

Modulation of carbohydrate and fat utilization by diet, exercise and environment

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Abstract

At rest and during exercise carbohydrate and fat are the predominant substrates. They are oxidized simultaneously but the relative contribution of these two substrates is dependent on a variety of factors including the exercise intensity and duration, diet, environmental conditions and training status. Changes in carbohydrate metabolism during the transition from rest to exercise and from low- to high-intensity exercise are mainly due to allosteric regulation. The factors that up-regulate fat metabolism in the transition to moderate-intensity exercise and the factors that result in a down-regulation of fat metabolism at higher intensities are incompletely understood. Substrate use is further modulated by the endocrine milieu (e.g. catecholamines, insulin, cortisol) and possibly cytokines (e.g. interleukin-6). With increasing duration of exercise there are marked increases in fat metabolism and decreases in carbohydrate metabolism and this has been ascribed mainly to substrate availability. Both acute food intake and chronic diets also have profound effects on substrate utilization. An increase in carbohydrate intake will rapidly suppress fat metabolism and increase carbohydrate metabolism whereas such an adaptation to a high-fat diet may take several days. The environmental conditions can also alter substrate use; high ambient temperatures can increase glycogen breakdown as a result of increased body core temperature and increased circulation catecholamines. Low temperatures can also increase carbohydrate metabolism, especially when shivering. In addition to these factors adaptation to training, in particular endurance training, will reduce the reliance on carbohydrate metabolism and increase fat oxidation, especially from intramuscular triacylglycerol stores.

Introduction

Carbohydrate and fat are the most important fuels at rest and during exercise. Although it has been shown that the branched-chain α -keto-acid dehydrogenase complex is activated during exercise [1,2] the quantitative contribution of branched-chain amino acids to energy expenditure is usually minimal (<1%). Even in extreme conditions (i.e. prolonged exercise in fasted conditions) amino acid oxidation only represents a relatively small fraction of total substrate utilization (<10%).

Carbohydrate is stored as glycogen in muscle and liver. Fat is stored in the form of triacylglycerol in subcutaneous adipose tissue and muscle. The liver typically contains about 80–100 g of glycogen in the post-absorptive state whereas muscle glycogen can vary from 50 g after strenuous exercise to 900 g in a well-fed, well-trained, muscular person (500–900 mmol/kg of dry mass) [3]. Fat stores are relatively large and there are considerable inter-individual differences, with body fat making up between 8 and 35% of body mass (5–40 kg). Fat is predominantly stored in adipose tissue but approx. 300 g can be found in the muscle as IMTAG (intramuscular triacylglycerol). At rest and during exercise, substrates are mobilized from these stores and utilized mainly within skeletal muscle. Clearly fat stores are very large,

representing 92–98% of all endogenously stored energy with carbohydrate contributing only about 2–8%.

In most conditions carbohydrate and fat are oxidized simultaneously but the relative contribution of these two substrates is dependent on a variety of factors including exercise intensity and duration, diet, environmental conditions, gender and training status. Some of these factors and their effects on substrate oxidation will be discussed below.

Exercise intensity and duration

At rest and during exercise skeletal muscle is the main site of oxidation of FA (fatty acids). After an overnight fast most of the energy requirement at rest is covered by the oxidation of FA derived from adipose tissue with carbohydrate only making a relatively small contribution (glucose is utilized mainly by the brain). During low-intensity exercise, the energy demand is increased several-fold compared with resting conditions and both carbohydrate and fat oxidation increase. When the exercise intensity increases, fat oxidation increases further until exercise intensities of about 65% $\dot{V}O_{2max}$, after which a decline in the rate of fat oxidation is observed [4,5]. In contrast to carbohydrate metabolism, which increases as a function of the aerobic work rate, fat oxidation is reduced at the high exercise intensities (Figure 1). The factors that up-regulate fat metabolism in the transition to moderate-intensity exercise and the factors that result in a down-regulation of fat metabolism at higher intensities

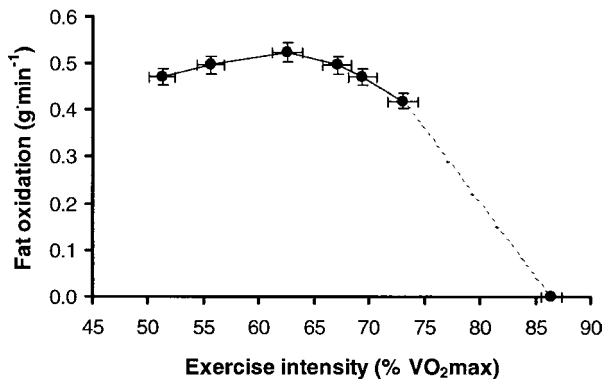
Key words: carbohydrate, diet, exercise, fat, metabolism, substrate utilization.

Abbreviations used: IMTAG, intramuscular triacylglycerol; FA, fatty acids; Ra, rate of appearance.

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Figure 1 | Fat oxidation during exercise and the effect of exercise intensity in trained individuals

It can be seen that fat oxidation peaks around 60–65% $\dot{V}O_{2max}$. Data from Achten and Jeukendrup [5].



are incompletely understood [6–8]. A detailed review of the mechanisms thought to be responsible for this regulation is beyond the scope of this article and the reader is referred to recent reviews [6,8].

Lipolysis in adipose tissue is mostly dependent on β -adrenergic stimulation and the endocrine environment [adrenaline ('epinephrine') to stimulate lipolysis and insulin to inhibit lipolysis]. When exercise is initiated, adrenaline concentrations increase and insulin concentrations decrease. As a result the rate of lipolysis and adipose-tissue blood flow increase, and more FA are released from the adipose tissue. During moderate-intensity exercise, lipolysis increases approx. 3-fold [9], mainly because of an increased β -adrenergic stimulation. In addition, during moderate-intensity exercise the blood flow to adipose tissue is doubled and the rate of re-esterification is halved [9,10], although others have found no change in re-esterification from rest to exercise [11,12]. Also, blood flow in skeletal muscle is increased dramatically [12] and therefore the delivery of FA to the muscle is increased several-fold. During the first 15 min of exercise, plasma FA concentrations usually decrease because the rate of FA uptake by the muscle exceeds the rate of FA appearance from lipolysis. Thereafter, the rate of appearance is in excess of the utilization by muscle, and plasma FA concentrations increase. FA are also mobilized from IMTAG and there is accumulating evidence that well-trained individuals have larger IMTAG stores [13] and oxidize more FA from IMTAG than untrained controls [14,15].

Liver glycogen breakdown will also be increased at the onset of exercise; the hepatic glucose output will increase as a function of the exercise intensity [16]. Glucose will be transported to the muscle and across the sarcolemma using GLUT4 transport proteins. In muscle, glucose can be oxidized along with glucose 1-phosphate derived from muscle glycogen. Muscle glycogen becomes the most important substrate when the exercise intensity increases above approx. 50% $\dot{V}O_{2max}$ [10,17] whereas plasma glucose typically contributes up to about 1 g/min. This seems mainly controlled by

the rate of appearance (Ra) of glucose because higher uptake rates can be achieved with artificially high Ra of glucose (by glucose infusion). It has been repeatedly demonstrated that 70–99% of all glucose taken up by the muscle is used for oxidative purposes [18,19] and non-oxidative glucose disposal is minimal unless the exercise intensity is very low.

The duration of exercise also affects substrate oxidation. Fat oxidation increases and carbohydrate oxidation decreases as the exercise duration increases. This increased fat oxidation is likely to be caused by a reduction in muscle glycogen stores towards the later stages of prolonged exercise. Reductions in muscle glycogen are thought to be responsible for the development of fatigue when these muscle glycogen concentrations reach very low levels and carbohydrate oxidation rates cannot be maintained at a sufficient rate to maintain ATP resynthesis (see [19a]). Typical fat oxidation rates are between 0.2 and 0.5 g/min [4,5] but values of over 1.0–1.5 g/min have been reported after 6 h of running [20]. The contribution of fat to energy expenditure can even increase to as much as 90%.

Diet

In 1920 Krogh and Lindhard [21] reported that a diet high in fat and low in carbohydrate reduced the respiratory exchange ratio, indicating increased fat oxidation. In the late 1960s, when the muscle biopsy technique was redeveloped, it was discovered that diets high in carbohydrate increased muscle glycogen concentrations and resulted in glycogen stores up to twice the normal resting level (e.g. approx. 500–900 mmol/kg of dry mass). Conversely, several days of a low-carbohydrate diet depleted muscle glycogen stores and decreased carbohydrate oxidation. It has been demonstrated repeatedly that the rate of glycogenolysis is directly related to muscle glycogen concentration [22].

High-carbohydrate diets

We recently studied the effects of high-carbohydrate, low-fat diets on metabolism and performance [23]. Eight well-trained cyclists received a diet containing 88% carbohydrate (901 g/day). Subjects trained for 2 h a day at 70% $\dot{V}O_{2max}$ for 7 days expending approx. 8000 kJ in each training session. After 7 days on this exercise and diet protocol muscle glycogen concentrations were extremely high and in fact among the highest values ever reported (824 mmol/kg of dry mass). Fat oxidation during exercise was reduced by 27% by the high-carbohydrate low-fat diet and this was partly attributed to reduced IMTAG stores. This may demonstrate that dietary fat has an important role to play after exercise, in that it helps to restore intramuscular fat stores. However, the role of these IMTAG stores in relation to performance is still unclear.

High-fat diets

Chronic high-fat diets (>3–7 days) have been shown to result in a shift towards fat metabolism. This adaptation

takes longer than the almost immediate adaptation to an increase in carbohydrate intake. The results of various studies suggest that after adaptation to a high-fat diet, the capacity to oxidize fatty acids is increased, because of an adaptation of the oxidative enzymes in the muscle cell. Such changes are similar to those observed after endurance training and result in a 'sparing' of glycogen during exercise.

Chronic high-fat diets (4–7 weeks) have been shown to result in increases in β -hydroxy-acyl-CoA dehydrogenase activity, carnitine palmitoyl transferase I activity [24], fatty acid-binding protein content in the sarcolemma [25] and decreases in hexokinase activity [24]. These changes suggest an increased capacity to oxidize fatty acids after such an adaptation period. It has been demonstrated that adaptation to a high-fat diet will lead to measurable changes in the capacity to store, mobilize, transport and oxidize fat.

Carbohydrate intake before or during exercise

Pre-exercise carbohydrate ingestion has a very strong inhibiting effect on fat oxidation. The ingestion of 50–100 g of carbohydrate in the hours before exercise will inhibit lipolysis and will also reduce fat oxidation by about 30–40% [26–28]. It has been demonstrated that the reduction is partly because less FA are available for oxidation (reduced lipolysis) [27] and partly because of an effect of hyperglycaemia or hyperinsulinaemia in the muscle [26]. The exact mechanism by which glucose and/or insulin reduce fat oxidation at an intramuscular level is still subject to debate. The likely sites of regulation are the transport of FA into the muscle by the fatty-acid transporter, FAT/CD36, and the transport of FA across the mitochondrial membrane [6–8].

Environmental conditions

Environmental conditions can also affect substrate utilization. It has been clearly demonstrated that environmental conditions such as heat and cold exposure can influence substrate use at rest and during exercise. Altitude will also affect substrate utilization at rest and during exercise.

Heat exposure

An increased body core temperature leads to increased carbohydrate oxidation during exercise and a concomitant decrease in fat oxidation. This is caused by increased muscle glycogen use [29,30] with no change in glucose uptake by the muscle [30]. Furthermore, it has been suggested that there is an increased hepatic glucose production with no alteration in glucose uptake, leading to hyperglycaemia [30].

A number of mechanisms have been proposed to account for the shift towards increased carbohydrate metabolism during exercise and heat stress [31]. It has been suggested that the increase in muscle glycogen utilization is due to an elevation in muscle temperature that occurs during exercise and heat stress [32]. The mechanism(s) for an increase

Table 1 | Factors affecting substrate utilization during exercise

Changes are expressed as the relative (%) and absolute (for example, kJ/min) contributions to energy expenditure (EE) for both carbohydrate (CHO) and fat. \blacktriangle indicates an increase or a higher amount; \blacktriangledown indicates a decrease or a lower amount.

	CHO contribution to EE		Fat contribution to EE	
	Relative	Absolute	Relative	Absolute
Exercise intensity \blacktriangle	\blacktriangle	\blacktriangle	\blacktriangledown	\blacktriangle^* , $\blacktriangledown^\dagger$
Exercise duration \blacktriangle	\blacktriangledown	\blacktriangledown	\blacktriangle	\blacktriangle
CHO feeding before exercise	\blacktriangle	\blacktriangle	\blacktriangledown	\blacktriangledown
CHO-rich diet	\blacktriangle	\blacktriangle	\blacktriangledown	\blacktriangledown
Endurance training	\blacktriangledown	\blacktriangledown	\blacktriangle	\blacktriangle
Hot conditions	\blacktriangle	\blacktriangle	\blacktriangledown	\blacktriangledown
Cold conditions	\blacktriangle	\blacktriangle	\blacktriangledown	\blacktriangledown
Altitude \blacktriangle	\blacktriangle	\blacktriangle	\blacktriangledown	\blacktriangledown
Gender (women compared with men)	\blacktriangledown	\blacktriangledown	\blacktriangle	\blacktriangle

* Up to about 65% $\dot{V}O_{2max}$.

† Higher than about 65% $\dot{V}O_{2max}$.

in muscle glycogen utilization with elevations in muscle temperature are not known at this time but may be related to the activity of key enzymes involved in carbohydrate metabolism, mitochondrial function, cross-bridge cycling and motor unit recruitment [32]. Furthermore, there is also evidence to suggest a potential role for adrenaline as a mechanism for increased muscle glycogenolysis during exercise in the heat [30,33,34]. It is well known that the adrenaline concentrations are higher during exercise in the heat compared with exercise in cooler environments [30,33,35]. Febbraio et al. [34] demonstrated that a 2-fold increase in circulating adrenaline increased muscle glycogen utilization, glycolysis and carbohydrate oxidation when subjects were exercising at 70% $\dot{V}O_{2max}$. The magnitude of the increase in adrenaline in that study was similar to those observed in previous studies that compared hot and thermoneutral environments [30,33]. Thus the increase in core temperature during exercise in the heat may result in an increased adrenaline secretion and this, in addition to the effect on increased muscle temperature itself, may increase muscle glycogen utilization.

Cold exposure

Compared with information about metabolism in the heat, far fewer studies have investigated the effects of cold exposure on substrate utilization. Studies have generally found increases in the relative contribution of carbohydrate and decreases in the relative contribution of fat [36,37] to energy expenditure although some studies have reported no change with moderate cold exposure [38]. During extreme cold shivering is a mechanism to increase energy expenditure

and heat production. It has been shown that during shivering hepatic glucose output and the rate of glucose utilization are increased [39]. These changes are somewhat similar to the changes observed during light-to-moderate exercise but should not be regarded as analogous processes [39].

Conclusions

Clearly, substrate selection at rest and during exercise depends on numerous factors including exercise intensity and duration, food intake before and during exercise, composition of the diet, environmental conditions, gender and training status of the subject (Table 1). Although these factors have been known for over 70 years the exact regulation of the interaction between carbohydrate and fat is still incompletely understood. In addition, there may be other factors that we are not yet aware of. There appears to be enormous inter-individual variation in substrate utilization despite low intra-individual variation, and only part of this variation can be explained by the factors mentioned above. More research is required to determine what other factors might be responsible for these apparent differences in substrate use.

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