Using Protein Kinetics to Maximise your Training Gains

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Protein kinetics is the study of the relationship between the speed of absorption of dietary proteins and the effects on protein turnover and retention.

INTRODUCTION

Anyone who has done any significant amount of training knows that protein supplementation plays a major role in training gains, that training increases protein requirements and that some protein supplements work better than others. This view has not been shared by the scientific community who have largely said that the most important factor in training success is providing energy for exercise, that protein has only a minor role in providing energy for exercise and that protein requirements are easily met by a regular western diet. Gradually this view is changing and increasingly there are positive statements in respected journals supporting protein supplementation e.g. "*There is a strong theoretical basis for expecting a beneficial effect of protein supplementation in active people*", (Wolf RR., Protein Supplements and Exercise, Am J Clin Nutr, 2000)

For many years scientists have looked at protein quality in terms of the amino acid composition. The focus of much of this research has been on the minimum amount of protein necessary to sustain growth, especially with regard to developing nations. There has been considerable debate in the scientific community about the relevance of measures of protein quality for these purposes and several different protein scoring systems have been developed.

Biological Value has largely been superseded by– PDCAAS scores for World Health Organisation yet is continually used to promote the value of protein supplements the world over. Possible to argue the relevance of any of these scores to athletic populations who are perhaps more concerned with optimising performance rather than surviving on the minimum amount of protein to maintain life.

Bodybuilders make it easy for the scientific community to disregard nutritional practices they know to work because all too often the justification for the nutritional strategy has been flawed.

There has been much debate in recent years about the classification of essential amino acids and indeed whether some amino acids may become conditionally essential etc. (e.g. hard physical exercise may increase the need for glutamine beyond the bodies ability to synthesise it and training gains etc may be improved by increasing dietary consumption of glutamine).

Methodological errors may be responsible for some of the discrepancies between what the scientific community regard as fact and what body builders know to work.
i.e. a successful body builder does much more than consume lots of protein the protein is consumed in a systematic manner with regard to training status, and type and timing of protein supplements in a nutritional strategy. There is no doubt that it is a commonly held belief that 30-40g of protein taken every 2 hours will promote muscular gains, and there is no doubt that the protein of choice is whey protein. The popularity of whey protein is not easily explained by protein quality scores and amino acid profiles– there are other proteins, or combinations of proteins which score as good if not better.

Some supplement manufactures have suggested that the superiority of different proteins may be due to bioactive proteins within certain proteins. However, attractive as this may be there is little evidence of bioactive proteins within milk protein fractions having any systemic effect when consumed in a normal manner. There is more evidence that bioactive peptides may work locally, for instance casomorphins may work locally to slow down gastro intestinal motility. (Danielle H, Vohwinkel M, and Rehner G. Effect of casein and beta-casomorphines on gastrointestinal motility in rats. J Nutr 120: 252-257, 1990)

There is some evidence of intrinsic factors within soy protein having beneficial effects, in particular emphasis has been placed on isoflavones e.g. Rossi et al (2000) have demonstrated an improved antioxidant status and reduced exercise induced muscle damage with soy consumption. (Rossi AL, Blostein-Fujii A, DiSilvestro RA, Soy beverage consumption by young men: increased plasma total antioxidant status and decreased acute, exercise-induced muscle damage, Journal of Nutraceuticals, Functional & Medical Foods, Vol. 3(1) 2000 www.HaworthPress.com)

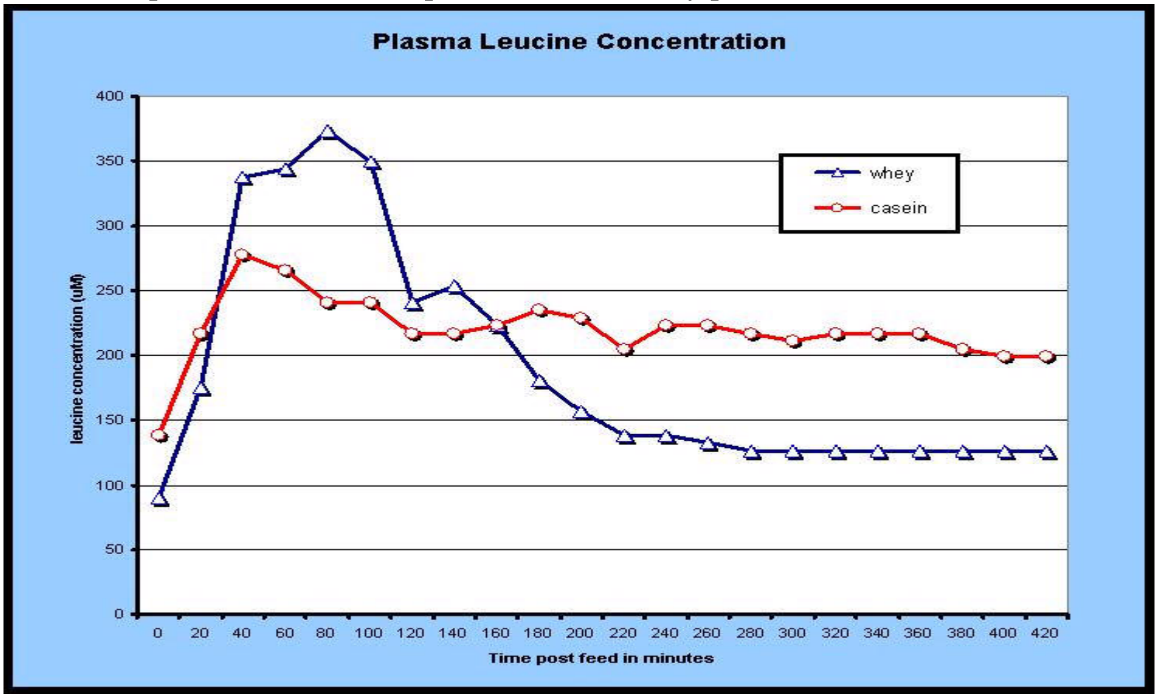
However, although there is increasing consumption of soy especially since modern isolation techniques make soy beverages far more easily digested than in the past soy has found it difficult to displace whey as a the protein supplement of choice.

What may explain the nutritional strategies which have become prevalent in body building population but also the choice of protein, particularly the choice of whey protein above casein for these nutritional strategies, is the concept of slow and fast dietary proteins.

The concept of slow and fast dietary proteins has been studied by a series of experiments reported by Boirie and co-workers. (Boirie Y., Dangin M., Gachon P., Vasson MP., Maubois JL., Beaufr'ere B., **Slow and Fast dietary proteins differentially modulate postprandial protein accretion**, Proc. Natl Acad Sci USA., 94(26): 14930-5 1997, Dangin M, Boirie Y, Garcia-Rodenas C, Gachon P, Fauquant J, Callier P, Ballever O, Beaufrere B, **The digestion rate of protein is an independent regulating factor of postprandial protein retention**, Am J Physiol Endocrinol Metab, 280: E340-E348, 2001)

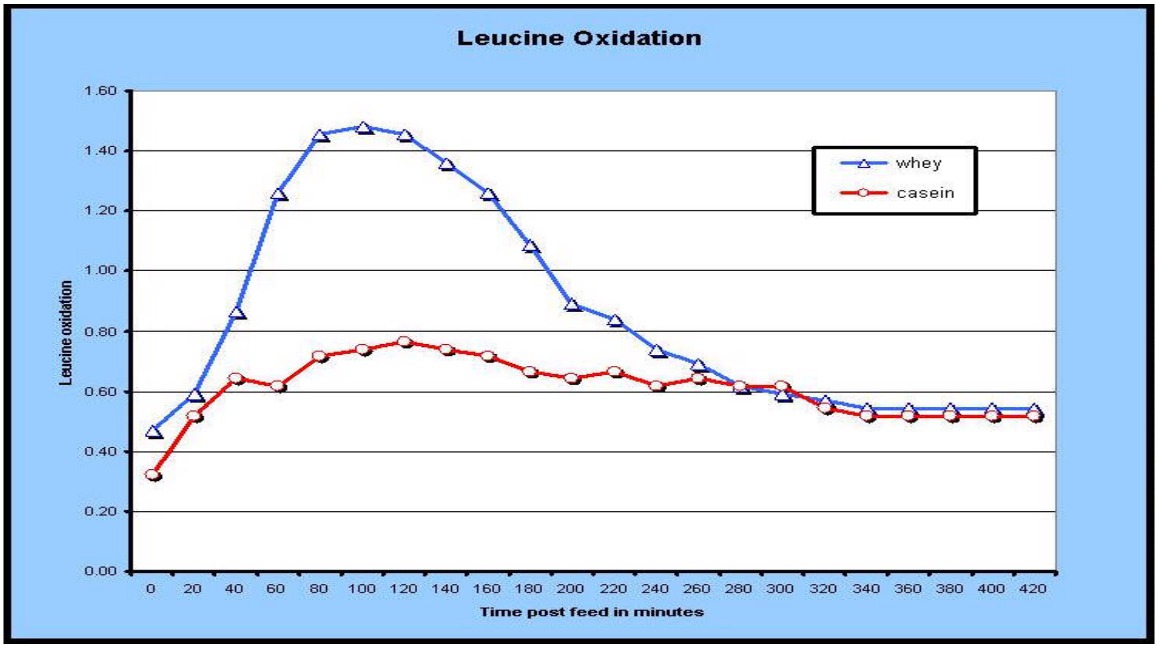
They have shown that the rate of absorption of dietary proteins may affect nitrogen balance independently of the amino acid composition in high biological value proteins.

In these studies they differentiated between protein which is rapidly absorbed and results in a rapid rise in plasma amino acids (whey and later amino acid mixtures) and protein which is slowly absorbed and resulted in slower more pronged but less extreme rise in plasma amino acids (casein). The slow release of amino acids into plasma with casein was later replicated with small repeated doses of whey protein.



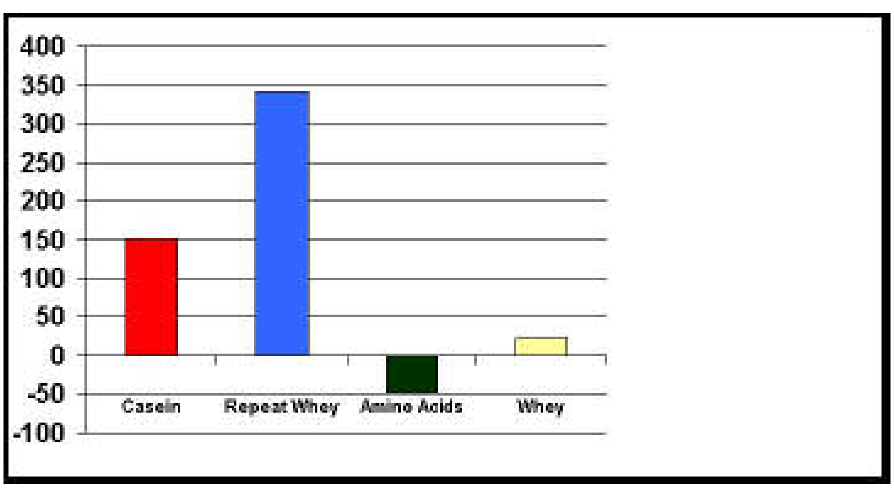
The slow increase in plasma amino acid levels in the casein treatment was thought to be due to delayed gastric emptying caused by casein clotting in the stomach and thus slowing down gastric emptying, and possible the effect of bioactive peptides within casein slowing down gastrointestinal motility.

The whey protein resulted in a rapid rise in plasma amino acids and this was associated with a big increase in protein synthesis but also a big increase in protein oxidation. So although the whey protein resulted in much greater anabolic activity in the short term, when the researchers looked at the nitrogen balance over 7 hours it was shown to be much higher in the casein treatments. Casein was shown inhibit protein breakdown in the postprandial period to a much greater extent than whey protein.



These papers were written from a clinical perspective where there are many conditions in which low protein diets are indicated, or occur, and there is a necessity to improve protein deposition and reduce muscle wasting the attractiveness of casein is obvious. I.e. using a slow protein enables a better nitrogen balance for less protein consumption. The relevance of this in athletic populations where there is not necessarily a contra-indication to high protein consumption is less obvious, -other than for those situations where it is not possible to practice repeat protein feedings i.e. during sleep. Casein based formulations thus have obvious applications for a night time drink in populations wishing to prevent night time protein catabolism.

Postprandial nitrogen balance over 7 hours derived from Dangin et al (2001) Postprandial leucine balance data x 3.93 (assumes tissue protein leucine content of 3.93mmol leucine/g N



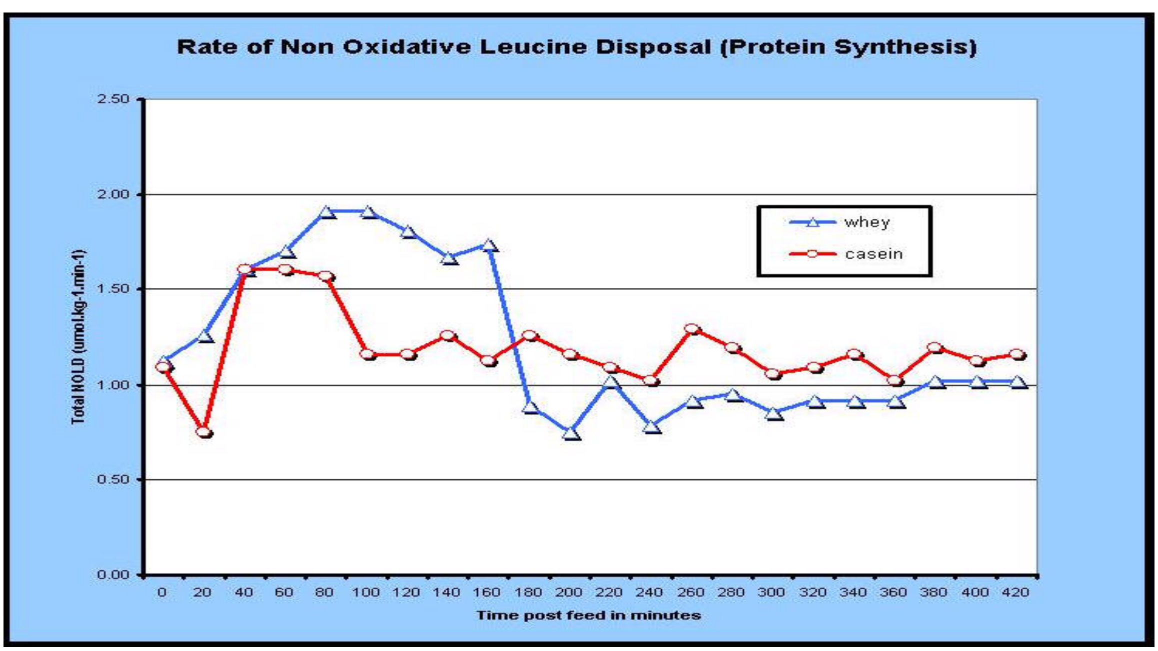
This may be important, not just for those populations who which to maintain bulk but perhaps also for endurance athletes who may be less concerned with maintaining muscle bulk but for whom losses in non-constitutionally expressed proteins may be more catastrophic. (Non-constitutionally expressed proteins include the regulatory and rate limiting enzymes which are responsible for instance for the production of energy). A casein based night time formula has recently been developed by Science in Sport, Rego nocté combines slow release protein with mineral supplementation and fructo-oligosaccharides.

What about those situations when repeat protein feeding is possible and high protein consumption is not contra indicated?

It can be seen that even in the study by Dangin (figure…) when very small doses of whey protein were given the nitrogen balance was greater than with casein, or the 40g of whey given in one dose. However, if we look at the time course of nitrogen balance over time using the data from Boirie it does appear to give scientific support to the strategies employed by bodybuilding populations.

In there studies Non-oxidative Leucine disappearance (NOLD) which is an index of whole body protein synthesis is seen to be much greater with the whey than with casein e.g. the rate of protein synthesis was stimulated by 68% with whey compared with 31% with casein (average between 40-140 minutes) in the Boirie paper. In both papers the rate of protein synthesis is higher with whey than with casein until between 2 and 3 hours (see figure …. Data from Dangin –NOLD)

It is also apparent that although the protein oxidation is much higher in the whey protein treatment it is not in the same order as protein synthesis. It is also important to remember that these are rates of synthesis and oxidation. Protein is still being synthesised at a much higher rate than casein up to about 3 hours although the rate may have peaked at 1 hour post supplement. .



You can see from the graph that net nitrogen gains for whey peak at about 2 hours and these peak gains are maintained up to about 3 hours post supplement. It is only after 3 hours that the net gains start to diminish with the fast protein, but it is only after approximately 5 hours that there is any advantage of the slow release protein.

The data from these studies would thus seem to support the supplementation of 30-40g doses of rapidly absorbed proteins every 2-3 hours for those wishing to maximise protein deposition, other than in those circumstances where repeat feeding will not take place for many hours. There is a possibility that repeated doses of rapidly absorbed protein may raise protein oxidation and thus make a slow release protein formulation for nigh time use additionally beneficial.

Is the answer not to combine different proteins, thus gaining the advantages of fast and slow dietary proteins?

This is not likely to work since the proposed mechanism of action, responsible for the anti-catabolic effects of the slow protein is that it is slowly absorbed and that the amino acids are drip fed into plasma. Similarly the anabolic effects of the fast protein are by virtue of the hyper aminoacidemia generated by the rapid absorbtion of the protein. It is well documented that stimulation of protein synthesis requires at least a 2 fold increase in plasma amino acids above base line levels. (Castellino P, Luzi L, Simonson DC, Haymond M and De Fronzo RA. **Effect of insulin and plasma amino acid concentrations on leucine metabolism in man. Role of substrate availability on estimates of whole body protein synthesis.** J Clin Invest 80: 1784-1793, 1987. Giordano M, Castellino P and DeFronzo RA. **Differential responsiveness of protein synthesis and degradation to amino acid availability in humans.** Diabetes 45: 393-399, 1996. Tessari P, Inchiostro S, Biolo G, Trevisan R, Fantin G, Marescotti MC, Iori E, Tiengo A and Crepaldi G. **Differential effects of hyperinsulinemia and hyperaminoacidemia on leucine-carbon metabolism in vivo. Evidence for distinct mechanisms in regulation of net amino acid deposition.** J Clin Invest 79: 1062-1069, 1987)

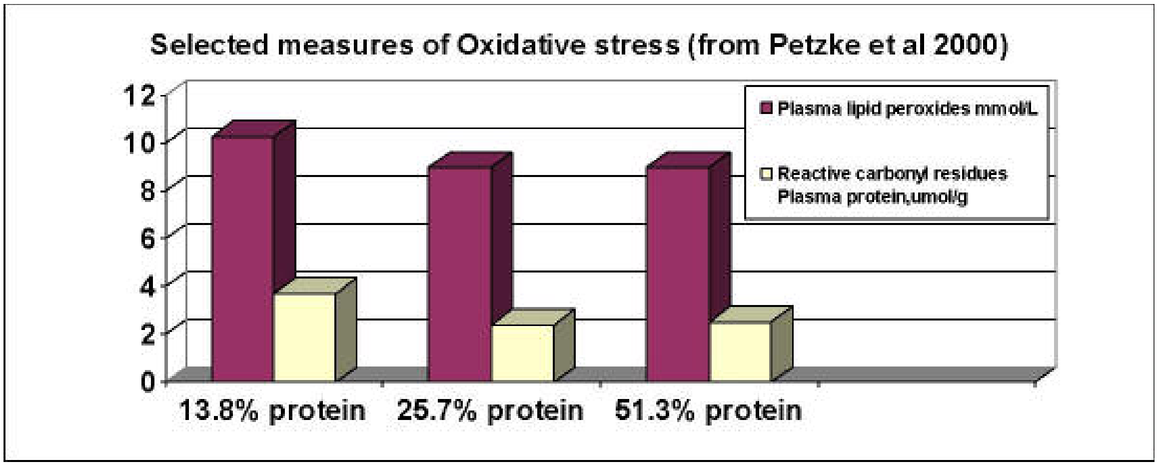
Those wishing to gain the anabolic effects of fast protein are thus advised to avoid casein and whole milk, which has a casein component, since any casein will slow gastric emptying and reduce the necessary rise in plasma amino acids.

Protein turnover etc inc = inc oxidation, not proven =faster adaptation etc.

Taking 30-40g of protein every 2-3 hours can result in high protein consumption eg. 8 x 40g doses results in a protein consumption of 320g of protein which is equivalent to 4g/Kg body weight for an 80Kg subject. Protein consumption of this magnitude is not uncommon in strength athletes. (Lemon P and Nagle F. **Effects of exercise on protein and amino acid metabolism.** Medicine and Science in Sports and Exercise 13: 141-149, 1981)

High protein diets are associated with increased protein oxidation and it is obvious from the studies by Boirie and co-workers that repeated fast protein feedings would result in very high protein oxidation. Since the oxidation of amino acids involves the mitochondrial redox chain it is a potential source of free radicals and researchers have speculated that high protein diets may result in increased oxidative stress. (Petzke KJ, Elsner

A, Proll J, Thielecke F and Metges CC. **Long-Term High Protein Intake Does Not Increase Oxidative Stress in Rats**, J. Nutr. 130: 2889-2896, 2000)



However, when rats were fed high protein diets 25.7 or 51.3% crude protein (casein) over an adequate protein diet 13.8% crude protein for 15 weeks measures of oxidative stress were found to be reduces.

Protein Turnover

Proteins are in a continual state of flux. A significant amount of protein turnover is necessary to facilitate rapid alterations in concentrations of certain proteins -enzymes etc and the need to continually replace damaged proteins. Researchers have estimated that as much as 20% of the energy expenditure of a fasting individuals energy is devoted to protein turnover, and this has been used to illustrate the importance of protein turnover in biological systems. (Welle 1999).

Constitutionally expressed proteins making up tissue structure and protein account for the bulk of body proteins. Rapid alterations in the concentrations of these proteins is not as necessary as for regulatory proteins and rate limiting enzymes and therefore the half lives of these proteins tend to be longer yet much energy is devoted to there turnover. Tend to think of adaptation to physical activity in terms of changes in constitutionally expressed proteins however physical performance may be dependent upon regulatory and rate limiting enzymes - speeding up protein turnover = reducing the half life of proteins = faster adaptation to training intervention.

Protein half life and adaptation

Wesse (1999) gave the following example to illustrate how the half life of protein could be applied to the adaptation to a physical challenge,

"Assuming a protein turnover in skelatal muscle of 1.5% per day in a sedentary individual who then takes up weight training and that this stimulates protein synthesis by

1/3 leaving fractional degradation unchanged. According to the concept that protein mass is proportional to the synthesis, the final protein mass will be 1/3 more. The time required to achieve 50% of the maximal response would be 46 days. The time required to achieve 95% of the final response would be 200 days and any study to examine changes in muscle mass after only a few weeks would underestimate the intervention.

APPLY INCREASES IN PROTEIN TURNOVER TO SPEED OF ADAPTATION

Any increase in protein turnover should reduce the time course necessary to adapt to a given training intervention.

There has been much research in recent years on the effects of exercise and free radical production and the role of free radicals in tissue degeneration. Research shows that anti-oxidant nutrition does offer some protection against oxidative stress however, some oxidative damage is inevitable. Researchers have also pointed to a role of free radicals as important signals for cellular adaptation. (Jackson 1999)

Protein turnover is another mechanism by which the body copes with the inevitable free radical mediated damage associated with cellular oxidation. Protein turnover has been shown to decline with age (Balagopal et al 1997) and this decline in protein turnover is associated with an increase in the presence of oxidatively damaged proteins (Stadtman 1992, Oliver et al 1987, Stadtman 1998, Stadtman 2000)

Assays have been developed to measure the carbonyl content of proteins (Levine et al 1990, Levine et al 1994, Nakamura and Goto 1996) and these have been shown to be a good indicator of oxidative damage, accepting that not all oxidative damage results in carbonyl formation and thus will represent an underestimation of the total oxidative modification. (Stadtman 1998, Stadtman 2000)

Oxidative damage is not restricted to constitutionally expressed proteins and protein carbonyls have been studied in erythrocytes (Oliver et al 1987), hepatocytes (Stark-Reed and Oliver 1989, Stark et al 1987), lung (Rad'ak et al 1998), brain (Rad'ak et al 1998, Carney et al 1991), and skeletal muscle (Witt et al 1992, Rad'ak et al 1997)
Carbonyl modification could be used to study the effect of dietary manipulation on body protein quality and possibly explain some of the discrepancies between common belief and scientific understanding.

Protein Turnover and Protein Quality

A major requirement for protein turnover in constitutionally expressed proteins occurs due to the need to repair free radical mediated damage. Free radicals oxidise amino acid side chains leading to a number of products that cause cross-linking fragmentation, or loss or reduction of protein activity. Oxidative damage to a few amino acid side chains does not necessarily inactivate a protein molecule but accumulation of random damage could have a major impact on the specific activity of the protein. (Stadtman 1988, 1992)

Some amino acid side chains are oxidised to carbonyl derivatives, and the carbonyl content of proteins has been used to estimate the extent of oxidative damage to protein. Carbonyl modification in young adults is evident in approximately 10% of protein molecules rising to over 20% in older individuals. Since not all oxidative damage results in carbonyl formation this does represent an underestimation of the total oxidative damage which may well be present in over 50% of proteins.

Stadtman (1992) has claimed experimental support for the accumulation of damaged proteins as a result of age-related increase in the oxygen free radical-mediated damage and/or a loss in the ability to degrade oxidised proteins. Since it is well documented that protein turnover decreases with age it would seem logical that the net accumulation of carbonyls would increase as a result. The age related decrease in protein turnover can partly be explained by a decrease in the cellular activity of cellular proteases that preferentially degrade abnormal enzyme forms. However, the possibility that an increase in protein turnover by dietary manipulation could result in a reduced net accumulation of free radical mediated damage.

Since carbonyl formation occurs as a result of oxidative stress the relationship between protein turnover, net carbonyl accumulation and exercise stress warrants further study.

Goto et al (1999) using immunoblot followed by one or two-dimensional polyacrymide gel electrophoresis with antibodies against 2,4,dinitrophenylhydrazones studied the effect of ageing and exercise on protein carbonyls. They were able to demonstrate that exhaustive exercise induced significant increases of selected but unspecified proteins in the lung. They also showed that exercise at high altitude caused higher carbonylation of skeletal muscle proteins than at sea level. IN WHAT ANIMAL OVER HOW LONG ETC

Oliver et al (1987) showed that the concentration of oxidised protein in human erythrocytes increases with the age of the cell (ie with cell density).

Protein Kinetics Summary

Understanding the absorption speed of different proteins may be used to help maximize training gains.

Rapidly absorbed proteins can promote protein synthesis but also increase protein oxidation, so should be taken every 2-3 hours in order that the gains made in the short term are not lost over the longer term.

If it is not possible to eat for longer than 5 hours a slow release protein will prevent protein catabolism.

When casein is added to a fast protein it is likely to slow the absorption of anything it is taken with- if the intention is to promote an anabolic effect then casein should be avoided, this includes whole milk which has a casein component.

More information www.proteinkinetics.com

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