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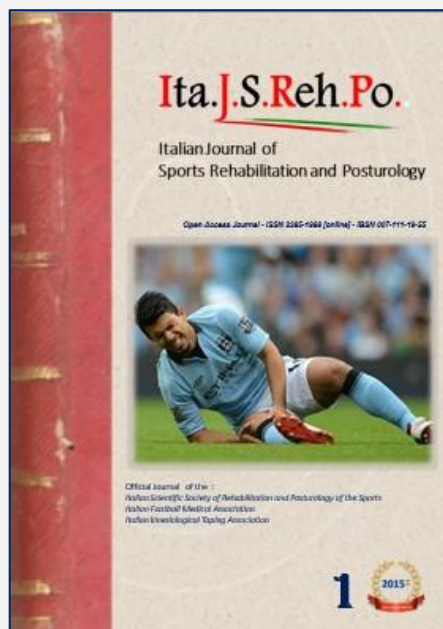
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
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
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
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
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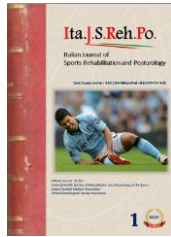
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The Role of Amino Acid Supplementation Following Musculoskeletal Injury

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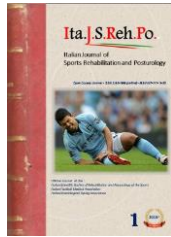
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Abstract

The intention of this article is to provide a fundamental understanding of proteins and amino acids and their role in potentiating recovery from exercise and injury. Potential benefits of amino acid supplementation and conveying recommendations will be availed by an unbiased review of existing scientific literature. (Victor M. Tringali, Christopher D. Policastro, and Joseph A. Giandonato The Role of Amino Acid Supplementation Following Musculoskeletal Injury - Ita J Sports Reh Po 2015 ; 2 ;1 ; 114 - 121 ; ISSN 2385-1988 [online] - IBSN 007-111-19-55

Introduction

Amino acid supplementation has been traditionally advocated by individuals partaking in resistance training activities for their purported conferrals of strength and muscle mass. While findings of correlations between amino acid supplementation and increases in strength and muscle mass in the literature have provided credence to long held beliefs (6), a comparative dearth of literature exists linking amino acid supplementation and injury recovery.



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Physiological Response to Stimulus and Threat

Exercise and injuries elicit a volley of catabolic responses which prominently include: the accretion of metabolites, such as lactate, hydrogen ions, and inorganic phosphate. The collective release of these metabolites elevates acidity which bollixes intracellular and extracellular amino acid content. Metabolic disruptions occur in the presence of a negative nitrogen balance. Localized trauma occurring from a newly introduced stimulus or foreign threat causes disruption of sacromeres and myofilaments and damages the transverse tubules (18).

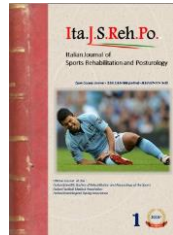
Damaged tissue stemming from exercise or injury prompts systemic immunological and hormonal invocations. When skeletal muscle becomes damaged via exercise or injury, satellite cells, located between the sarcolemmal membrane and basal lamina, are activated and dispatched to the damaged fiber, where they donate their nuclei to facilitate the reparation of contractile matter contained within the muscle fiber. An inflammatory response elicits the proliferation and differentiation of macrophages and cytokines, whereby nitrogen is cleaved from amino acids, particularly glutamine. Cytokines signal the activation of prostaglandins, lymphocytes, neutrophils, and monocytes which inaugurate the recovery process. A varying degree of endogenous growth factors, peptides, and steroid hormones are secreted, thus enabling longer term responses and pursuant adaptations.

While both metabolic stress and muscle damage are precursors in facilitating hypertrophic adaptations, an abundance of both may trigger acute illness, such as rhabdomyolysis, a potentially fatal ailment characterized by muscle tissue necrosis and the release of constituents into the bloodstream leading to kidney failure.

Proteins

Proteins are polymeric structures composed of amino acid chains and comprised of carbon, hydrogen, oxygen, and nitrogen molecules. Proteins are involved in host of physiological functions and are classified as structural, transport, enzymes, or messengers. While protein can be utilized as a fuel, it is not a preferred source of energy.

Structural proteins are fibrous proteins which protect the body and enable movement. These proteins can be found in hair (keratin) in muscle fibers (actin, myosin, titin), and within tendons and the extracellular matrix (collagen and elastin). Transport proteins are water soluble proteins which carry biological constituents throughout the body. These proteins consist of hemoglobin, which carries oxygen to working tissue in bronchial circulation; myoglobin, which sequesters oxygen from the hemoglobin and stores it until needed by the working tissue; and cytochromes, which are instrumental in the conversion of ADP to ATP, as they carry electrons from hydrogen atoms in the citric acid cycle and bind them to oxygen molecules.



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Protein Supplementation

As it pertains to supplementation, most prevailing authorities advocate increased protein intakes for strength and endurance athletes to repair damaged structural proteins, support increases in fat free mass, and ensure optimal levels of all physiologically required proteins. The Academy of Nutrition and Dietetics (AND) and the American College of Sports Medicine (ACSM) opined that strength athletes ingest 1.7g of protein per kg of body weight per day. Protein needs among individuals in energy deficit may be even higher (1). For proteins to be used by the body they need to be metabolized into their simplest form, amino acids.

Amino Acids

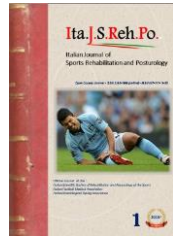
Amino acids are biologically indispensable compounds which consist of amine and carboxylic acid functional groups and a side-chain specific to each amino acid and are composed of carbon, hydrogen, oxygen, and nitrogen molecules. While over 500 amino acids that have been identified in nature, only 20 amino acids are found within proteins (31), which are classified as essential and non-essential. Essential amino acids cannot be synthesized by our body on its own so they must be obtained from our diet. The essential amino acids are leucine, isoleucine, valine, lysine, methionine, phenylalanine, threonine, histidine, and tryptophan. Non-essential amino acids can be synthesized by our body and are not necessary to obtain from our diet. These include glutamate, alanine, aspartate, glutamine, arginine, proline, serine, tyrosine, cysteine, taurine and glycine.

Branched Chain Amino Acid Supplementation

Essential amino acids leucine, isoleucine, and valine possess a similar structure with a branched-chain residue and therefore are referred to as branched-chain amino acids (BCAA). BCAA are among the nine essential amino acids for humans and constitute 35–40% of the dietary essential amino acids in body protein and 14–18% of the total amino acids in muscle proteins. BCAA are among the most widely studied supplements, therefore, a majority of our literature review is comprised of studies which investigated their benefits.

Numerous studies have shown that consumption of BCAA, either at rest, or following exercise is capable of concurrently increasing skeletal muscle protein synthesis and decreasing muscle protein breakdown (4, 5, 7, 28, 29). Based on current evidence, it appears BCAA stimulate protein synthesis and/or decrease muscle protein breakdown (112). Recent research suggests that supplementation of BCAA may lead to increased lean mass and strength when added to a properly designed resistance training routine.

Some of the common indicators of muscle damage after a period of eccentric exercise consist of drop in active tension as well as ensuing sensations of stiffness and swelling. The muscles become tender to local palpation, stretch, and contraction in the hours and days following exercise. This is commonly known as



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delayed-onset muscle soreness (DOMS) and is the most recognizable symptom of exercise-induced muscle damage (EIMD). Collectively, these signs and symptoms can impair muscle function and inhibit the ability to engage in high intensity exercise.

In an attempt to allay the negative effects of EIMD, a number of interventions have been explored, however, nutritional intervention with BCAA have been shown to have a reasonable effect in curtailing the effects of EIMD from strenuous exercise. Furthermore, BCAA supplementation conserves muscle mass in conditions characterized by protein loss and catabolism (3) and studies examining recovery from heavy endurance activity (17) have shown evidence that BCAA are beneficial in not only reducing muscle damage but also in accelerating the recovery process.

Amino acid supplementation (containing around 60% BCAA) was effective in reducing muscle damage and soreness when consumed immediately before and during the four recovery days that followed a damaging bout of eccentric contractions (19). BCAA were found to reduce the negative effects of damaging exercise by attenuating creatine kinase efflux, reducing residual muscle soreness and improving recovery of muscle function to a greater extent than a placebo control (13).

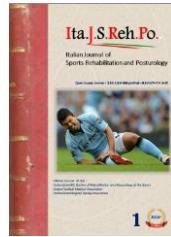
Shimomura and colleagues (2006) examined the effects of BCAA supplementation on delayed-onset muscle soreness (DOMS) and muscle fatigue induced by squat exercise in humans. The results showed that BCAA supplementation prior to squat exercise decreased DOMS and muscle fatigue occurring for a few days after exercise. The findings suggested that BCAAs may be useful for muscle recovery following exercise (26).

In recent years, leucine has become of particular interest due to its interaction with metabolic pathways associated with anabolism, particularly mammalian target of rapamycin (mTOR). mTOR regulates myogenic differentiation and influences the rate of muscle protein synthesis, thus gating increases in muscle mass and strength. Literature has suggested that the proportion of leucine content within an amino acid or protein supplement is correlative with improvements in muscle mass and strength (26, 28, 29). An investigation of leucine supplementation among young rats undergoing cryolesioning revealed that those receiving leucine attenuated strength losses and experienced improvements in myofibril size in comparison to control subjects (20).

Hydroxy Methylbutric Acid (HMB), a metabolite of leucine, has been shown to stave off protein breakdown. Research has indicated that HMB increases collagen deposition while improving nitrogen balance among critically injured adult patients (23). Leucine supplementation has been shown to escalate protein synthesis in the presence of elevated free radicals caused by smoking (30).

Amino Acids and their roles in health and recovery

Essential amino acid supplementation among adults undergoing total knee arthroplasty, staved off post-surgical decrements in functional mobility and tempered muscle loss stemming from disuse (33). Supplementation of the amino acids phenylalanine, tyrosine, and tryptophan have been shown to elevate bone resorption and downregulate osteoclastic activity (23). Arginine, a non-essential amino acid, is composed of substrates that arginase and nitric oxide synthase which are used to produce nitric oxide. Nitric oxide, a signaling molecule which is rooted in numerous physiological and pathological processes, elicits profound vasodilatory effects.



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Nitric oxide facilitates the relaxation of the endothelium which lines the blood vessels, permitting greater perfusion, thus proliferating the transport of nutrients and removal of waste products. Arginine supplementation may prove beneficial in preventing muscle wasting occurring from injury or illness as research has shown that it is capable of activating and regulating mTOR (26). Further, arginine stimulates the secretion of growth hormone, which serves an assistive role in tissue repair (27).

Combining arginine with the amino acid, ornithine, elicits the production of insulin (28), a peptide hormone intimately involved with growth and recovery. Glutamine, another non-essential amino acid which is found in the most abundant amounts of the amino acids in the body, supplies a bulk of the nitrogen needed to fuel the production of cytokines and macrophages during injury or illness. Glutamine supplementation has been indicated as a viable remedy for those suffering from traumatic brain injury (30), compromised gastrointestinal functioning (2), and burn injuries (27). Proline, a non-essential amino acid, catalyzes collagen and cartilage production, which may warrant its supplementation in recovering from traumatic injuries as well as those experiencing age and activity associated degradations of cartilaginous structures (27).

Methionine, an essential amino acid, has been shown to improve cartilaginous integrity as well as serving in an assistive capacity in treating rheumatoid arthritis (32). Supplementation with phenylalanine, an essential amino acid, which has been proven to alleviate conditions associated with decreased endorphin levels may be of benefit if an individual wishes to dull pain accompanying musculoskeletal injuries (20).

Practical Considerations

Assessing the quality of a protein can be determined by assessing its essential amino acid composition, bioavailability, and digestibility. The digestibility of a protein is determined by measuring the amounts of amino acids absorbed by the body and the protein's contribution to human amino acid and nitrogen requirements. Proteins which are readily digestible and contain the dietary essential amino acids in quantities that correspond to human requirements are regarded as "high quality".

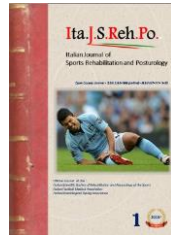
Increased protein intakes for strength and endurance athletes to repair and replace damaged proteins, support increases in fat free mass, and ensure optimal levels of all physiologically required proteins.

Energy deficits are generally associated with a decline in body weight. While the loss of body weight may be due to declines in body fat, skeletal muscle mass is also lost and may account for 25% or more of the total body weight loss. Research shows that consuming a high-protein diet during energy deficit can reduce the loss of fat-free mass. This muscle-sparing effect may be positively shifting the nitrogen balance, accounting for less protein degradation, thus facilitating increased muscle protein synthesis.

Phillips & Van Loon (2011) suggest that a protein intake of 1.8-2.7 g/kg for athletes training in energy deficit may be optimal. Recent literature has suggested increased protein intakes among resistance-trained, lean athletes during caloric restriction. A range of 2.3-3.1 g/kg of lean body mass (LBM) was proposed.

Conclusion

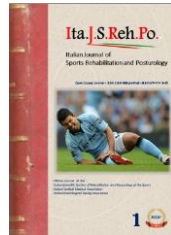
Based on the referenced literature it can be inferred that individuals recovering from injuries will benefit from an increased protein intake, particularly of high quality sources which contain greater quantities of amino acids to accelerate recovery and regain pre-injury functionality.



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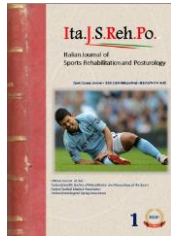
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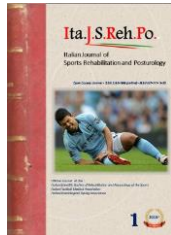
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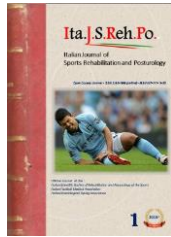
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Physiological Response to Stimulus and Threat

Exercise and injuries elicit a volley of catabolic responses which prominently include: the accretion of metabolites, such as lactate, hydrogen ions, and inorganic phosphate. The collective release of these metabolites elevates acidity which bollixes intracellular and extracellular amino acid content. Metabolic disruptions occur in the presence of a negative nitrogen balance. Localized trauma occurring from a newly introduced stimulus or foreign threat causes disruption of sacromeres and myofilaments and damages the transverse tubules (18).

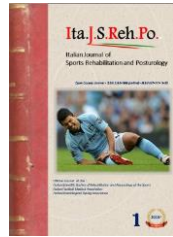
Damaged tissue stemming from exercise or injury prompts systemic immunological and hormonal invocations. When skeletal muscle becomes damaged via exercise or injury, satellite cells, located between the sarcolemmal membrane and basal lamina, are activated and dispatched to the damaged fiber, where they donate their nuclei to facilitate the reparation of contractile matter contained within the muscle fiber. An inflammatory response elicits the proliferation and differentiation of macrophages and cytokines, whereby nitrogen is cleaved from amino acids, particularly glutamine. Cytokines signal the activation of prostaglandins, lymphocytes, neutrophils, and monocytes which inaugurate the recovery process. A varying degree of endogenous growth factors, peptides, and steroid hormones are secreted, thus enabling longer term responses and pursuant adaptations.

While both metabolic stress and muscle damage are precursors in facilitating hypertrophic adaptations, an abundance of both may trigger acute illness, such as rhabdomyolysis, a potentially fatal ailment characterized by muscle tissue necrosis and the release of constituents into the bloodstream leading to kidney failure.

Proteins

Proteins are polymeric structures composed of amino acid chains and comprised of carbon, hydrogen, oxygen, and nitrogen molecules. Proteins are involved in host of physiological functions and are classified as structural, transport, enzymes, or messengers. While protein can be utilized as a fuel, it is not a preferred source of energy.

Structural proteins are fibrous proteins which protect the body and enable movement. These proteins can be found in hair (keratin) in muscle fibers (actin, myosin, titin), and within tendons and the extracellular matrix (collagen and elastin). Transport proteins are water soluble proteins which carry biological constituents throughout the body. These proteins consist of hemoglobin, which carries oxygen to working tissue in bronchial circulation; myoglobin, which sequesters oxygen from the hemoglobin and stores it until needed by the working tissue; and cytochromes, which are instrumental in the conversion of ADP to ATP, as they carry electrons from hydrogen atoms in the citric acid cycle and bind them to oxygen molecules.



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Protein Supplementation

As it pertains to supplementation, most prevailing authorities advocate increased protein intakes for strength and endurance athletes to repair damaged structural proteins, support increases in fat free mass, and ensure optimal levels of all physiologically required proteins. The Academy of Nutrition and Dietetics (AND) and the American College of Sports Medicine (ACSM) opined that strength athletes ingest 1.7g of protein per kg of body weight per day. Protein needs among individuals in energy deficit may be even higher (1). For proteins to be used by the body they need to be metabolized into their simplest form, amino acids.

Amino Acids

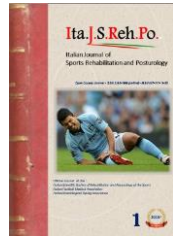
Amino acids are biologically indispensable compounds which consist of amine and carboxylic acid functional groups and a side-chain specific to each amino acid and are composed of carbon, hydrogen, oxygen, and nitrogen molecules. While over 500 amino acids that have been identified in nature, only 20 amino acids are found within proteins (31), which are classified as essential and non-essential. Essential amino acids cannot be synthesized by our body on its own so they must be obtained from our diet. The essential amino acids are leucine, isoleucine, valine, lysine, methionine, phenylalanine, threonine, histidine, and tryptophan. Non-essential amino acids can be synthesized by our body and are not necessary to obtain from our diet. These include glutamate, alanine, aspartate, glutamine, arginine, proline, serine, tyrosine, cysteine, taurine and glycine.

Branched Chain Amino Acid Supplementation

Essential amino acids leucine, isoleucine, and valine possess a similar structure with a branched-chain residue and therefore are referred to as branched-chain amino acids (BCAA). BCAA are among the nine essential amino acids for humans and constitute 35–40% of the dietary essential amino acids in body protein and 14–18% of the total amino acids in muscle proteins. BCAA are among the most widely studied supplements, therefore, a majority of our literature review is comprised of studies which investigated their benefits.

Numerous studies have shown that consumption of BCAA, either at rest, or following exercise is capable of concurrently increasing skeletal muscle protein synthesis and decreasing muscle protein breakdown (4, 5, 7, 28, 29). Based on current evidence, it appears BCAA stimulate protein synthesis and/or decrease muscle protein breakdown (112). Recent research suggests that supplementation of BCAA may lead to increased lean mass and strength when added to a properly designed resistance training routine.

Some of the common indicators of muscle damage after a period of eccentric exercise consist of drop in active tension as well as ensuing sensations of stiffness and swelling. The muscles become tender to local palpation, stretch, and contraction in the hours and days following exercise. This is commonly known as



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delayed-onset muscle soreness (DOMS) and is the most recognizable symptom of exercise-induced muscle damage (EIMD). Collectively, these signs and symptoms can impair muscle function and inhibit the ability to engage in high intensity exercise.

In an attempt to allay the negative effects of EIMD, a number of interventions have been explored, however, nutritional intervention with BCAA have been shown to have a reasonable effect in curtailing the effects of EIMD from strenuous exercise. Furthermore, BCAA supplementation conserves muscle mass in conditions characterized by protein loss and catabolism (3) and studies examining recovery from heavy endurance activity (17) have shown evidence that BCAA are beneficial in not only reducing muscle damage but also in accelerating the recovery process.

Amino acid supplementation (containing around 60% BCAA) was effective in reducing muscle damage and soreness when consumed immediately before and during the four recovery days that followed a damaging bout of eccentric contractions (19). BCAA were found to reduce the negative effects of damaging exercise by attenuating creatine kinase efflux, reducing residual muscle soreness and improving recovery of muscle function to a greater extent than a placebo control (13).

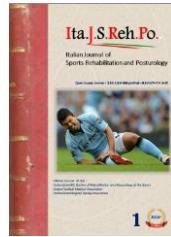
Shimomura and colleagues (2006) examined the effects of BCAA supplementation on delayed-onset muscle soreness (DOMS) and muscle fatigue induced by squat exercise in humans. The results showed that BCAA supplementation prior to squat exercise decreased DOMS and muscle fatigue occurring for a few days after exercise. The findings suggested that BCAAs may be useful for muscle recovery following exercise (26).

In recent years, leucine has become of particular interest due to its interaction with metabolic pathways associated with anabolism, particularly mammalian target of rapamycin (mTOR). mTOR regulates myogenic differentiation and influences the rate of muscle protein synthesis, thus gating increases in muscle mass and strength. Literature has suggested that the proportion of leucine content within an amino acid or protein supplement is correlative with improvements in muscle mass and strength (26, 28, 29). An investigation of leucine supplementation among young rats undergoing cryolesioning revealed that those receiving leucine attenuated strength losses and experienced improvements in myofibril size in comparison to control subjects (20).

Hydroxy Methylbutric Acid (HMB), a metabolite of leucine, has been shown to stave off protein breakdown. Research has indicated that HMB increases collagen deposition while improving nitrogen balance among critically injured adult patients (23). Leucine supplementation has been shown to escalate protein synthesis in the presence of elevated free radicals caused by smoking (30).

Amino Acids and their roles in health and recovery

Essential amino acid supplementation among adults undergoing total knee arthroplasty, staved off post-surgical decrements in functional mobility and tempered muscle loss stemming from disuse (33). Supplementation of the amino acids phenylalanine, tyrosine, and tryptophan have been shown to elevate bone resorption and downregulate osteoclastic activity (23). Arginine, a non-essential amino acid, is composed of substrates that arginase and nitric oxide synthase which are used to produce nitric oxide. Nitric oxide, a signaling molecule which is rooted in numerous physiological and pathological processes, elicits profound vasodilatory effects.



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Nitric oxide facilitates the relaxation of the endothelium which lines the blood vessels, permitting greater perfusion, thus proliferating the transport of nutrients and removal of waste products. Arginine supplementation may prove beneficial in preventing muscle wasting occurring from injury or illness as research has shown that it is capable of activating and regulating mTOR (26). Further, arginine stimulates the secretion of growth hormone, which serves an assistive role in tissue repair (27).

Combining arginine with the amino acid, ornithine, elicits the production of insulin (28), a peptide hormone intimately involved with growth and recovery. Glutamine, another non-essential amino acid which is found in the most abundant amounts of the amino acids in the body, supplies a bulk of the nitrogen needed to fuel the production of cytokines and macrophages during injury or illness. Glutamine supplementation has been indicated as a viable remedy for those suffering from traumatic brain injury (30), compromised gastrointestinal functioning (2), and burn injuries (27). Proline, a non-essential amino acid, catalyzes collagen and cartilage production, which may warrant its supplementation in recovering from traumatic injuries as well as those experiencing age and activity associated degradations of cartilaginous structures (27).

Methionine, an essential amino acid, has been shown to improve cartilaginous integrity as well as serving in an assistive capacity in treating rheumatoid arthritis (32). Supplementation with phenylalanine, an essential amino acid, which has been proven to alleviate conditions associated with decreased endorphin levels may be of benefit if an individual wishes to dull pain accompanying musculoskeletal injuries (20).

Practical Considerations

Assessing the quality of a protein can be determined by assessing its essential amino acid composition, bioavailability, and digestibility. The digestibility of a protein is determined by measuring the amounts of amino acids absorbed by the body and the protein's contribution to human amino acid and nitrogen requirements. Proteins which are readily digestible and contain the dietary essential amino acids in quantities that correspond to human requirements are regarded as "high quality".

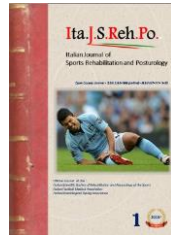
Increased protein intakes for strength and endurance athletes to repair and replace damaged proteins, support increases in fat free mass, and ensure optimal levels of all physiologically required proteins.

Energy deficits are generally associated with a decline in body weight. While the loss of body weight may be due to declines in body fat, skeletal muscle mass is also lost and may account for 25% or more of the total body weight loss. Research shows that consuming a high-protein diet during energy deficit can reduce the loss of fat-free mass. This muscle-sparing effect may be positively shifting the nitrogen balance, accounting for less protein degradation, thus facilitating increased muscle protein synthesis.

Phillips & Van Loon (2011) suggest that a protein intake of 1.8-2.7 g/kg for athletes training in energy deficit may be optimal. Recent literature has suggested increased protein intakes among resistance-trained, lean athletes during caloric restriction. A range of 2.3-3.1 g/kg of lean body mass (LBM) was proposed.

Conclusion

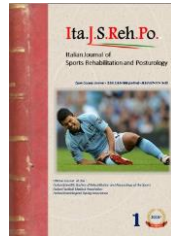
Based on the referenced literature it can be inferred that individuals recovering from injuries will benefit from an increased protein intake, particularly of high quality sources which contain greater quantities of amino acids to accelerate recovery and regain pre-injury functionality.



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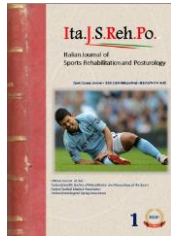
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