Meat Science 109 (2015) 96–100

Contents lists available at ScienceDirect

Meat Science

journal homepage: www.elsevier.com/locate/meatsci

Review

The muscle protein synthetic response to food ingestion

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ARTICLE INFO

Article history:
Received 8 March 2015
Received in revised form 12 May 2015
Accepted 15 May 2015
Available online 20 May 2015

Keywords:
Muscle mass maintenance
Meat
Muscle protein synthesis
Protein digestion and absorption
Aging

ABSTRACT

Preservation of skeletal muscle mass is of great importance for maintaining both metabolic health and functional capacity. Muscle mass maintenance is regulated by the balance between muscle protein breakdown and synthesis rates. Both muscle protein breakdown and synthesis rates have been shown to be highly responsive to physical activity and food intake. Food intake, and protein ingestion in particular, directly stimulates muscle protein synthesis rates. The postprandial muscle protein synthetic response to feeding is regulated on a number of levels, including dietary protein digestion and amino acid absorption, splanchnic amino acid retention, postprandial insulin release, skeletal muscle tissue perfusion, amino acid uptake by muscle, and intramyocellular signaling. The postprandial muscle protein synthetic response to feeding is blunted in many conditions characterized by skeletal muscle loss, such as aging and muscle disuse. Therefore, it is important to define food characteristics that modulate postprandial muscle protein synthesis. Previous work has shown that the muscle protein synthetic response to feeding can be modulated by changing the amount of protein ingested, the source of dietary protein, as well as the timing of protein consumption. Most of this work has studied the postprandial response to the ingestion of isolated protein sources. Only few studies have investigated the postprandial muscle protein synthetic response to the ingestion of protein dense foods, such as dairy and meat. The current review will focus on the capacity of proteins and protein dense food products to stimulate postprandial muscle protein synthesis and identifies food characteristics that may modulate the anabolic properties.

Contents

1. Introduction

Muscle mass maintenance is achieved through sinusoidal fluctuations in muscle protein synthesis and breakdown rates that are eventually counterbalanced such that net muscle protein balance remains zero by the end of each day (Burd, Tang, Moore, & Phillips, 2009). However, aging, muscle disuse, and chronic metabolic diseases are characterized by a decline in skeletal muscle mass. This decline in muscle mass must be attributed to an imbalance between protein breakdown and synthesis rates, resulting in a negative net muscle protein balance. Since basal muscle protein synthesis rates do not seem to differ between healthy young and older men (Volpi, Sheffield-Moore, Rasmussen, & Wolfe, 2001), researchers have been assessing whether derangements in the muscle protein synthetic response to the main anabolic stimuli, physical activity and

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http://dx.doi.org/10.1016/j.meatsci.2015.05.009
0309-1740/

food intake, underpin the loss of skeletal muscle mass. Several studies have shown that muscle protein synthesis rates are not increased to the same extent in older when compared with young individuals following ingestion of amino acids (Cuthbertson et al., 2005; Katsanos, Kobayashi, Sheffield-Moore, Aarsland, & Wolfe, 2005; Volpi, Mittendorfer, Rasmussen, & Wolfe, 2000). This phenomenon has been referred to as 'anabolic resistance' (Burd, Gorissen, & van Loon, 2013; Rennie, 2009). Optimizing food intake to allow for maximal stimulation of postprandial muscle protein synthesis rates may yield valuable information that can be used to develop more effective strategies to attenuate the loss of skeletal muscle mass in various clinical settings.

2. Postprandial muscle protein synthesis

Food intake, and protein ingestion in particular, has been shown to stimulate muscle protein synthesis. The postprandial muscle protein synthetic response to protein ingestion is regulated on a number of levels (Burd et al., 2013). Protein digestion and amino acid absorption kinetics have a major impact on the postprandial anabolic response. Rapidly digestible proteins (such as whey) may stimulate protein synthesis to a greater extent and for a shorter time period, whereas slowly digestible proteins (such as casein) may stimulate protein synthesis for a longer time period (Boirie, Gachon, & Beaufrere, 1997). Modulating protein digestion and amino acid absorption kinetics by ingesting whey in repeated small boluses (simulating digestion and absorption kinetics of a slowly digestible protein) or by ingesting hydrolyzed casein (rapidly digestible) affects the postprandial muscle protein synthetic response (Dangin et al., 2001; Koopman et al., 2009; Pennings et al., 2011; West et al., 2011). Moreover, splanchnic retention of dietary protein-derived amino acids (which includes amino acid uptake by gut and liver tissue) may modulate postprandial muscle protein synthesis by affecting the postprandial availability of circulating amino acids (Boirie, Gachon, & Beaufrere, 1997; Gorissen et al., 2014; Volpi, Mittendorfer, Wolf, & Wolfe, 1999). Furthermore, the postprandial rise in insulin concentrations can modulate the muscle protein synthetic response through its vasodilatory properties, i.e., stimulating endothelial nitric oxide synthase (eNOS), resulting in greater capillary recruitment, increased microvascular volume and nutritive blood flow to skeletal muscle tissue (Timmerman et al., 2010; Timmerman et al., 2010). It could be speculated that the postprandial increase in muscle tissue perfusion will increase the exposure of muscle tissue to nutrients and growth factors and, as such, stimulate muscle protein synthesis rates. The stimulation of muscle protein synthesis has been shown to be blunted in insulin resistant subjects under hyperinsulinemic–euglycemic conditions (Fujita, Glynn, Timmerman, Rasmussen, & Volpi, 2009; Rasmussen et al., 2006), further emphasizing the proposed role of insulin in the postprandial stimulation of muscle protein synthesis. Finally, the postprandial increase in muscle protein synthesis may also be regulated through amino acid uptake by amino acid transporters located on the cell membrane of muscle cells (Drummond et al., 2010) and subsequent intramyocellular mTORC1 signaling towards protein synthesis (Cuthbertson et al., 2005; Guillet et al., 2004). One or more of these processes may be compromised in conditions that are characterized by skeletal muscle loss such as aging, disuse, or chronic metabolic diseases. Several protein (intake) characteristics may influence the postprandial muscle protein synthetic response and may need consideration when trying to develop more effective dietary strategies to prevent or attenuate the loss of skeletal muscle mass.

2.1. Protein source

Various studies have reported improved net protein balance and/or increased muscle protein synthesis rates following the ingestion of isolated protein sources such as whey (Pennings et al., 2012), casein (Koopman, Walrand, et al., 2009), casein hydrolysate (Koopman, Crombach, et al., 2009; Pennings, Boirie, et al., 2011), soy (Fouillet, Mariotti, Gaudichon, Bos, & Tome, 2002; Tang, Moore, Kujbida, Tarnopolsky, & Phillips, 2009; Yang et al., 2012), and egg protein (Moore et al., 2009). Even though all of these protein sources have the capacity to stimulate muscle protein anabolism, postprandial muscle protein fractional synthetic rates can vary substantially following the ingestion of these different protein sources. The question arises what protein characteristics may influence the postprandial muscle protein synthetic response. It has previously been suggested that the consumption of more rapidly digestible proteins results in a greater stimulation of postprandial muscle protein synthesis when compared with slowly digestible proteins. This concept has been developed by measuring dietary protein digestion and absorption kinetics and subsequent postprandial protein accretion following whey compared with casein protein (Boirie et al., 1997; Dangin et al., 2001). However, these proteins differ not only in their digestion and absorption kinetics (Mahe et al., 1996), but also in their amino acid composition. Even when casein was hydrolyzed prior to ingestion it was still unable to stimulate postprandial muscle protein synthesis rates to the same extent as the ingestion of whey protein (Pennings, Boirie, et al., 2011). This suggests that the amino acid composition, and leucine content in particular, represents another key determinant of the postprandial muscle protein synthetic response following protein ingestion. In agreement, addition of free leucine to a bolus of amino acids, protein, or a meal has been shown to further enhance postprandial muscle protein synthesis rates (Katsanos, Kobayashi, Sheffield-Moore, Aarsland, & Wolfe, 2006; Rieu et al., 2006; Wall et al., 2013).

2.2. Amount of protein

Though it has been well established that dietary protein effectively stimulates muscle protein synthesis, less information is available on the amount of protein that should be ingested to maximize the postprandial muscle protein synthetic response. It has been shown that graded intakes of essential amino acids (EAA) up to 10 g (equivalent to ~25 g of a high-quality protein) stimulate myofibrillar protein synthesis rates in a dose-dependent manner (Cuthbertson et al., 2005). However, this response is lower in older individuals, and higher intakes of EAA (20 and 40 g) failed to promote a greater muscle protein anabolic response (Cuthbertson et al., 2005). Recently, postprandial muscle protein synthesis rates following the ingestion of increasing amounts of whey protein (i.e., 10, 20, and 40 g) have been assessed in both young (Witard et al., 2014) and older individuals (Yang et al., 2012). In both age groups, 20 g of whey protein was required to significantly stimulate muscle protein synthesis rates, and ingesting a higher dose of 40 g had no additive effect (Witard et al., 2014; Yang et al., 2012). However, greater amounts of protein may result in prolonged hyperaminoacidemia (rather than higher peak values) and, as such, stimulate muscle protein synthesis for a more prolonged time period following protein ingestion. Therefore, future dose–response studies should include an assessment of muscle protein synthesis rates over an appropriate postprandial period.

2.3. Timing of protein ingestion

Daily protein intake is mainly consumed at breakfast, lunch, and dinner (Tieland, Borgonjen-Van den Berg, van Loon, & de Groot, 2012). Some researchers suggest that the distribution of protein intake throughout the day affects net protein balance over a longer period (Areta et al., 2013; Arnal et al., 1999; Arnal et al., 2000; Bouillanne et al., 2013; Bouillanne et al., 2014; Mamerow et al., 2014; Moore et al., 2012), while others did not observe an effect of protein feeding pattern (Adechian et al., 2012; Arnal et al., 2000; Kim et al., 2015). Despite the ongoing debate on the impact of protein intake pattern throughout the day, it is generally accepted that at least 20 g of high-quality protein needs to be consumed per meal to maximize the postprandial muscle