Z Ernährungswiss 36: 336–339 (1997)

*V.V.A.M. Schreurs
R.E. Koopmanschap
H.A. Boekholt

Short-term dynamics in protein and amino acid metabolism

Kurzzeitdynamik des Protein- und Aminosäurenstoffwechsels

Summary Actual amounts of free amino acids in the blood are sufficient to support whole body protein synthesis for some minutes only. This indicates that the levels of free amino acids in the circulation are kept small and constant relative to the amounts of amino acids supplied by daily intake and turnover of body proteins. The clearance of the amino acids originating from either endogenous or exogenous sources is mainly due to protein synthesis and metabolic degradation. The partitioning of dietary amino acids between these processes, on the short term, is supposed to play an important role in whole body amino acid economy. Therefore whole body amino acid economy could be improved by nutritional measures that favour the clearance of dietary amino acids by protein synthesis instead of by metabolic degradation. These nutritional measures should to be focused on threshold values for metabolic degradation of individual amino acids.

Zusammenfassung Die aktuellen Mengen an freien Aminosäuren im Blut reichen nur aus, um die Ganzkörper-Proteinsynthese für einige Minuten aufrecht zu erhalten. Das zeigt, daß die freien Aminosäurenkonzentrationen in der Zirkulation klein und konstant gehalten werden im Vergleich zu den Mengen der Aminosäuren, die täglich aufgenommen und über die Körperproteine umgesetzt werden. Das Verschwinden der Aminosäuren exogenen oder endogenen Ursprungs aus dem freien Aminosäuren-Pool, findet hauptsächlich durch die Proteinsynthese und den Aminosäurenabbau statt. Die Partitionierung der Nahrungs-Aminosäuren zwischen diesen beiden Prozessen im Kurzzeitbereich werden als bedeutsam für die Ökonomie der Ganzkörper-Aminosäuren angesehen. Eine Verbesserung der Aminosäurenökonomie könnte durch solche nutritiven Maßnahmen erreicht werden, welche die Clearance der Nahrungsaminosäuren durch die Proteinsynthese anstelle des Aminosäurenabbaus begünstigen. Diese nutritiven Maßnahmen sollten sich an den „Schwellenwerten" des Abbaus der individuellen Aminosäuren orientieren.

Key words Amino acids – protein – metabolism – meal feeding – oxidation – breath test

Schlüsselwörter Aminosäuren – Protein – Stoffwechsel – Fütterung – Oxidation – Atemtest

*V.V.A.M. Schreurs
R.E. Koopmanschap · H.A. Boekholt
Wageningen Insitute of Animal Sciences (WIAS)
Department of Human and Animal Physiology
Wageningen Agricultural University
Haarweg 10
NL-6709 PJ Wageningen
The Netherlands

Introduction

A clear function of metabolism is to synthonize the dietary supply of nutrients to the physiological demands of the body. Therefore nutrient metabolism, during and between meals, is thought to have an important influence on the overall efficiency of utilization. Meal feeding creates a temporal oversupply of nutrients (post-prandial phase) necessary to meet the requirements between the meals (post-absorptive phase). It is questionable whether different ways of deposition and mobilisation always lead to the same utilization. This paper discusses possible

interactions between the feeding strategy and the utilization of dietary amino acids.

Whole body protein and amino acid metabolism

The metabolic utilization of dietary amino acids may range from incorporation in body proteins to excretion as metabolic end products CO_2, H_2O and urea (mammals) or uric acid (birds). The metabolic fate of an amino acid is strongly influenced by all kinds of nutritional, physiological, metabolic and biochemical aspects.

A two-compartment model for whole body protein and amino acid metabolism is presented in Fig. 1. The pool of free amino acids is considered to hold only the 'currency' of nitrogen metabolism and comprises not more than 1% of the total. The currency in the free pool mainly originates from endogenous sources (protein turnover and occasionally *'de novo'* synthesis) and intermittently from the feed as the exogenous source. The Fig. 1 illustrates that amino acids or their functional parts remain available to support physiological functions as long as their metabolic end products are not excreted. The nature and site of utilization is variable and will be determined by physiological circumstances and metabolic constraints.

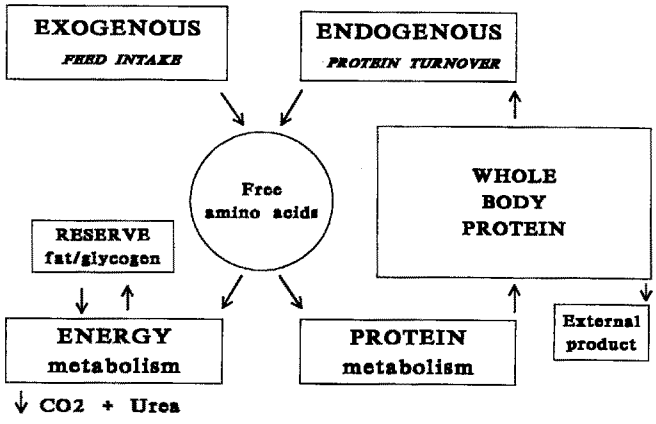

Fig. 1 Whole body protein and amino acid metabolism

It should be emphasized that the pool of free amino acids in the body is kept small and constant relative to the amounts of free amino acids supplied by daily intake and turnover of body proteins. The amount of free amino acids in the blood plasma is only sufficient to support whole body protein synthesis for some minutes. The discrepancy between the influx of amino acids and the buffering capacity of the free pool implies that amino acids are rapidly used for either protein synthesis or other metabolic processes. In case protein synthesis capacity is exceeded by the influx of amino acids due to feed intake or turnover of body proteins, the excess is mainly subject to metabolic degradation. In this respect it should be mentioned that the efficiency of protein deposition immediately after a meal (post-prandial phase) has to be considered as the upper limit for the long term efficiency of protein production.

Diurnal protein cycling

A direct consequence of the introductory remarks is that the nutritional and metabolic condition of meal fed animals changes during the day. These animals require a system of post-prandial gain and post-absorptive mobi-lization of dietary protein. Millward and Rivers (1) have discussed such a system as 'diurnal protein cycling' This process, relevant to both producing and non-producing animals, is thought to play an important role in whole body amino acid economy. Amino acids available from meal feeding are clearly not stored in the body pool of free amino acids. Metabolic degradation of amino acids in the post-prandial and the post-absorptive phase can be monitored by breath test measurements.

$^{14}CO_2$ breath test measurements

Oxidative losses of amino acids, as discussed in this paper, have been studied by $^{14}CO_2$ breath tests, according to the method of Schreurs et al. (2). [Carboxyl-^{14}C; 1-^{14}C] and [universal-^{14}C; U-^{14}C] labeled amino acids can be used as substrates. The cumulative recovery of label in the breath during 4 hours is expressed as percentage of the dose applied intraperitoneally (Fig. 2). The recovery values indicate which part of the labeled amino acid flux has been subject to decarboxylation and total oxidation, respectively.

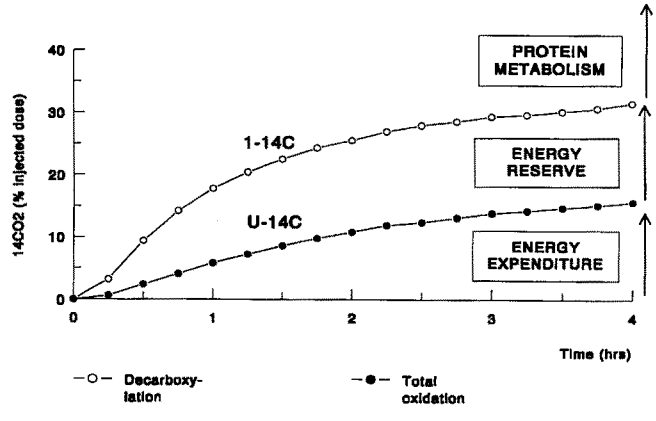

Fig. 2 The cumulative recovery of label

Measurements in a steady metabolic state

In a previous study oxidative losses of two amino acids under different nutritional conditions have been compared. The post-absorptive phase can be considered as a relative steady metabolic state. Decarboxylation and total oxidation were measured for tyrosine and leucine in adult male rats conditioned for 3 weeks on iso-energetic diets containing 210, 75 or 0 gram protein/kg (2).

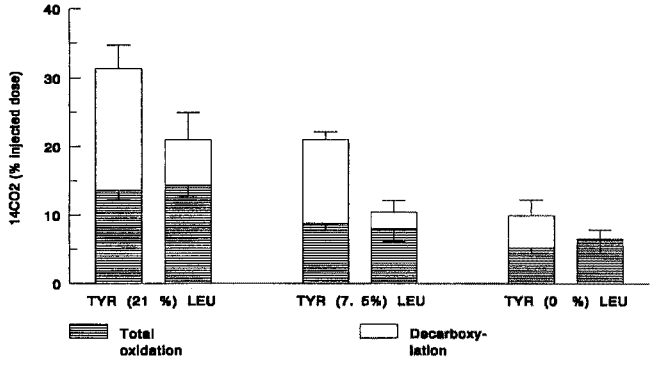

Fig. 3 Breath test measurements in a steady metabolic state

The level of dietary protein influences both decarboxylation and total oxidation. Although the responses of leucine and tyrosine were not different for total oxidation, there was a difference between the amino acids in their relative rate of decarboxylation (Fig. 3). These breath test measurements in adult rats show a higher level of amino acid oxidation during the post-absorptive phase if the protein intake is higher and therefore support a mechanism of diurnal protein cycling.

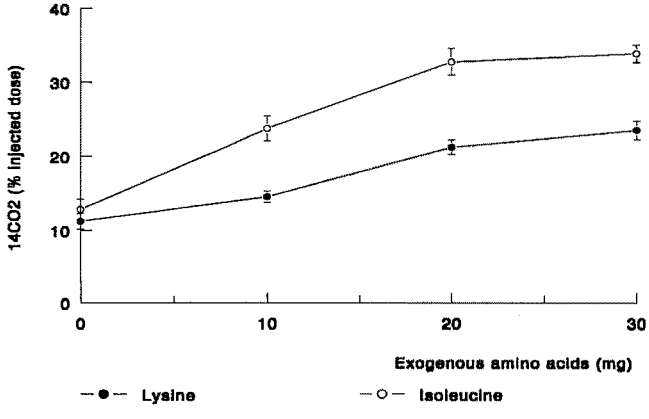

Fig. 4 Comparison of dose-response relation of lysine and isoleucine

Measurements in a perturbed metabolic state

Similar breath test measurements have shown a rapid catabolic response for the metabolic degradation of amino acids upon an increase of the free pool. The nutritional protein status and the nature of the amino acid were, however, of great influence on the catabolic responses observed. For lysine, as compared to branched chain amino acids, the catabolic response was modest especially in the lower range dose (Fig. 4).

These breath test observations based the hypothesis that also rather normal physiological fluctuations in the availability, as caused by meal feeding, could have adverse effects on the metabolic utilisation of dietary amino acids.

Effect of meal size on metabolic utilisation of amino acids

Direct evidence for an interaction between meal size or meal frequency and the utilisation of dietary amino acids was shown in an experiment with adult rats fed two large vs. six small meals at a fixed marginal level of daily protein intake (3).

Adult male Wistar rats (16 wks) were fitted with a gastric cannula and randomly divided over 3 groups. From 17 wks on, all rats received a feeding solution [Nutrison Standard (Nutricia, The Netherlands) mixed with glucose syrup to contain 350 kJ ME and 1 gram protein in a final volume of 32 ml]. Group 1 had *ad libitum* access to a drinking bottle with the feeding solution. Groups 2 and 3 were both pair fed with group 1 by gastric infusion of the daily amount by 2 or 6 meals, respectively. Development of body weight is shown in Fig. 5.

Due to habituation to the drinking nipple *ad libitum* feed intake was initially low but became relative constant

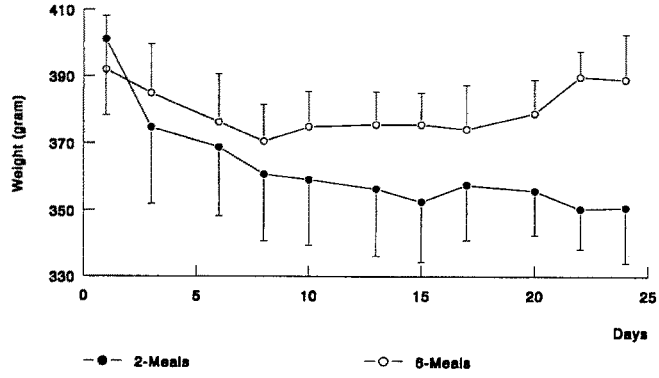

Fig. 5 Development of body weights

(ca. 30 ml per day) within a week. Consequently there was a fall in body weight for all animals in the first days. The *ad libitum* rats stabilized their body weight at the end of the first week and almost regained their original weight in another 2 weeks (not shown). For the pair fed rats development of body weight was strongly influenced by the number of meals. For rats receiving 6 small meals the development of body weight was roughly similar as described for the *ad libitum* rats. Rats receiving the daily amount by 2 large meals not only failed to regain but also failed to stabilize their body weight. They continued to loose weight at least till the end of the third week. These results indicate that long term metabolic utilization of nutrients can be influenced by the number of meals.

Previously we showed that the level of amino acid oxidation in the post-absorptive phase is sensitive to the level of dietary protein (2). In this experiment we compared decarboxylation and total oxidation of leucine in the post absorptive phase for the pair fed rats receiving two or six meals. Values for rats fed 6 small meals [23.5, sd 1.8; 15.8, sd 2.5] were slightly higher as for rats fed 2 large meals [19.2, sd 1.1; 12.2, sd 1.4]. It is concluded that relative large meals, at least at a marginal level of daily protein intake, can have a negative effect on amino acid economy by a wasting of amino acids in the post prandial phase. As a consequence large meals may have adverse effects on the nutritional protein status as reflected in this study by a lower body weight and a lower level of amino acid oxidation in the post absorptive phase. Therefore meal size should be taken into account for an adequate utilization of dietary amino acids in cases of marginal supply, e.g., food shortage or attempts to improve N efficiency. In a similar experiment with young growing rats the same tendencies were found (4).

Acknowledgement Nutricia (Zoetermeer, The Netherlands) is acknowledged for the kind supply of Nutrison Standard.

References

1. Millward DJ, Rivers JPW (1988) The nutritional role of indespensable amino acids and the metabolic basis for their requirements. Eur J Clin Nutr 42:367-393
2. Schreurs VVAM, Boekholt HA, Koopmanschap RE, Weijs PJM (1992) The metabolic utilization of amino acids: potentials of $^{14}CO_2$ breath test measurements. Brit J Nutr 67:207-214
3. Schiffelers SLH, Schreurs VVAM, Krawielitzki K, Koopmanschap RE Effect of meal size on metabolic utilisation of amino acids at a marginal level of protein intake. Proc 7th Int Symp Protein Metabolism and Nutrition (Vale de Santarém, P) EAAP publication 81, 345-347
4. Bujko J, Schreurs VVAM, Koopmanschap RE, Fürstenberg E, Keller J (1997) Benefit of more but smaller meals at a fixed daily protein intake. Z Ernährungswiss 36:347–349