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REVIEW ARTICLE

Nutritional strategies to support concurrent training

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Abstract
Concurrent training (the combination of endurance exercise to resistance training) is a common practice for athletes looking to maximise strength and endurance. Over 20 years ago, it was first observed that performing endurance exercise after resistance exercise could have detrimental effects on strength gains. At the cellular level, specific protein candidates have been suggested to mediate this training interference; however, at present, the physiological reason(s) behind the concurrent training effect remain largely unknown. Even less is known regarding the optimal nutritional strategies to support concurrent training and whether unique nutritional approaches are needed to support endurance and resistance exercise during concurrent training approaches. In this review, we will discuss the importance of protein supplementation for both endurance and resistance training adaptation and highlight additional nutritional strategies that may support concurrent training. Finally, we will attempt to synergise current understanding of the interaction between physiological responses and nutritional approaches into practical recommendations for concurrent training.

Keywords: *Concurrent training, training interference, nutrition, hypertrophy, AMPK, mTORC1*

Introduction

Training interference was first conceptualised by Robert C. Hickson (Hickson, 1980). Utilising high-intensity cycling and running as the endurance component of a concurrent training programme (i.e. the combination of resistance and endurance type exercise in the same training session), Hickson demonstrated that endurance exercise blunted gains in strength compared to strength training alone (Hickson, 1980). This data demonstrated for the first time that high-intensity endurance training was capable of interfering with the adaptive response to strength training (Figure 1). Despite numerous experimental studies, the mechanisms underlying training interference remain unclear (Fyfe, Bishop, & Stepto, 2014; Hamilton & Philp, 2013). What is also uncharacterised is the role of nutrition in the concurrent training response and whether nutritional strategies might be an effective approach to offset the strength declines reported by Hickson (1980) and others (Ronnestad, Hansen, & Raastad, 2012). The aim of this review is to (1) briefly highlight the molecular processes thought to regulate skeletal muscle adaptation to endurance, resistance and concurrent exercise, (2) discuss nutritional strategies to improve recovery from and/or adaptation to endurance and resistance exercise in isolation, and (3) attempt to formulate nutritional strategies that might be suitable for supporting concurrent training.

Molecular regulation of endurance exercise adaptations

Endurance exercise relies to a great extent on skeletal muscle oxidative capacity, which in turn is highly dependent on mitochondrial function and blood supply (Egan & Zierath, 2013). Accordingly, chronic endurance exercise training augments the

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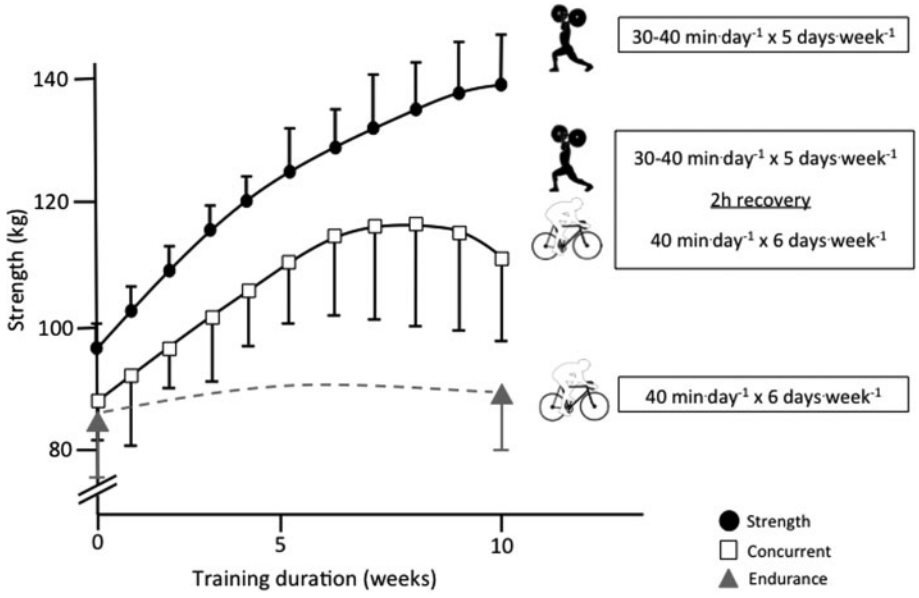

Figure 1. Concurrent training blocks strength gains during 10 weeks training. The addition of endurance training to resistance-training programme blunts gains in strength compared to resistance training alone. Data is redrawn from Hickson (1980) with relative training regimes detailed for resistance, concurrent and endurance training designs.

capacity for aerobic adenosine triphosphate (ATP) synthesis by increasing the expression of genes regulating biological processes like mitochondrial biogenesis and angiogenesis (Egan & Zierath, 2013). Skeletal muscle metabolic and mechanical stress induced by endurance exercise are thought to modulate different signal pathways controlling the transcriptional networks regulating these adaptations (Egan & Zierath, 2013). It is well established that following the initiation of contraction, there is a rapid, transient flux of substrates, metabolites and nucleotides within skeletal muscle, such as Ca^{2+}, adenosine monophosphate (AMP) and nicotinamide adenine dinucleotide (NAD^{+}) (Egan & Zierath, 2013). From an adaptation perspective, this is extremely important, as many of these signalling molecules have been identified as key activators of signal transduction cascades, which ultimately enhance the adaptive response. We will briefly highlight these factors and the cascades they govern in the context of endurance training adaptations.

Metabolic stress leads to skeletal muscle adaptation

Among the wide range of proteins regulated by endurance exercise, AMP-activated protein kinase (AMPK) is probably the most studied in the context of skeletal muscle remodelling. The relevance of this protein kinase relies on its capacity to sense both metabolic stress and energy storage (Hardie, Ross, & Hawley, 2012). Exercise activates skeletal muscle AMPK in an intensity-dependent manner, with exercise at high intensities (thus higher ATP turnover) resulting in higher AMPK activation (Wojtaszewski, Nielsen, Hansen, Richter, & Kiens, 2000). Furthermore, energy restriction and glycogen depletion in rodent and human skeletal muscle significantly enhances AMPK activity both under basal conditions and following acute exercise (Philp et al., 2013; Wojtaszewski et al., 2003).

In the long-term, repeated activation of AMPK via endurance exercise can enhance skeletal muscle oxidative capacity through the modulation of different transcription factors and co-regulators (Egan & Zierath, 2013); these include nuclear respiratory factor 1, nuclear respiratory factor 2, mitochondrial transcription factor A and the co-activator peroxisome proliferative activated receptor, gamma, coactivator 1 alpha (PGC-1α), all of which are central modulators of mitochondrial biogenesis (Garcia-Roves, Osler, Holmstrom, & Zierath, 2008; Rockl et al., 2007). The positive effects of AMPK on mitochondrial function are PGC-1α dependent, which can be phosphorylated and activated by AMPK *in vitro* (Jager, Handschin, St-Pierre, & Spiegelman, 2007), indicating dynamic interaction between the two proteins. Another post-translational modification controlling PGC-1α activity is its acetylation, with deacetylation of PGC-1α shown to increase its transcriptional activity. PGC-1α acetylation levels are regulated by the acetyltransferase GCN5 and the deacetylase sirtuin 1 (SIRT1), respectively (Lerin et al., 2006; Rodgers et al., 2005). This acetylation balance adds another way by which skeletal muscle metabolism can be modulated by energy status, since SIRT1 activity is

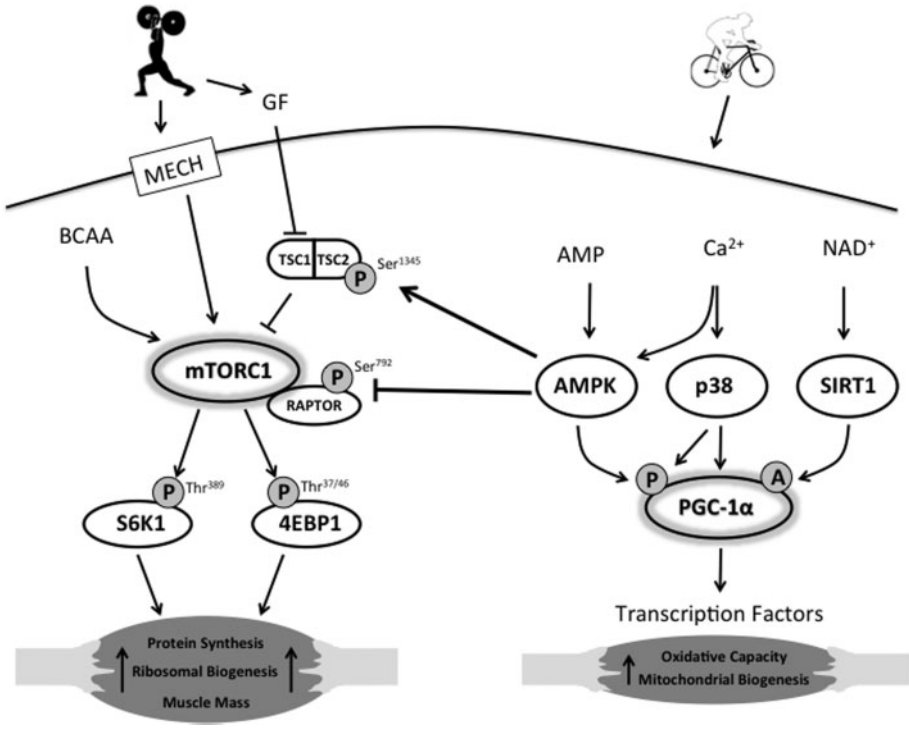

Figure 2. Molecular signalling pathways involved in endurance and resistance-training adaptation. mTORC1 is activated in skeletal muscle via three distinct mechanisms (1) Branch-chain amino acids (BCAA), (2) Mechanical loading (MECH) and (3) growth factor (GF) stimulation. Through phosphorylation of downstream targets S6K1 and 4E-BP1, mTORC1 increases protein synthesis and ribosomal biogenesis, which ultimately leads to hypertrophy. In contrast, endurance-training adaptation is initiated via the increased production of AMP, Ca^{2+} and NAD^{+}, which activate the sensing proteins AMPK, p38 MAPK and SIRT1. These proteins initiate a programme of mitochondrial biogenesis through the activation of the transcriptional co-activator PGC-1α, which in turn drives mitochondrial gene transcription through a subset of transcription factors. The interference effect of endurance exercise has been suggested to occur through AMPK mediated phosphorylation of TSC2 Ser^{1345} and Raptor Ser^{792} which both serve to blunt mechanical and nutritional activation of mTORC1. *P* = phosphorylation, *A* = acetylation.

efficiently induced by an increase in cytosolic $[NAD^{+}]$ and GCN5 activity thought to be regulated by increased acetyl-CoA availability (Philp & Schenk, 2013).

In addition to alterations in the metabolic environment, other signals induced by skeletal muscle contraction have also been shown to be an important signal controlling exercise adaptation, with the p38 mitogen-activated protein kinase (MAPK) and calcium dependent (CaMKII) and cAMP (PKA-CREB) signalling thought to play a key role (Egan & Zierath, 2013). However, how these proteins could affect strength adaptations has yet to be demonstrated.

Molecular regulation of resistance exercise-mediated skeletal muscle hypertrophy

In contrast to endurance exercise, adaptations to chronic resistance exercise require the activation of anabolic processes that ultimately promote increased protein accretion, enhanced skeletal muscle cross-sectional area (CSA) and maximal force (Egan & Zierath, 2013). Skeletal muscle mechanical loading mediates these adaptations mainly through an increase in the rate of protein synthesis and ribosomal biogenesis (Moore, Robinson, et al., 2009; Tipton, Ferrando, Phillips, Doyle, & Wolfe, 1999; Witard et al., 2014).

Activation of the mechanistic target of rapamycin (mTOR) complex 1 (mTORC1) seems to be a mandatory step and a point of convergence of pathways sensing both mechanical load and amino acid levels (Philp, Hamilton, & Baar, 2011). Skeletal muscle overload has been proposed to increase mTORC1 activity by increasing cytosolic calcium $[Ca^{2+}]$, phosphatidic acid and leucine, in addition to the activation of focal adhesion kinase, extracellular signal-regulated kinase and diacylglycerol kinase ζ (Miyazaki, McCarthy, Fedele, & Esser, 2011; Philp et al., 2011; You et al., 2014). mTORC1 activation by amino acids, on the other hand, involves the activation of the Rag GTPases that mediate the translocation of mTORC1 from the cytosol to the lysosome surface (Shimobayashi & Hall, 2014). Since the two mechanisms are distinct, administration of essential amino acids potentiates the positive effects of resistance exercise on mTORC1 activity in human skeletal muscle (Kakigi et al., 2014).

Following its activation, mTORC1 drives protein synthesis via two main mechanisms (Figure 2): (1) the direct phosphorylation of the eukaryotic translation initiation factor 4E (eIF4E)-binding protein 1 (4E-BP1) and (2) S6 kinase 1 (S6K1) (Shimobayashi & Hall, 2014). 4E-BP1 phosphorylation exerts an inhibitory effect that releases eIF4E, thus promoting the initiation of cap-dependent translation, whereas phosphorylation of S6K1 increases its activity and the regulation of its downstream targets controlling translation, including S6 and eIF4B (Shimobayashi & Hall, 2014). In accordance, the increase in protein synthesis induced by resistance exercise in human skeletal muscle has been shown to coincide with higher levels of 4E-BP1 and S6K1 phosphorylation, although reports have also identified that surrogate markers of mTORC1 activation might not always correlate with the protein synthetic response (Mitchell et al., 2013) or adaptation to chronic resistance exercise training (Phillips et al., 2013).

Intracellular signalling regulated by concurrent exercise in skeletal muscle

It has been proposed that AMPK-mediated suppression of mTORC1 is the principal mechanism by which endurance exercise may blunt strength gains following resistance exercise (Hamilton & Philp, 2013). In fact, while the growth stimulus provided by resistance exercise inhibits the upstream mTORC1 repressor TSC1-TSC2 complex, endurance exercise seems to promote the opposite effects in an AMPK-dependent way (Figure 2). Practically, however, although the molecular mechanism controlling anabolic (mTORC1) and catabolic (AMPK) processes coincide with the concurrent effect reported in humans, some studies have also reported conflicting results, making the molecular events underpinning concurrent training at present unclear. For example, chronic concurrent exercise training has been shown to induce similar effects on maximal force and CSA as strength training, while $\dot{V}O_{2max}$ and exercise performance improved to a similar extent as induced by interval training (de Souza et al., 2013). Moderate intensity endurance exercise does not seem to impair the effects of acute resistance exercise on mTORC1 and S6K phosphorylation (Apro, Wang, Ponten, Blomstrand, & Sahlin, 2013) or the hypertrophy response to short-term single-leg resistance training (Lundberg, Fernandez-Gonzalo, Gustafsson, & Tesch, 2013); however, high-intensity interval exercise does blunt S6K1 phosphorylation (Coffey et al., 2009). Furthermore, performing aerobic exercise prior to resistance exercise in a concurrent model has no detrimental effects on anabolic signalling (Lundberg, Fernandez-Gonzalo, Gustafsson, & Tesch, 2012) or adaptive growth to chronic single-leg training (Lundberg et al., 2013). In fact, contrary to the concept of exercise interference during concurrent training, concurrent exercise actually enhances myofibrillar (Camera et al., 2014) or myofibrillar and mitochondrial protein fractional synthesis rates (Donges et al., 2012) in the fed state to a greater extent than resistance exercise alone. These data, therefore, indicate that the physiological and acute molecular responses to concurrent exercise are highly dependent on training status, the order of the concurrent exercise regime, the mode of exercise and the time course studied (acute vs. chronic models). As such, contemporary studies still have not identified a unifying molecular mechanism accounting for Hickson's initial observations. Given that training interference occurs after 8 weeks of concurrent training (Hickson, 1980; Ronnestad et al., 2012), chronic training protocols combined with specific acute studies appear to represent the most appropriate approach to delineate the molecular mechanisms mediating training interference in human skeletal muscle (Fyfe et al., 2014; Hamilton & Philp, 2013).

Nutritional approaches to improve resistance and endurance performance – implications for concurrent training

Whilst the interference effect makes concurrent training technically challenging, it also adds additional complexity when considering the nutritional requirements for a concurrent athlete. In general terms, energy restriction in skeletal muscle appears to amplify the endurance training signalling environment, whereas a positive energy balance is optimal to maximise the anabolic environment post-resistance exercise (Hamilton & Philp, 2013). Detailed investigation of the nutritional requirements for concurrent training has not been conducted, and so much of our knowledge about nutritional strategies that may influence the concurrent training comes from isolated studies examining the impact of nutritional interventions on endurance or resistance training alone. Based on these studies, the following section will examine nutritional strategies utilised in isolated endurance or resistance exercise settings to highlight common practices between modes that might be suitable for consideration for the concurrent athlete. Additionally, given the need to synthesise new muscle proteins (e.g. force-generating myofibrillar and/or energy-producing mitochondrial protein) in order to facilitate muscle recovery and ultimately improve training adaptations for the concurrent athlete, the following section will focus heavily on the role dietary protein plays in the remodelling of skeletal muscle.

Beneficial effects of protein supplementation for both resistance and endurance exercise

Exercise in the fasted state increases both the synthesis and breakdown (i.e. "turnover") of muscle protein with the algebraic difference between these processes determining the net protein balance (i.e. synthesis – breakdown; Burd, Tang, Moore, & Phillips, 2009). This enhanced protein turnover functions to remodel skeletal muscle and ultimately underpins its plasticity. It is well known that the ingestion of essential amino acids enhances muscle protein synthesis (MPS) and net protein balance after exercise (Tipton et al., 1999). The stimulatory effect of exogenous amino acids on MPS is uninfluenced by the co-ingestion of carbohydrate (Glynn et al., 2010; Staples et al., 2011), demonstrating that dietary protein is the primary nutritional factor regulating skeletal muscle remodelling after exercise and, in the case of resistance exercise, can enhance training-induced muscle growth (Burd et al., 2009). Recent studies have demonstrated that it is the myofibrillar protein fraction that is primarily responsive to exogenous amino acids after resistance (Moore, Tang, et al., 2009), endurance (Breen et al., 2011), and/or concurrent exercise (Camera et al., 2014; Donges et al., 2012). While there appears to be little effect of dietary protein on post-exercise rates of mitochondrial protein synthesis (Moore, Camera, Areta, & Hawley, 2014), this enhanced myofibrillar protein remodelling could still reflect an adaptive advantage for the athlete engaged in concurrent training. Moreover, during periods of chronic energy restriction, such as would be encountered during voluntary weight loss or inadvertent suboptimal energy intake, protein ingestion is essential to enhance post-exercise MPS (Areta et al., 2014) and the maintenance of lean mass (Churchward-Venne, Murphy, Longland, & Phillips, 2013; Mettler, Mitchell, & Tipton, 2010). Therefore, dietary protein should be viewed as a core component of the recovery nutrition for the concurrent athlete (and especially weight restricted athletes) through its ability to enhance muscle protein remodelling.

MPS is enhanced after both resistance (Moore, Robinson, et al., 2009) and endurance-based exercise (Levenhagen et al., 2002) with the ingestion of as little as ~10 g of dietary protein. However, athletes aiming to maximise recovery from each training bout would benefit from greater post-exercise protein ingestion, as demonstrated by recent ingested protein dose–response studies (Moore, Robinson, et al., 2009; Witard et al., 2014). Therefore, the "optimal" protein ingestion (i.e. one that maximises MPS yet minimises irreversible amino acid oxidation) would be ~20 g (or the equivalent of ~0.25 g/kg) of high-quality protein (such as whey protein). Understanding of the specific protein requirements to maximise MPS after endurance exercise are at a relative infancy compared to resistance exercise (Moore et al., 2014). Nevertheless, MPS is similarly enhanced after endurance-based exercise with ~16–20 g of dietary protein in both untrained and trained athletes (Breen et al., 2011; Lunn et al., 2012), suggesting post-exercise protein requirements for skeletal muscle remodelling are likely consistent across training modalities (Moore et al., 2014). Therefore, based on currently available literature, the "optimal" protein ingestion would likely be similar after endurance exercise, meaning that concurrent athletes can likely interchange dosing across the training regime.

In general, there are three occasions in which athletes may ingest nutrients to facilitate their training and/or recovery: before, during and/or after exercise. These clear distinctions between eating occasions are not always evident for athletes who train on consecutive days or, more importantly, multiple times per day, as would be the case with many concurrent athletes. Nevertheless, the following sections will discuss the relative importance of these general opportunities for protein intake on the ability to enhance skeletal muscle remodelling with training.

Prior to exercise

Although early research suggested that pre-exercise essential amino acid ingestion induced a greater increase in muscle net protein balance with resistance exercise (Tipton et al., 2001), subsequent studies have failed to support these initial positive findings (Tipton et al., 2007). The digestion and absorption of high-quality dietary protein typically result in peak blood amino acid concentrations occurring within 1 h after ingestion and being sustained for up to 2–3 h, although this depends on the protein type, energy density and food matrix of the nutrition (Burke et al., 2012). Nevertheless, post-exercise MPS after relatively short duration training bouts (e.g. ≤1 h) has been reported to be enhanced by pre-exercise protein/amino acid ingestion (Tipton et al., 2007), possibly through a "priming" of the muscle intracellular amino acid pool for subsequent post-exercise muscle remodelling. However, MPS is generally depressed during muscle contraction due to the shunting of cellular energy away from non-essential energy-consuming processes such as protein remodelling (Atherton & Rennie, 2006), which ultimately lessens the importance of pre-exercise protein ingestion for the greater muscle remodelling and adaptive process. Therefore, athletes performing brief (e.g. ≤1 h) exercise bouts would arguably obtain a greater benefit from a pre-exercise feeding strategy that would prioritise fuelling

a quality training session (e.g. adequate carbohydrate and/or fluid ingestion), rather than promoting muscle remodelling (e.g. protein ingestion).

During exercise

Aerobic exercise is associated with an enhanced oxidative disposal of amino acids (especially the branched-chain amino acids) (Millward, Bowtell, Pacy, & Rennie, 1994) that arise from the catabolism of skeletal muscle protein, which ultimately results in a negative muscle and whole body protein balance during exercise (Howarth et al., 2010). For athletes who perform relatively long (e.g. ≥1.5 h) bouts and/or multiple endurance training sessions per day, the inclusion of protein during their workout may help limit the endogenous use of amino acids as a source of fuel and improve whole body protein balance during exercise (Beelen et al., 2011). It is presently unclear, however, as to what extent protein intake could improve muscle protein remodelling and/or net protein balance during a bout of endurance exercise (Beelen et al., 2011), given the general suppression of anabolic pathways during periods of high ATP demand (e.g. muscle contraction; Atherton & Rennie, 2006).

Resistance exercise differs from traditional constant load endurance exercise as it is typically characterised by brief inter-set "rest" (i.e. recovery) periods, which may represent an opportunity to initiate skeletal muscle remodelling. In potential support, protein ingestion during a relatively prolonged (i.e. ~2 h) resistance training bout has been reported to support greater rates of MPS during exercise than a protein-free carbohydrate control (Beelen et al., 2008). Therefore, athletes who have long resistance training sessions and/or who train concurrently after their endurance exercise sessions may benefit from the co-ingestion of dietary protein during their training bouts.

Following exercise

Protein ingestion immediately after exercise unquestionably enhances MPS and net protein balance in young adults after all forms of exercise (Burd et al., 2009; Moore et al., 2014). Resistance exercise has been shown to enhance the sensitivity of skeletal muscle to dietary protein for up to 24 h, meaning that protein consumed at any time within this extended "window of opportunity" will contribute to enhanced muscle remodelling and adaptation (Burd et al., 2011). This may explain, in part, the recent suggestion that the timing of protein intake around a resistance exercise session (i.e. ±2 h) plays a limited role in the ability to augment training-induced gains in muscle mass or strength primarily in novice athletes (Schoenfeld, Aragon, & Krieger, 2013). However, resistance-trained individuals may have a relatively abbreviated "window of opportunity", given that rates of MPS are enhanced by protein ingestion 4 h, but not 28 h, after an acute bout of resistance exercise (Tang, Perco, Moore, Wilkinson, & Phillips, 2008). Moreover, compared to immediately post-exercise, delaying protein ingestion by as little as 3 h after constant load aerobic exercise markedly blunts its anabolic effects as demonstrated by a lack of stimulation of MPS (Levenhagen et al., 2001). Therefore, it would be prudent for athletes aiming to rapidly initiate muscle remodelling and recovery to consume dietary protein as soon as possible after an exercise bout, regardless of training modality.

Aside from the immediate post-exercise feeding period, the pattern of protein ingestion outside of this early (i.e. < 3 h) recovery period can also impact the extent of muscle protein remodelling. For instance, the repeated ingestion of 20 g of protein [i.e. an "optimal" amount for the stimulation of MPS (Moore, Robinson, et al., 2009; Witard et al., 2014)] every 3 h over 12 h supported greater rates of myofibrillar protein synthesis and induced a more positive whole-body protein balance after a bout of resistance exercise than the identical amount (i.e. 80 g) of protein ingested as 10 g feedings every 1.5 h or 40 g feedings every 6 h (Areta et al., 2013; Moore et al., 2012). This demonstrates that the pattern, and not merely the amount, of protein ingested can influence the efficiency of post-exercise muscle remodelling after resistance exercise. While such prolonged recovery studies have not been performed after endurance and/or concurrent exercise, it is likely that a similar feeding pattern (both of protein amount and frequency) would also support the greatest rates of MPS after these training modalities, given that 20–25 g (0.25–0.30 g protein/kg/meal) of protein has been established to saturate the protein synthetic capacity of the muscle in multiple studies at rest and after exercise (Moore, Robinson, et al., 2009; Witard et al., 2014). Additionally, protein consumed immediately prior to sleep has been reported to sustain greater rates of MPS during the overnight post-exercise recovery period (Res et al., 2012), which may help athletes who, due to scheduling or personal preference, must train in the evening but want to maximise their recovery. Therefore, athletes aiming to support the greatest rates of muscle remodelling would benefit from targeting protein consumption immediately after exercise and every 3–4 h thereafter.

It should also be highlighted that beyond altering anabolic processes, influencing protein accretion, protein ingestion can also play a role in glycogen synthesis and by extension in skeletal muscle metabolic conditioning (Burke, Hawley, Wong, & Jeukendrup,

2011). Co-ingesting protein with suboptimal doses of carbohydrate (<1.2 $g.kg^{-1}$ h^{-1}) elicits a glycogen re-synthesis response comparable to higher carbohydrate ingestion (Burke et al., 2011). As such, combined protein and carbohydrate ingestion could be advantageous for a concurrent athlete looking to restore glycogen levels quickly prior to a second exercise bout or to avoid ingesting high amounts of carbohydrate. In this respect, however, under some circumstances, it may also be beneficial for the concurrent athlete to delay glycogen re-synthesis, allowing endurance exercise to be performed in a glycogen-depleted state (see review in this issue from Morton and Hawley). However, the payoff for this strategy may be a greater rate of muscle catabolism with low glycogen levels (Howarth et al., 2010). It is, therefore, likely that periodising protein and combined protein–carbohydrate ingestion in respect to the mode/intensity of exercise during a concurrent training regime could be the most practical approach. Clearly, this topic will provide numerous avenues of experimentation for concurrent-based research in the future.

General protein requirements

General protein recommendations highlight that athletes require a greater daily protein intake than their sedentary counterparts. Provided energy needs are met, current recommendations suggest that ~1.2–1.7 g protein/kg/d is required to satisfy the metabolic demands of this macro-nutrient for both resistance and endurance-trained athletes (Phillips, 2012; Tarnopolsky, 2004), which is generally in line with habitual dietary intakes of elite athletes (Burke et al., 2003). As highlighted previously, balanced daily protein ingestion supports greater rates of MPS both at rest (Mamerow et al., 2014) and during prolonged recovery from exercise (Areta et al., 2013). If one were to accept that ~0.25 g/kg maximises MPS (Moore, Robinson, et al., 2009) and that the repeated ingestion every ~3 h would sustain these elevated rates (Areta et al., 2013), then a typical ~16 h waking period (i.e. ~5 meal occasions) would result in a total protein intake of ~1.25 g/kg/d. However, a greater protein intake (i.e. 40 g or ~0.50 g/kg) may be required prior to bedtime to offset overnight catabolic losses (Res et al., 2012), which when factored into this repeated feeding paradigm to replace the final meal occasion would yield a total protein intake of ~1.5 g/kg/d. This "optimal" feeding pattern would result in a total protein intake that would be in line with recommendations for all athletes and would be generally consistent with the habitual meal frequency and protein intake of most elite athletes (Burke et al., 2003).

Are there other "active" ingredients that might support concurrent training practice?

Omega 3 fish oil. Omega 3 fatty acids have a unique ability to reorganise cell membrane structure and effect intermediate signalling precursors with a range of bioactivities including anti-inflammatory actions (Maskrey, Megson, Rossi, & Whitfield, 2013). Recently, Omega 3 supplementation (8 weeks/4 g/day) has been shown to improve anabolic responsiveness in 16 older adult subjects (>65 years of age; Smith et al., 2011). In response to simulated feeding (hyperinsulinaemic–hyperaminoacidaemic clamp), those subjects supplemented with fish oil increased their MPS by ~60% above the pre-supplementation value (Smith et al., 2011). The same response was observed in a follow-up study by the same group in nine young and middle-aged men and women (25–45 years old) indicating that the effect of Omega 3 supplementation is maintained in young and old individuals. Furthermore, an Omega 3 supplementation (2 g/day fish oil) trial superimposed on a 90-day resistance-training programme in 45 elderly women resulted in greater training-induced strength gains in the groups receiving fish oil (Rodacki et al., 2012). These studies highlight that Omega 3 supplementation can have a substantial impact on the nutritional response of MPS and also (in elderly subjects at least) Omega 3 supplementation can enhance the training effect achieved by a resistance-training programme.

The impact of Omega 3 supplementation on endurance adaptations is less defined. With specific focus on skeletal muscle adaptation, Peoples and McLennan have shown that male Wistar rats supplemented with *n*-3 PUFAs for 8 weeks display greater fatigue resistance to electrical stimulation (1 Hz, 6–12 V, 0.05 ms), improved recovery rates between contraction bouts and a significantly higher O_2 efficiency index during the recovery period (Peoples & McLennan, 2010). A possible explanation for the improvements reported by Peoples and McLennan (2010) was recently provided by Herbst et al. who demonstrated that 12-weeks of *n*-3 supplementation in humans improved adenosine diphosphate (ADP) kinetics in human skeletal muscle mitochondria through alterations in membrane structure and/or post-translational modification of ATP synthase and adenine nucleotide translocator isoforms (Herbst et al., 2014). However, to our knowledge, no studies have found a beneficial effect of fish oil/Omega 3 supplementation on endurance exercise performance in trained individuals. Only one study in sedentary subjects has reported improvements in training-induced changes in $\dot{V}O_{2max}$ when supplemented with fish oil throughout the training period (Brilla & Landerholm, 1990). So

from the endurance training perspective, there seems to be a benefit of fish oil on $\dot{V}O_{2max}$ only in untrained subjects with a potential to reduce inflammation in response to an acute bout of endurance exercise (Ernst, Saradeth, & Achhammer, 1991). Irrespective of exercise mode, it would appear that in order to gain a benefit, doses need to be high (>3 g Omega 3 per day) with a minimum supplementation period of 2 weeks to increase skeletal muscle Omega 3 content (McGlory et al., 2014). As a recommendation, it would seem wise for those on concurrent training programmes to supplement at least 3 g/day fish oil with the potential for the supplementation to enhance the strength training responses.

Modulators of nitric oxide (L-arginine, citrulline and nitrates)

The signalling molecule nitric oxide (NO) represents another nutritional target that might promote both endurance and resistance adaptation. NO can be synthetised from L-arginine and molecular O_2 through a reaction catalysed by different NO synthase (NOS) isoforms (endothelial, neuronal and inducible; Stamler & Meissner, 2001). In addition, NO can be synthetised in a NOS-independent manner through an alternative mechanism requiring nutritional nitrate (NO_3^-; Jones, Vanhatalo, & Bailey, 2013). Nitrate is especially enriched in green-leafed vegetables and is converted into nitrite (NO_2^-) by oral bacteria prior to its absorption, where it can subsequently be converted to NO *in vivo* (Jones et al., 2013). NO regulates a number of biological processes determining skeletal muscle metabolism and exercise performance, such as blood flow, glucose/fatty acid oxidation, angiogenesis and mitochondrial biogenesis (Stamler & Meissner, 2001).

Nitrate supplementation in the form of $NaNO_3^-$ or NO_3^--rich beetroot juice has been reported to improve metabolic efficiency, which is reflected in lower oxygen consumption (VO_2) during sub-maximal exercise when compared to a placebo (Bescós, Sureda, Tur, & Pons, 2012; Jones et al., 2013). Importantly, consistent with the effects on metabolic efficiency, ~7 days of nitrate consumption has been demonstrated to increase fatigue resistance by ~20% (Bescós et al., 2012; Jones et al., 2013). Maximal exercise performance, on the other hand, seems to be less sensitive to nitrate supplementation, with short-term nitrate supplementation inducing ~2% improvement in peak power output (Bescós et al., 2012; Jones et al., 2013). These short-term effects of nutritional nitrate on metabolic efficiency are related to a more efficient coupling between ATP utilisation and skeletal muscle force generation (Bailey et al., 2010), while mitochondrial function seems to be also improved following long-term administration (Vanhatalo et al., 2010). Administration of nitrate for a longer period of time (15 days) increases maximal exercise performance and $\dot{V}O_{2max}$ (Vanhatalo et al., 2010); however, the mechanisms behind these ergogenic effects remain to be elucidated. In addition, a different strategy to modulate NO levels involves the consumption of the L-arginine precursor L-citrulline (Bescós et al., 2012). However, even though some reports suggest that L-arginine and L-citrulline supplementation can exert ergogenic effects, the efficiency of these nutrients remain controversial and its effects appear to be NO-independent (Bescós et al., 2012). Collectively, these data suggest that increasing NO levels might be a potential strategy to potentiate the improvement in endurance performance following concurrent exercise. However, the effects of nutritional supplements increasing NO synthesis on skeletal muscle force generation and adaptive growth need to be experimentally explored.

Creatine

The performance-enhancing effects of the biologically active compound creatine have been extensively studied in both endurance and resistance settings (Bemben & Lamont, 2005) due to the fact that the main biological function of creatine is to rapidly replenish high-energy phosphate stores (Bemben & Lamont, 2005). During high-intensity and explosive exercises, such as brief (~10 s) sprinting or weightlifting, are predominantly fuelled by phosphocreatine as this intracellular energy buffer provides an immediate phosphate source for ADP re-phosphorylation (catalysed by the enzyme creatine kinase (CK)) that ultimately leads to ATP re-synthesis. Another function of creatine is pH buffering, since hydrogen ions are utilised during the enzymatic reaction catalysed by CK, suggesting that increased levels of skeletal muscle phosphocreatine can also delay fatigue by attenuating metabolic acidosis (Bemben & Lamont, 2005).

Nutritional supplementation of this active compound in the form of creatine monohydrate efficiently increases phosphocreatine levels in skeletal muscle tissue, implying that this nutritional supplement improves skeletal muscle energetics and function. Accordingly, creatine supplementation has been extensively shown to induce a significant ~2% improvement of high-intensity exercise performance, representing an important ergogenic effect for elite athletes competing in disciplines involving sprinting and jumping (Tarnopolsky, 2010). In addition to the beneficial effects in sprint-related sports, creatine can also potentiate the effects of chronic resistance exercise on skeletal muscle mass, potentially through a greater work capacity and, subsequently, training

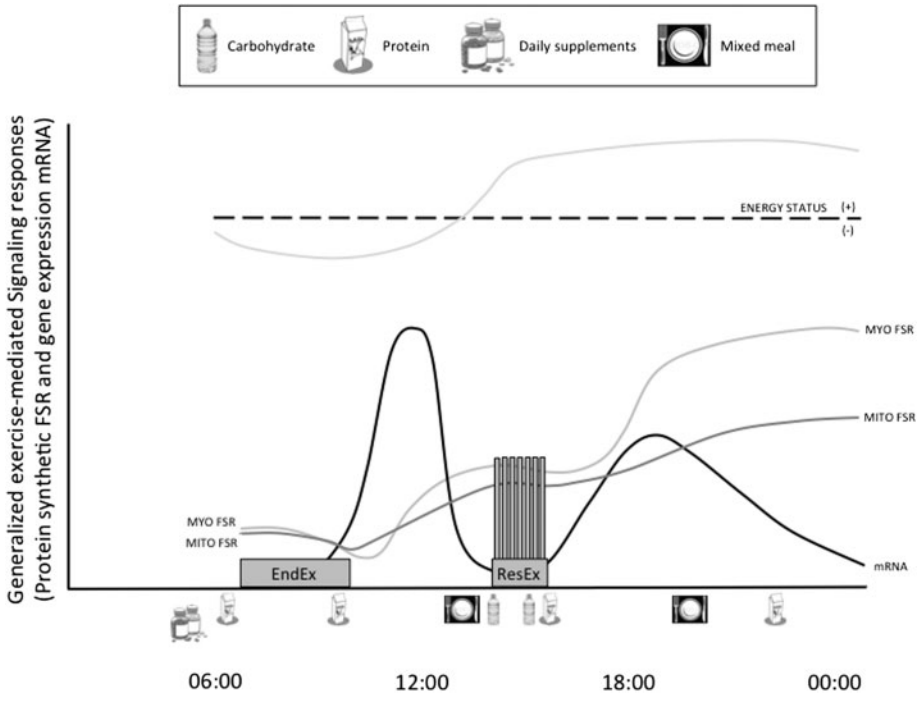

Figure 3. Integrating nutritional approaches relative to molecular signalling events in skeletal muscle. Exercise-mediated signalling responses representing transcriptional (mRNA) and fractional protein synthesis rate (MITO – Mitochondrial and MYO – myofibrillar) in relation to generalised skeletal muscle energy status are depicted. To maximise adaptation, it would be advised to complete endurance training with a low energy status. The most practical approach to achieve this would be to perform endurance exercise in the AM, following an overnight fast. Protein ingestion can be performed during this period, whereas high CHO intake should be avoided during low intensity – long duration exercise bouts. Prior to resistance exercise, the nutritional focus would be to restore CHO/PRO availability so that the individual enters the resistance exercise session in positive energy status. Typically, this can be achieved with a mixed meal prior to exercise, supported with CHO/PRO ingestion. Post-resistance exercise, the nutritional goal is to maintain PRO availability during the adaptive period, maintaining positive energy status and maximising the protein synthetic response. This can be achieved through a mixed meal and pulse ingestion of PRO.

stimulus. Even though higher fat-free mass induced by creatine ingestion is partially due to increased intracellular water, when combined with resistance exercise, this active compound induces positive effects on skeletal muscle function (Bemben & Lamont, 2005). Consistently, resistance exercise training combined with creatine supplementation induces greater improvements in skeletal muscle strength compared to placebo (Bemben & Lamont, 2005). The main nutritional approach to induce such ergogenic effects has traditionally involved an initial loading period in which high doses (~20 g/day) of creatine are consumed during a short period of time (~5 days). Subsequently, a maintenance period in which lower doses (~4 g/days) of creatine are consumed is continued for a longer period of time (~4 weeks). Alternatively, similar effects can be obtained by consuming lower doses (~5 g/days) of creatine during a long period of time (> 4 weeks) without the necessity of a loading period.

Practical implications

The most practical approach to combine endurance and resistance training within the same day is likely an endurance session in the morning, followed by resistance training in the afternoon (Figure 3). This approach is advantageous as it allows the athlete to conduct the endurance training bout in a fasted state, to promote signalling adaptation associated with metabolic and mechanical stress. For long duration/moderate-intensity sessions, ingestion of high amounts of carbohydrates (CHO) are likely detrimental for many of the pro-adaptive signals (Philp, Hargreaves, & Baar, 2012). In contrast, protein ingestion during this phase could support muscle remodelling and offset proteolysis during exercise. Post-exercise, CHO replenishment should be gradual and likely avoided in the immediate post-exercise period (Figure 3).

In preparation for subsequent resistance exercise, the concurrent athlete should attempt to gradually increase skeletal muscle energy status so that resistance exercise is ultimately performed in an energy-rich fed state. In this respect, a mixed meal and CHO replenishment are advised, with post-exercise protein intake of 0.25 g/kg of a leucine-rich food required to maximise the anabolic effects of the exercise bout and maintenance of the pro-hypertrophic effects thereafter. Further, gains may be

achieved by habitual supplementation of active ingredients such as Omega 3 fish oils, NO precursors and creatine which may enhance the training response and improve recovery in between successive exercise bouts.

References

Apro, W., Wang, L., Ponten, M., Blomstrand, E., & Sahlin, K. (2013). Resistance exercise induced mTORC1 signaling is not impaired by subsequent endurance exercise in human skeletal muscle. *American Journal of Physiology – Endocrinology and Metabolism*, *305*(1), E22–E32. doi:10.1152/ajpendo.00091.2013

Areta, J. L., Burke, L. M., Camera, D. M., West, D. W., Crawshay, S., Moore, D. R., … Coffey, V. G. (2014, April). Reduced resting skeletal muscle protein synthesis is rescued by resistance exercise and protein ingestion following short-term energy deficit. *American Journal of Physiology – Endocrinology and Metabolism*, *306*(8), E989–E997. doi:10.1152/ajpendo.00590.2013

Areta, J. L., Burke, L. M., Ross, M. L., Camera, D. M., West, D. W., Broad, E. M., … Coffey, V. G. (2013). Timing and distribution of protein ingestion during prolonged recovery from resistance exercise alters myofibrillar protein synthesis. *The Journal of Physiology*, *591*(Pt 9), 2319–2331.

Atherton, P. J., & Rennie, M. J. (2006). Protein synthesis a low priority for exercising muscle. *The Journal of Physiology*, *573* (Pt 2), 288–289. doi:10.1113/jphysiol.2006.110247

Bailey, S. J., Fulford, J., Vanhatalo, A., Winyard, P. G., Blackwell, J. R., DiMenna, F. J., … Jones, A. M. (2010). Dietary nitrate supplementation enhances muscle contractile efficiency during knee-extensor exercise in humans. *Journal of Applied Physiology*, *109*(1), 135–148. doi:10.1152/japplphysiol.00046.2010

Beelen, M., Koopman, R., Gijsen, A. P., Vandereyt, H., Kies, A. K., Kuipers, H., … van Loon, L. J. (2008). Protein coingestion stimulates muscle protein synthesis during resistance-type exercise. *American Journal of Physiology – Endocrinology and Metabolism*, *295*(1), E70–E77. doi:10.1152/ajpendo.00774.2007

Beelen, M., Zorenc, A., Pennings, B., Senden, J. M., Kuipers, H., & van Loon, L. J. (2011). Impact of protein coingestion on muscle protein synthesis during continuous endurance type exercise. *American Journal of Physiology – Endocrinology and Metabolism*, *300*, E945–E954.

Bemben, M. G., & Lamont, H. S. (2005). Creatine supplementation and exercise performance: Recent findings. *Sports Medicine*, *35*(2), 107–125. doi:10.2165/00007256–200535020-00002

Bescós, R., Sureda, A., Tur, J. A., & Pons, A. (2012). The effect of nitric-oxide-related supplements on human performance. *Sports Medicine*, *42*(2), 99–117. doi:10.2165/11596860-000000000-00000

Breen, L., Philp, A., Witard, O. C., Jackman, S. R., Selby, A., Smith, K., … Tipton, K. D. (2011). The influence of carbohydrate-protein co-ingestion following endurance exercise on myofibrillar and mitochondrial protein synthesis. *The Journal of Physiology*, *589*(Pt 16), 4011–4025. doi:10.1113/jphysiol.2011.211888

Brilla, L. R., & Landerholm, T. E. (1990). Effect of fish oil supplementation and exercise on serum lipids and aerobic fitness. *The Journal of Sports Medicine and Physical Fitness*, *30*, 173–180.

Burd, N. A., Tang, J. E., Moore, D. R., & Phillips, S. M. (2009). Exercise training and protein metabolism: Influences of contraction, protein intake, and sex-based differences. *Journal of Applied Physiology*, *106*, 1692–1701. doi:10.1152/japplphysiol.91351.2008

Burd, N. A., West, D. W., Moore, D. R., Atherton, P. J., Staples, A. W., Prior, T., … Phillips, S. M. (2011). Enhanced amino acid sensitivity of myofibrillar protein synthesis persists for up to 24 h after resistance exercise in young men. *The Journal of Nutrition*, *141*, 568–573. doi:10.3945/jn.110.135038

Burke, L. M., Hawley, J. A., Wong, S. H., & Jeukendrup, A. E. (2011). Carbohydrates for training and competition. *Journal of Sports Sciences*, *29*(Suppl. 1), S17–S27. doi:10.1080/02640414.2011.585473

Burke, L. M., Slater, G., Broad, E. M., Haukka, J., Modulon, S., & Hopkins, W. G. (2003). Eating patterns and meal frequency of elite Australian athletes. *International Journal of Sport Nutrition & Exercise Metabolism*, *13*, 521–538.

Burke, L. M., Winter, J. A., Cameron-Smith, D., Enslen, M., Farnfield, M., & Decombaz, J. (2012). Effect of intake of different dietary protein sources on plasma amino acid profiles at rest and after exercise. *International Journal of Sport Nutrition & Exercise Metabolism*, *22*, 452–462.

Camera, D. M., West, D. W., Phillips, S. M., Rerecich, T., Stellingwerff, T., Hawley, J. A., & Coffey, V. G. (2014). Protein ingestion increases myofibrillar protein synthesis after concurrent exercise. *Medicine and Science in Sports and Exercise*. [Epub ahead of print].

Churchward-Venne, T. A., Murphy, C. H., Longland, T. M., & Phillips, S. M. (2013). Role of protein and amino acids in promoting lean mass accretion with resistance exercise and attenuating lean mass loss during energy deficit in humans. *Amino Acids*, *45*, 231–240. doi:10.1007/s00726-013-1506-0

Coffey, V. G., Jemiolo, B., Edge, J., Garnham, A. P., Trappe, S. W., & Hawley, J. A. (2009). Effect of consecutive repeated sprint and resistance exercise bouts on acute adaptive responses in human skeletal muscle. *American Journal of Physiology – Regulatory, Integrative and Comparative Physiology*, *297*, R1441–R1451.

de Souza, E. O., Tricoli, V., Roschel, H., Brum, P. C., Bacurau, A. V., Ferreira, J. C., … Ugrinowitsch, C. (2013). Molecular adaptations to concurrent training. *International Journal of Sports Medicine*, *34*, 207–213.

Donges, C. E., Burd, N. A., Duffield, R., Smith, G. C., West, D. W., Short, M. J., … Edge, J. A. (2012). Concurrent resistance and aerobic exercise stimulates both myofibrillar and mitochondrial protein synthesis in sedentary middle-aged men. *Journal of Applied Physiology*, *112*, 1992–2001. doi:10.1152/japplphysiol.00166.2012

Egan, B., & Zierath, J. R. (2013). Exercise metabolism and the molecular regulation of skeletal muscle adaptation. *Cell Metabolism*, *17*, 162–184. doi:10.1016/j.cmet.2012.12.012

Ernst, E., Saradeth, T., & Achhammer, G. (1991). n-3 fatty acids and acute-phase proteins. *European Journal of Clinical Investigation*, *21*(1), 77–82. doi:10.1111/j.1365-2362.1991.tb01362.x

Fyfe, J. J., Bishop, D. J., & Stepto, N. K. (2014). Interference between concurrent resistance and endurance exercise: Molecular bases and the role of individual training variables. *Sports Medicine*, *44*, 743–762. doi:10.1007/s40279-014-0162-1

Garcia-Roves, P. M., Osler, M. E., Holmstrom, M. H., & Zierath, J. R. (2008). Gain-of-function R225Q mutation in AMP-activated protein kinase gamma3 subunit increases mitochondrial biogenesis in glycolytic skeletal muscle. *The Journal of Biological Chemistry*, *283*, 35724–35734. doi:10.1074/jbc.M805078200

Glynn, E. L., Fry, C. S., Drummond, M. J., Dreyer, H. C., Dhanani, S., Volpi, E., … Rasmussen, B. B. (2010). Muscle protein breakdown has a minor role in the protein anabolic response to essential amino acid and carbohydrate intake following resistance exercise. *American Journal of Physiology – Regulatory, Integrative and Comparative Physiology*, 299, R533–R540.

Hamilton, D. L., & Philp, A. (2013). Can AMPK mediated suppression of mTORC1 explain the concurrent training effect? *Cellular and Molecular Exercise Physiology*, *2*(1), 1–8. doi:10.7457/cmep.v2i1.e4

Hardie, D. G., Ross, F. A., & Hawley, S. A. (2012). AMPK: A nutrient and energy sensor that maintains energy homeostasis. *Nature Reviews – Molecular Cell Biology*, *13*, 251–262.

Herbst, E. A., Paglialunga, S., Gerling, C., Whitfield, J., Mukai, K., Chabowski, A., … Holloway, G. P. (2014). Omega-3 supplementation alters mitochondrial membrane composition and respiration kinetics in human skeletal muscle. *The Journal of Physiology*, *592*(Pt 6), 1341–1352. doi:10.1113/jphysiol.2013.267336

Hickson, R. C. (1980). Interference of strength development by simultaneously training for strength and endurance. *European Journal of Applied Physiology and Occupational Physiology*, *45*, 255–263.

Howarth, K. R., Phillips, S. M., MacDonald, M. J., Richards, D., Moreau, N. A., & Gibala, M. J. (2010). Effect of glycogen availability on human skeletal muscle protein turnover during exercise and recovery. *Journal of Applied Physiology*, *109*, 431–438. doi:10.1152/japplphysiol.00108.2009

Jager, S., Handschin, C., St-Pierre, J., & Spiegelman, B. M. (2007). AMP-activated protein kinase (AMPK) action in skeletal muscle via direct phosphorylation of PGC-1alpha. *Proceedings of the National Academy of Sciences of the United States of America*, *104*, 12017–12022.

Jones, A. M., Vanhatalo, A., & Bailey, S. J. (2013). Influence of dietary nitrate supplementation on exercise tolerance and performance. *Nestlé Nutrition Institute Workshop Series*, *75*, 27–40.

Kakigi, R., Yoshihara, T., Ozaki, H., Ogura, Y., Ichinoseki-Sekine, N., Kobayashi, H., & Naito, H. (2014, April). Whey protein intake after resistance exercise activates mTOR signaling in a dose-dependent manner in human skeletal muscle. *European Journal of Applied Physiology*, *114*(4), 735–742. doi:10.1007/s00421-013-2812-7.

Lerin, C., Rodgers, J. T., Kalume, D. E., Kim, S. H., Pandey, A., & Puigserver, P. (2006). GCN5 acetyltransferase complex controls glucose metabolism through transcriptional repression of PGC-1alpha. *Cell Metabolism*, *3*, 429–438. doi:10.1016/j.cmet.2006.04.013

Levenhagen, D. K., Carr, C., Carlson, M. G., Maron, D. J., Borel, M. J., & Flakoll, P. J. (2002). Postexercise protein intake enhances whole-body and leg protein accretion in humans. *Medicine and Science in Sports and Exercise*, *34*, 828–837.

Levenhagen, D. K., Gresham, J. D., Carlson, M. G., Maron, D. J., Borel, M. J., & Flakoll, P. J. (2001). Postexercise nutrient intake timing in humans is critical to recovery of leg glucose and protein homeostasis. *American Journal of Physiology – Endocrinology and Metabolism*, *280*, E982–E993.

Lundberg, T. R., Fernandez-Gonzalo, R., Gustafsson, T., & Tesch, P. A. (2012). Aerobic exercise alters skeletal muscle molecular responses to resistance exercise. *Medicine and Science in Sports and Exercise*, *44*, 1680–1688.

Lundberg, T. R., Fernandez-Gonzalo, R., Gustafsson, T., & Tesch, P. A. (2013). Aerobic exercise does not compromise muscle hypertrophy response to short-term resistance training. *Journal of Applied Physiology*, *114*(1), 81–89. doi:10.1152/japplphysiol.01013.2012

Lunn, W. R., Pasiakos, S. M., Colletto, M. R., Karfonta, K. E., Carbone, J. W., Anderson, J. M., & Rodriguez, N. R. (2012). Chocolate milk and endurance exercise recovery: Protein balance, glycogen, and performance. *Medicine and Science in Sports and Exercise*, *44*, 682–691.

Mamerow, M. M., Mettler, J. A., English, K. L., Casperson, S. L., Arentson-Lantz, E., Sheffield-Moore, M., … Paddon-Jones, D. (2014, June). Dietary Protein Distribution Positively Influences 24-h Muscle Protein Synthesis in Healthy Adults. *The Journal of Nutrition*, *144*(6), 876–880. doi:10.3945/jn.113.185280

Maskrey, B. H., Megson, I. L., Rossi, A. G., & Whitfield, P. D. (2013). Emerging importance of omega-3 fatty acids in the innate immune response: Molecular mechanisms and lipidomic strategies for their analysis. *Molecular Nutrition & Food Research*, *57*, 1390–1400.

McGlory, C., Galloway, S. D. R., Lee Hamilton, D., McClintock, C., Breen, L., Dick, J. R., … Tipton, K. D. (2014, June). Temporal changes in human skeletal muscle and blood lipid composition with fish oil supplementation. *Prostaglandins, Leukotrienes and Essential Fatty Acids*, *90*(60), 199–206. doi:10.1016/j.plefa.2014.03.001

Mettler, S., Mitchell, N., & Tipton, K. D. (2010). Increased protein intake reduces lean body mass loss during weight loss in athletes. *Medicine and Science in Sports and Exercise*, *42*, 326–337.

Millward, D. J., Bowtell, J. L., Pacy, P., & Rennie, M. J. (1994). Physical activity, protein metabolism and protein requirements. *The Proceedings of the Nutrition Society*, *53*, 223–240.

Mitchell, C. J., Churchward-Venne, T. A., Bellamy, L., Parise, G., Baker, S. K., & Phillips, S. M. (2013). Muscular and systemic correlates of resistance training-induced muscle hypertrophy. *PLoS One*, *8*, e78636.

Miyazaki, M., McCarthy, J. J., Fedele, M. J., & Esser, K. A. (2011). Early activation of mTORC1 signalling in response to mechanical overload is independent of phosphoinositide 3-kinase/Akt signalling. *The Journal of Physiology*, *589*(Pt 7), 1831–1846.

Moore, D. R., Areta, J., Coffey, V. G., Stellingwerff, T., Phillips, S. M., Burke, L. M., … Hawley, J. A. (2012). Daytime pattern of post-exercise protein intake affects whole-body protein turnover in resistance-trained males. *Nutrition and Metabolism*, *9*(1), 91.

Moore, D. R., Camera, D. M., Areta, J. L., & Hawley, J. A. (2014, May). Beyond muscle hypertrophy: Why dietary protein is important for endurance athletes. *Applied Physiology, Nutrition, and Metabolism*, *7*, 1–11.

Moore, D. R., Robinson, M. J., Fry, J. L., Tang, J. E., Glover, E. I., Wilkinson, S. B., … Phillips, S. M. (2009). Ingested protein dose response of muscle and albumin protein synthesis after resistance exercise in young men. *The American Journal of Clinical Nutrition*, *89*, 161–168.

Moore, D. R., Tang, J. E., Burd, N. A., Rerecich, T., Tarnopolsky, M. A., & Phillips, S. M. (2009). Differential stimulation of myofibrillar and sarcoplasmic protein synthesis with protein ingestion at rest and after resistance exercise. *The Journal of Physiology*, *587*(Pt 4), 897–904.

Peoples, G. E., & McLennan, P. L. (2010). Dietary fish oil reduces skeletal muscle oxygen consumption, provides fatigue resistance and improves contractile recovery in the rat in vivo hindlimb. *The British Journal of Nutrition*, *104*, 1771–1779.

Phillips, B. E., Williams, J. P., Gustafsson, T., Bouchard, C., Rankinen, T., Knudsen, S., … Atherton, P. J. (2013). Molecular networks of human muscle adaptation to exercise and age. *PLoS Genetics*, *9*, e1003389.

Phillips, S. M. (2012). Dietary protein requirements and adaptive advantages in athletes. *The British Journal of Nutrition*, *108* (Suppl. 2), S158–S167.

Philp, A., Hamilton, D. L., & Baar, K. (2011). Signals mediating skeletal muscle remodeling by resistance exercise: PI3-kinase independent activation of mTORC1. *Journal of Applied Physiology*, *110*, 561–568.

Philp, A., Hargreaves, M., & Baar, K. (2012). More than a store: Regulatory roles for glycogen in skeletal muscle adaptation to exercise. *American Journal of Physiology – Endocrinology and Metabolism*, *302*, E1343–E1351.

Philp, A., MacKenzie, M. G., Belew, M. Y., Towler, M. C., Corstorphine, A., Papalamprou, A., … Baar, K. (2013). Glycogen content regulates peroxisome proliferator activated receptor- partial differential (PPAR- partial differential) activity in rat skeletal muscle. *PLoS One*, *8*, e77200.

Philp, A., & Schenk, S. (2013). Unraveling the complexities of SIRT1-mediated mitochondrial regulation in skeletal muscle. *Exercise and Sport Sciences Reviews*, *41*, 174–181.

Res, P. T., Groen, B., Pennings, B., Beelen, M., Wallis, G. A., Gijsen, A. P., … Van Loon, L. J. (2012). Protein ingestion before sleep improves postexercise overnight recovery. *Medicine and Science in Sports and Exercise*, *44*, 1560–1569.

Rockl, K. S., Hirshman, M. F., Brandauer, J., Fujii, N., Witters, L. A., & Goodyear, L. J. (2007). Skeletal muscle adaptation to exercise training: AMP-activated protein kinase mediates muscle fiber type shift. *Diabetes*, *56*, 2062–2069.

Rodacki, C. L., Rodacki, A. L., Pereira, G., Naliwaiko, K., Coelho, I., Pequito, D., … Fernandez, L. C. (2012). Fish-oil supplementation enhances the effects of strength training in elderly women. *The American Journal of Clinical Nutrition*, *95*, 428–436.

Rodgers, J. T., Lerin, C., Haas, W., Gygi, S. P., Spiegelman, B. M., & Puigserver, P. (2005). Nutrient control of glucose homeostasis through a complex of PGC-1alpha and SIRT1. *Nature*, *434*(7029), 113–118.

Ronnestad, B. R., Hansen, E. A., & Raastad, T. (2012). High volume of endurance training impairs adaptations to 12 weeks of strength training in well-trained endurance athletes. *European Journal of Applied Physiology*, *112*, 1457–1466.

Schoenfeld, B. J., Aragon, A. A., & Krieger, J. W. (2013). The effect of protein timing on muscle strength and hypertrophy: A meta-analysis. *Journal of the International Society of Sports Nutrition*, *10*(1), 53.

Shimobayashi, M., & Hall, M. N. (2014). Making new contacts: The mTOR network in metabolism and signalling crosstalk. *Nature Reviews – Molecular Cell Biology*, *15*, 155–162.

Smith, G. I., Atherton, P., Reeds, D. N., Mohammed, B. S., Rankin, D., Rennie, M. J., & Mittendorfer, B. (2011). Dietary omega-3 fatty acid supplementation increases the rate of muscle protein synthesis in older adults: A randomized controlled trial. *The American Journal of Clinical Nutrition*, *93*, 402–412.

Stamler, J. S., & Meissner, G. (2001). Physiology of nitric oxide in skeletal muscle. *Physiological Reviews*, *81*, 209–237.

Staples, A. W., Burd, N. A., West, D. W., Currie, K. D., Atherton, P. J., Moore, D. R., … Phillips, S. M. (2011). Carbohydrate does not augment exercise-induced protein accretion versus protein alone. *Medicine and Science in Sports and Exercise*, *43*, 1154–1161.

Tang, J. E., Perco, J. G., Moore, D. R., Wilkinson, S. B., & Phillips, S. M. (2008). Resistance training alters the response of fed state mixed muscle protein synthesis in young men. *American Journal of Physiology – Regulatory, Integrative and Comparative Physiology*, *294*, R172–R178.

Tarnopolsky, M. (2004). Protein requirements for endurance athletes. *Nutrition*, *20*, 662–668. doi:10.1016/j.nut.2004.04.008

Tarnopolsky, M. A. (2010). Caffeine and creatine use in sport. *Annals of Nutrition & Metabolism*, 57(Suppl. 2), 1–8. doi:10.1159/000322696

Tipton, K. D., Elliott, T. A., Cree, M. G., Aarsland, A. A., Sanford, A. P., & Wolfe, R. R. (2007). Stimulation of net muscle protein synthesis by whey protein ingestion before and after exercise. *American Journal of Physiology – Endocrinology and Metabolism*, *292*(1), E71–E76.

Tipton, K. D., Ferrando, A. A., Phillips, S. M., Doyle, D., Jr., & Wolfe, R. R. (1999). Postexercise net protein synthesis in human muscle from orally administered amino acids. *American Journal of Physiology*, *276*(4 Pt 1), E628–E634.

Tipton, K. D., Rasmussen, B. B., Miller, S. L., Wolf, S. E., Owens-Stovall, S. K., Petrini, B. E., & Wolfe, R. R. (2001). Timing of amino acid-carbohydrate ingestion alters anabolic response of muscle to resistance exercise. *American Journal of Physiology – Endocrinology and Metabolism*, *281*, E197–E206.

Vanhatalo, A., Bailey, S. J., Blackwell, J. R., DiMenna, F. J., Pavey, T. G., Wilkerson, D. P., … Jones, A. M. (2010). Acute and chronic effects of dietary nitrate supplementation on blood pressure and the physiological responses to moderate-intensity and incremental exercise. *American Journal of Physiology – Regulatory, Integrative and Comparative Physiology*, *299*, R1121–R1131.

Witard, O. C., Jackman, S. R., Breen, L., Smith, K., Selby, A., & Tipton, K. D. (2014). Myofibrillar muscle protein synthesis rates subsequent to a meal in response to increasing doses of whey protein at rest and after resistance exercise. *The American Journal of Clinical Nutrition*, *99*(1), 86–95.

Wojtaszewski, J. F., MacDonald, C., Nielsen, J. N., Hellsten, Y., Hardie, D. G., Kemp, B. E., … Richter, E. A. (2003). Regulation of 5'AMP-activated protein kinase activity and substrate utilization in exercising human skeletal muscle. *American Journal of Physiology – Endocrinology and Metabolism*, *284*, E813–E822.

Wojtaszewski, J. F., Nielsen, P., Hansen, B. F., Richter, E. A., & Kiens, B. (2000). Isoform-specific and exercise intensity-dependent activation of 5'-AMP-activated protein kinase in human skeletal muscle. *The Journal of Physiology*, *528*(Pt 1), 221–226.

You, J. S., Lincoln, H. C., Kim, C. R., Frey, J. W., Goodman, C. A., Zhong, X. P., … Hornberger, T. A. (2014). The role of diacylglycerol kinase zeta and phosphatidic acid in the mechanical activation of mammalian target of rapamycin (mTOR) signaling and skeletal muscle hypertrophy. *Journal of Biological Chemistry*, *289*, 1551–1563. doi:10.1074/jbc.M113.531392