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REVIEW ARTICLE

Ramadan and Its Effect on Fuel Selection during Exercise and Following Exercise Training

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Abstract

Fasting induces short-term physiological adaptations which spare the body's remaining carbohydrate stores and mobilize lipid stores to provide a substitute fuel for many tissues and organs, especially skeletal muscle. Rodent studies show that regular occurrence of fasting then refeeding, stimulates adaptations in muscle which make the animal better placed to withstand a further period of fasting by possessing a better ability to oxidise lipid.

This review explores the research describing these adaptations, with an emphasis on Ramadan, a human model of repeated fasting/refeeding. Separately, a single bout of endurance exercise places similar metabolic stress on the body as fasting since the exercising muscle must reduce its use of carbohydrate and utilize lipid more readily as exercise progresses. Not surprisingly therefore, adaptations in muscle to repeated bouts of endurance exercise (endurance training) are similar to those seen with repeated fasting/refeeding. Superimposing the stressors of repeated fasting/refeeding and exercise training, and subsequent adaptations to the muscle and exercise response, are examined by describing the published research which has investigated the situation where athletes continue their training whilst participating in Ramadan.

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INTRODUCTION

Lipid stored in adipose tissue depots theoretically contain sufficient energy to support the body's metabolism for many days or weeks in the absence of food [1]. In contrast, carbohydrate stores of liver and skeletal muscle glycogen are small and quickly depleted if food is not consumed [2], fasting induces rapid physiological adaptations which are centred on maintaining blood glucose concentration, but at the same time making sure there is sufficient alternative energy substrate (fuel) to support the other tissues such as skeletal muscle. The latter adaptation is particularly important in enabling physical work to be done during a period of fasting [3].

Endurance exercise results in depletion of the body's carbohydrate stores because the contracting muscle consumes blood glucose and muscle glycogen quickly. As exercise becomes prolonged, the body quickly responds to rapidly decreasing carbohydrate stores by mobilizing fat, presenting this to the contracting muscle for oxidation, and thus sparing any remaining carbohydrate for the brain [3]. This situation, which can be described as carbohydrate "stress", although occurring within a shorter space of time, is very similar to that which occurs during a fast [4].

Thus, during each period of carbohydrate stress (whether it be due to fasting or prolonged exercise), there is mobilization of triglyceride in adipose tissue into the circulation, making this fuel source available to metabolically active tissue. This substitute lipid-based fuel, primarily existing as (free) fatty acid (FFA), is able to support skeletal muscle energetic requirements at a significant rate, thereby allowing muscle function to continue even though blood glucose and muscle glycogen concentrations are becoming lower [5]. In both fasting and prolonged exercise, the biochemical pathways which are involved in fatty acid mobilization and oxidation are activated to permit increased rates of utilization of FFAs in support of metabolic requirements, including the vastly increased metabolic rate which results from muscular work.

Repeated short duration fasting, such as what occurs during Ramadan, would regularly expose the active tissue to periods of increased lipid availability and utilization [6]. Research in animals and humans presented below shows that when this occurs through periods of intermittent starvation or low carbohydrate dieting, tissues such as skeletal muscle become more adept at utilizing lipid. Endurance exercise training, perhaps not surprisingly, is well known to have a similar adaptive effect on muscle, and in this way enables a trained person to be able to exercise for longer [7]. This comparison then begs the question as to whether repeated fasting/refeeding, such as what occurs with participation in Ramadan, can improve the ability to use lipid during exercise and thus potentially improve endurance capacity.

The purpose of this review, therefore, is to describe the results of published scientific studies which have examined the effect of repeated fasting/refeeding on skeletal muscle metabolism and the fuel selection response to exercise. Since participation in Ramadan is an excellent model for a repeated fasting/refeeding regime, a specific focus will be on describing changes in whole body fuel selection at rest and with exercise during Ramadan. Further, undertaking endurance exercise training during participation in Ramadan would superimpose the metabolic stressors or fasting and endurance exercise, and theoretically this could result in a rapid adaptation in skeletal muscle to be able to better utilize lipid. A secondary purpose of this review therefore is to describe published studies which have superimposed exercise on a period of food restriction, including those which have studied the physiological response to endurance training during Ramadan.

Published scientific literature investigating the metabolic effects of repeated fasting/refeeding were identified through internet searches using the databases of PubMed and Google Scholar. Key words used to identify relevant studies included, but were not limited to: fasting, intermittent starvation, period starvation, and Ramadan. The reference lists of these articles were then examined to identify older material of relevance.

RODENT STUDIES

Investigations into the effect of repeated periods of fasting/refeeding in rodents variously term their interventions as food restriction [8], meal feeding [9], stuff and starve [10], infrequent feeding [11], nibbling versus gorging [12], periodic hyperphagia [13], and intermittent starvation [14]. Collectively they describe the effects of an increased time interval between meals on various physiologic parameters compared with much smaller time intervals, usually ad libitum fed controls. In the context of this article, the term repeated fasting/refeeding will be used.

Published research suggests that animals adapted to repeated fasting/refeeding develop a greater capacity to store, spare and perhaps manufacture carbohydrate in the liver [9,10,14,17]. Knowledge of the metabolic adaptations to muscle metabolism induced by repeated fasting/refeeding is limited compared with the liver (Table 1), but like the liver, a greater capacity to store and spare glycogen is suggested. Importantly, in intermittently starved rats Petrasek [18] observed a significant increase in cytochrome oxidase activity compared with ad libitum fed controls and rats with simple chronic caloric undernutrition. This indicates a greater capacity of the muscle to utilize lipid is, at least in part, a function of the timing of eating because the

Table 1: Changes in skeletal muscle fibre characteristics of rats resulting from repeated fasting/refeeding

Effect	Reference
Greater muscle glycogen content in the soleus and diaphragm 24 hrs after refeeding	Gutman and Vrbova study [17]
Increased muscle glycogen levels on refeeding	Krizova and Simek study [19]
Increased rate of muscle glycogen synthesis after intraperitoneal glucose injection	Gutman study [20]
Greater cytochrome oxidase activity in mixed skeletal muscle and diaphragm	Petrasek study [18]

total energy intake and weight changes were the same between the chronic underfed and intermittently starved groups.

Repeated Fasting/Refeeding and the Metabolic Response to Exercise

Curi et al [8] compared the response of rats adapted to repeated fasting/refeeding for four weeks and ad libitum fed rats to "moderate" submaximal exercise. The regularly fasted/refed group showed a lower resting plasma FFA concentration, but a relatively greater increase in circulating FFA concentration during exercise. They also had a higher liver glycogen content at the beginning and throughout exercise, greater skeletal muscle glycogen content before exercise, though a greater rate of muscle glycogen utilization during exercise. No measure was made of fuel selection during exercise nor were any markers of muscle oxidative capacity measured. Nevertheless, this animal study seems to indicate that repeated fasting/refeeding primes the liver and muscle for exercise by providing a greater ability to store carbohydrate prior to exercise, and at the same time mobilizing lipid more effectively during exercise.

Because of known species differences in skeletal adaptations to fuel selection [21] it is unwise to simply extrapolate the results of the aforementioned rodent studies to humans. Unfortunately there is a paucity of laboratory-based human research investigating the effects of repeated fasting/refeeding on tissue metabolism and fuel selection. This is possibly due to the severity of the intervention required for a well-controlled study [22].

One study by Vondra et al [23] investigated the effect of fasting, then refeeding on the *quadriceps femoris* muscle enzyme concentration in obese women. Study participants experienced five-day fasts alternating with three days of low calorie eating for a total of 37 days. No improvements in skeletal muscle markers of oxidative and lipid handling capacity were observed during the course of the experiment. However, obesity, particularly of the upper body, is associated with an inflexibility of the muscle to adapt to changes in macronutrient availability [24]; so for any changes to be observed with such an intervention, a lean cohort may need to be used.

HUMAN STUDIES

Ramadan - A Human Model of Repeated Fasting/ Refeeding

The festival of Ramadan occurs during the 9th lunar month of the Islamic calendar and lasts between 29 and 30 days. During this holy month, Muslims are allowed to eat and drink only between sunset and sunrise. The effective period of fasting that is experienced each day during Ramadan depends upon the latitude in which the participant is living and the season. However, given that the majority of studies have been undertaken in countries of lower latitudes, the period of food restriction studied is in the order of 11-18 hours. Subsequently, meal frequency decreases, but caloric intake per meal increases with increased preference for fatty foods [25,26]. This situation is similar to that imposed on laboratory animals subjected to a repeated fasting/refeeding regime, but with less severity. The feeding time period allows sufficient food intake such that caloric deficit is not mandatory and no significant weight change is [27,28] or only a small weight loss (1.5-3.2% body weight) [29,33] is observed. The latter observation coupled with a lack of change in percentage of body fat [29; 31, 33] suggests a small net fat loss often occurs.

Ramadan and resting metabolism

The use of respiratory gas analysis provides a non-invasive method of measuring whole body fuel selection at rest and during exercise. Some studies employing this technique have shown resting whole body fuel selection, indicated by a reduction in respiratory exchange ratio (RER), to favour lipid oxidation [27,31] as Ramadan progresses. In contrast, others have observed no significant change in resting RER with participation in Ramadan [33]. Increased fasting plasma glucose [28] and decreased serum insulin levels [27] have also been recorded, an observation similar to that seen in rats subjected to repeated fasting/refeeding. By the final week of Ramadan, there is consistent reporting of a reduced resting rate of oxygen consumption (VO_2) [27,31] and heart rate [31,33] indicating a reduced rate of energy expenditure. This observation could be mediated by a reduced sympathetic nervous activity [34], reduced thermic effect of food [35], or a reduction in resting metabolic rate associated with a reduced body weight.

Ramadan and exercise

During submaximal exercise in subjects who did not participate in physical training during Ramadan, submaximal exercise RER decreases [32] or remains unchanged [33]. However, these changes in fuel utilization are subtle and appear to occur only at the lower submaximal intensities [36]. By the final week of Ramadan, there is reporting of improved economy (i.e. reduced submaximal exercise VO_2) [33,36] and heart rate [28,26].

Adaptive Effect of Exercise Training Whilst in the Fasted State

Recently, a number of studies have examined the effect of regular exercise after an overnight fast. The results of these studies indicate that endurance training undertaken without breaking the overnight fast leads to an increased capacity of the trained muscle to utilize lipid and also store glycogen in the fed state [37,40]. Despite this increased potential to utilize lipid, increased lipid oxidation during submaximal exercise was not observed even when exercise became prolonged [38,40]. A longer training period or a more stressful period of daily fasting may be required for this to occur.

Ramadan and exercise training

Partaking in endurance exercise training during participation in Ramadan would superimpose the metabolic stressors associated with repeated fasting/refeeding in the same way as the aforementioned training studies [38,40]. However, since the daily fasting period is during the waking hours rather than during sleep (as in the aforementioned studies), the total level of metabolic stress experienced by those training during Ramadan would be greater. Theoretically therefore, greater changes in skeletal muscle fuel selection could potentially occur and indeed measureable changes to fuel selection during exercise may be able to be detected.

To date, no study has set out to test this hypothesis thoroughly in well controlled fashion; to do so would require great compliance, a control group who trained in the same fashion but did not partake in Ramadan, and invasive procedures. Nevertheless, the one study by Brouhlel et al [26] has investigated the combined effect of physical training and participation in Ramadan on the metabolic response to exercise. Rather than prescribing controlled endurance exercise, these researchers observed an elite rugby team who trained consistently through Ramadan, measuring the physiological response to submaximal exercise before, early in, and late in Ramadan. Similarly, but more convincingly than the study of Stannard and Thompson [36], Brouhlel et al [26] observed a significantly increased reliance upon lipid during submaximal exercise as Ramadan progressed. Further, these researchers noted that the intensity at which carbohydrate became the dominant fuel during exercise was increased following participation in Ramadan. This was in contrast to the results of Stannard and Thompson [36], who showed no change in RER at a higher intensity, but may be due to the probably greater metabolic stimulus that regular physical training produced.

In essence, there is emerging evidence that adaptations to fuel selection favouring lipid oxidation occur during Ramadan. Together these results seem to indicate that when exposed to repeated fasting/refeeding, as occurs in Ramadan, the skeletal muscle adapts to be able to better utilize lipid, and therefore spare carbohydrate during exercise. Furthermore, these adaptations appear stronger if exercise training continues during participation in Ramadan.

However, without invasive techniques which are able to measure the muscle's oxidative capacity or leg respiratory quotient during exercise, the mechanisms behind these changes in whole body fuel selection cannot be fully explained. For example, a slight body fat loss, noted by both Brouhlel et al [26] and Stannard and Thompson indicates caloric deficit during Ramadan. Increased lipid utilization during exercise may thus reflect an acute response to caloric deficit rather than a muscle adaptation to repeated fasting/refeeding. Though counter to this, a reduced resting RER has been observed with no significant change in body weight or composition [27], indicating a distinct effect of Ramadan participation on fuel selection. Also however, increased dietary fat, and decreased dietary carbohydrate intake, as reported by Brouhlel et al [26] and others [27], may produce a greater reliance upon lipid fuel during rest and exercise.

Amino acids are increasingly relied upon to support energy metabolism in the latter stages of prolonged exercise [41] and also starvation [42]. Further, an effect of endurance training is to increase the biochemical potential of muscle to support energy metabolism using amino acids as fuel [43]. However, the impact of repeated fasting/refeeding, including participation in Ramadan, on the turnover of amino acids is as yet unknown.

An important confounder in the Ramadan model for repeated fasting/refeeding is that the daily fast also means that no water or other fluid can be ingested. Thus, adaptation to participation in Ramadan may involve hormones that regulate fluid and electrolyte status. These, in turn, may partly explain the cardiovascular and circulatory changes reported[30,31,33].

Some of the discrepancies between the results of research described in this review may be due to the fact that all the aforementioned studies employed weight-bearing (treadmill) exercise. It is possible that the losses in body weight reported during Ramadan in some of these studies resulted in a reduction of 'real' exercising workload. Clearly, further study using non-weight bearing exercise, such as cycling, is required to investigate whether changes in submaximal exercise substrate selection actually do occur with participation in Ramadan. The knowledge garnered from such research will enable a better understanding of the effects of repeated fasting/refeeding, for which Ramadan provides a suitable human model, on metabolism during exercise.

Further research might also consider empirical measurement of endurance performance before and in the latter stages of Ramadan. Certainly, if oxidative capacity of skeletal muscle is increased with participation in Ramadan, it could be hypothesised that endurance capacity would follow a similar trend.

Finally, it is interesting to note that the whole body and muscular adaptations seen with participation in Ramadan parallel those of the improved metabolic profile which occurs following exercise training alone. These, which include a reduced exercising heart rate and increased oxidative capacity of muscle, are associated with a reduced risk of non-communicable diseases such as type 2 diabetes and coronary heart disease. More effort should be placed on research investigating the health benefits of participation in Ramadan. These studies may be able to use non-invasive techniques, such as magnetic resonance spectroscopy (MRS), to study how repeated fasting/refeeding impacts on skeletal muscle fuel selection. For example, MRS has previously been employed successfully to show how starvation alters intramyocellular lipid content [6]; accretion of this fuel is associated with obesity-induced insulin resistance[44].

CONCLUSION

Repeated fasting, then refeeding, results in adaptations which result in increased reliance upon lipid oxidation at rest and during exercise, and an increased capacity of the skeletal muscle and liver to store carbohydrate. Ramadan is an excellent human model for this dietary regime. There is strong evidence that participation in Ramadan promotes the ability of the body to better utilize lipid at rest and during exercise. If exercise training is done during Ramadan, these adaptations are more pronounced.

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