Clin Lab Invest 1974; 33: 5-10
123. Casey A, Mann R, Banister K, et al. Effect of carbohydrate ingestion on glycogen resynthesis in human liver and skeletal muscle, measured by 13C MRS. Am J Physiol 2000; 278: E65-75
124. Burke LM, Collier GR, Hargreaves M. Glycemic index: a new tool in sport nutrition? Int J Sport Nutr 1998; 8: 401-15
125. Kiens B, Raben B, Valeur AK, et al. Benefit of dietary simple carbohydrates on the early postexercise muscle glycogen repletion in male athletes [abstract 524]. Med Sci Sports Exerc 1990; 22 (Suppl. 4): S88
126. Coleman E. Update on carbohydrate: solid versus liquid. Int J Sport Nutr 1994; 4 (2): 80-8
127. Ebeling P, Bourey R, Koranyi L, et al. Mechanism of enhanced insulin sensitivity in athletes: increased blood flow, muscle glucose transport protein (GLUT-4) concentration, and glycogen synthase activity. J Clin Invest 1993; 92 (4): 1623-31
128. Hardin DS, Azzarelli B, Edwards J, et al. Mechanism of enhanced insulin sensitivity in endurance-trained athletes: effects on blood flow and differential expression of GLUT-4 in skeletal muscles. J Clin Endocrinol Metab 1995; 80 (8): 2437-46
129. Gulve EA, Spina RJ. Effect of 7-10 days of cycle ergometer exercise on skeletal muscle glut-4 protein content. J Appl Physiol 1995; 79 (5): 1562-6
130. Host HH, Hansen PA, Nolte LA, et al. Rapid reversal of adaptive increases in muscle GLUT-4 and glucose transport capacity after training cessation. J Appl Physiol 1998; 84 (3): 798-802
131. Philips SM, Han XX, Green HJ, et al. Increments in skeletal muscle GLUT-1 and GLUT-4 after endurance training in humans. Am J Physiol 1996; 270: E456-62
132. Houmard JA, Shaw CD, Hickey MS, et al. Effect of short-term exercise training on insulin-stimulated PI 3- kinase activity in human skeletal muscle. Am J Physiol 1999; 277 (6 Pt 1): E1055-60
133. Kirwan JP, del Aguila LF, Hernandez JM, et al. Regular exercise enhances insulin activation of IRS-1-associated PI3-kinase in human skeletal muscle. J Appl Physiol 2000; 88 (2): 797-803
134. Nakatani A, Han HD, Hansen PA, et al. Effect of endurance exercise training on muscle glycogen supercompensation in rats. J Appl Physiol 1997; 82: 711-5
135. Kawanaka K, Tabata I, Katsuta S, et al. Changes in insulin-stimulated glucose transport and GLUT-4 protein in rat skeletal muscle after training. J Appl Physiol 1997; 83 (6): 2043-7
136. Host HH, Hansen PA, Nolte LA, et al. Glycogen supercompensation masks the effect of a training-induced increase in GLUT-4 on muscle transport. J Appl Physiol 1998; 85 (1): 133-8
137. Piehl K, Adolfsson S, Nazar K. Glycogen storage and glycogen synthase activity in trained and untrained muscle of man. Acta Physiol Scand 1974; 90: 779-88
138. Bonen A, Ness GW, Belcastro AN, et al. Mild exercise impedes glycogen repletion in muscle. J Appl Physiol 1985; 58 (5): 1622-9
139. Price TB, Laurent D, Petersen KF, et al. Glycogen loading alters muscle glycogen resynthesis after exercise. J Appl Physiol 2000; 88 (2): 698-704
140. Azpiazu I, Manchester J, Skurat AV, et al. Control of glycogen synthesis is shared between glucose transport and glycogen synthase in skeletal muscle fibers. Am J Physiol Endocrinol Metab 2000; 278 (2): E234-43
141. Vollestad NK, Blom PCS, Gronnerod O. Resynthesis of glycogen in different muscle fibre types after prolonged exhaustive exercise in man. Acta Physiol Scand 1989; 137: 15-21
142. Essen B, Henriksson J. Glycogen content of individual muscle fibres in man. Acta Physiol Scand 1974; 90: 645-7
143. Lillioja S, Young AA, Culter CL, et al. Skeletal muscle capillary density and fiber type are possible determinants of *in vivo* insulin resistance in man. J Clin Invest 1987; 80 (2): 415-24
144. Defronzo RA, Jacot E, Maeder E, et al. The effect of insulin on the disposal of intravenous glucose: results from indirect calorimetry and hepatic and femoral venous catherization. Diabetes 1981; 30: 1000-7
145. Gaster M, Poulsen P, Handberg A, et al. Direct evidence of fiber type-dependent GLUT-4 expression in human skeletal muscle. Am J Physiol Endocrinol Metab 2000; 278 (5): E910-6
146. Daugaard JR, Nielsen JN, Kristiansen S, et al. Fiber type-specific expression of GLUT4 in human skeletal muscle: influence of exercise training. Diabetes 2000; 49 (7): 1092-5
147. Pascoe DD, Gladden LB. Muscle glycogen resynthesis after short term, high intensity exercise and resistance exercise. Sports Med 1996; 21 (2): 98-118
148. Bangsbo J, Golnick PD, Graham TE, et al. Substrates for muscle glycogen synthesis in recovery from intense exercise in man. J Physiol 1991; 434: 423-40
149. MacDougall JD, Ward GR, Sale DG, et al. Muscle glycogen repletion after high-intensity intermittent exercise. J Appl Physiol 1977; 42 (2): 129-32

150. O'Reilly KP, Warhol MJ, Fielding RA, et al. Eccentric exercise-induced muscle damage impairs muscle glycogen repletion. J Appl Physiol 1987; 63 (1): 252-6

151. Sherman WM, Costill DL, Fink WJ, et al. Effect of a 42.2-km footrace and subsequent rest or exercise on muscle glycogen enzymes. J Appl Physiol 1983; 55 (4): 1219-24

152. Widrick JJ, Costill DL, Fink WJ, et al. Carbohydrate feedings and exercise performance: effect of initial glycogen concentration. J Appl Physiol 1993; 74: 2998-3005

153. Asp S, Daugaard JR, Richter EA. Eccentric exercise decreases glucose transporter GLUT-4 protein in human skeletal muscle. J Physiol 1995; 482: 705-12

154. Kirwan JP, Hickner RC, Yarashesis KE, et al. Eccentric exercise induces transient insulin resistance in healthy individuals. J Appl Physiol 1992; 72 (6): 2197-202

155. Forster J, Morris AS, Shearer JD, et al. Glucose uptake and flux through phosphofructokinase in wounded rat skeletal muscle. Am J Physiol 1989; 256 (19): E788-97

156. Schearer JD, Amaral JF, Caldwell MD. Glucose metabolism of injured skeletal muscle: the contribution of inflammatory cells. Circ Shock 1988; 25: 131-8

157. Costill DL, Pascoe DD, Fink WJ, et al. Impaired muscle glycogen resynthesis after eccentric exercise. J Appl Physiol 1990; 69 (1): 46-50

158. Smith LL. Acute inflammation: the underlying mechanism in delayed onset muscle soreness? Med Sci Sports 1991; 23 (5): 542-51

159. Moodley D, Noakes TD, Bosch AN, et al. Oxidation of exogenous carbohydrate during prolonged exercise: the effects of the carbohydrate type and its concentration. Eur J Appl Physiol 1992; 64 (4): 328-34

160. Rehrer NJ, Wagenmakers AJM, Beckers EJ, et al. Gastric emptying, absorption and carbohydrate oxidation during prolonged exercise. J Appl Physiol 1992; 72: 468-75

161. Duchman SM, Ryan AJ, Schedl HP, et al. Upper limit for intestinal absorption of a dilute glucose solution in men at rest. Med Sci Sports Exerc 1997; 29 (4): 482-8

162. Radziuk J, Bondy DC. Abnormal oral glucose tolerance and glucose malabsorption after vagotomy and pyloroplasty. Gastroenterology 1982; 83: 1017-25

163. Hamilton KS, Gibbons FK, Bracy DP, et al. Effect of prior exercise on the partitioning of an intestinal glucose load between splanchnic bed and skeletal muscle. J Clin Invest 1996; 98 (1): 125-35

164. Rose AJ, Howlett K, King DS, et al. Effect of prior exercise on glucose metabolism in trained men. Am J Physiol Endocrinol Metab 2001; 281 (4): E766-71

165. Gollnick PD, Pernow B, Essen B, et al. Availability of glycogen and plasma FFA for substrate utilization in leg muscle of man during exercise. Clin Physiol 1981; 1: 27-42

Correspondence and offprints: *Asker E. Jeukendrup*, Human Performance Laboratory, School of Sport of Exercise Science, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK.
E-mail: A.E.JEUKENDRUP@bham.ac.uk