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PHYSICAL ACTIVITY: IMPACT ON PROTEIN AND AMINO ACID METABOLISM AND IMPLICATIONS FOR NUTRITIONAL REQUIREMENTS.

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INTRODUCTION

Although the molecular basis for the events leading to the contraction of muscles remains to be defined in detail, it is generally accepted that they include an interaction between actin and myosin, during which ATP is hydrolyzed to ADP (e.g. Bessman and Geiger, 1981). Thus, an essential metabolic aspect of exercise is the generation of utilization of chemical energy in the course of muscular work or its transformation with a generation of heat. But because the concentration of ATP in muscle is small, as indicated in Table 1, and the store of high energy phosphate bonds in the form of creatine phosphate is sufficient for only a limited number of contractions, a continuous generation of

TABLE 1

STORES OF ENERGY IN THE NORMAL ADULT[1]

Fuel	Amount	
	kcal	kJ
ATP	1.5	6
Creatine phosphate	3.5	15
Glycogen	1,200	
Fat	140,000	

[1] From Astrand (1979) and Felig and Wahren (1975): Stores for 20 kg muscle, except for fat (based on total body wt of 75 kg).

these bonds, through anaerobic and oxidative metabolism of fuels, is necessary to support a continuous output of muscular work for any significant period of time. In this brief review, we will consider the extent to which amino acid catabolism participates in the formation of the ATP required for muscular activity and if so whether this is of significance in relation to the protein and amino acid requirement of physically active human subjects.

In addition to the acute effects of physical exercise on the sources and utilization of major energy substrates, it is necessary also to consider the more prolonged effects of muscular activity on the status of tissue and body protein and amino acid metabolism. This is important because chronic periods of altered physical activity as, for example, in the case of an extended bed rest (e.g. MacDougal et al., 1977) bring about changes in body protein mass and may also influence the nutritional requirement for nitrogen and indispensable amino acids.

In the following sections we review selectively various observations reported in the literature and consider some of our unpublished work in an attempt to assess the relationships between physical activity, protein and amino acid metabolism and nutrition in the human. Our purpose is to highlight areas that appear to deserve more complete study, particularly because national (e.g. US/FNB, 1980) and international (FAO/WHO, 1973) allowances for dietary protein and amino acids do not make specific recommendations for persons whose physical activity differs widely.

Major Sources of Energy

Recognition of the importance of carbohydrate and fat as the major fuels in overall energy expenditure during exercise is based on numerous studies in the intact organism, including man, and in isolated muscles (reviewed by di Prompero, 1981). In summary, various factors influence the relative contribution of these two fuel sources, including intensity and duration of the exercise, body carbohydrate stores, physical conditioning, whether carbohydrate is consumed during the period of exercise and the prior nutritional history of the subject (e.g. Lemon and Nagle, 1981). The prevailing view, however, is expressed by Astrand (1979) who states, "the choice of fuels for working muscles, therefore,

is limited to carbohydrate and fat" and by di Prompero (1981) who concludes that "the energy for muscular work is entirely derived from carbohydrates and fat".

The importance of carbohydrate in relation to meeting the energy need of the exercised muscle is revealed by studies, involving application of a needle biopsy technique, that show a reduction in muscle glycogen with the continuation of exercise (e.g. Bergstrom and Hultman, 1972) and that the concentration of muscle glycogen may limit work performance (Costill and Miller, 1980). It should be noted, however, that reduced glycogen stores do not inevitably prevent prolonged exercise, provided the supply of FFA is adequate (Phinney et al., 1980).

Based on the arteriovenous difference studies, Ahlborg et al. (1974) estimated, as depicted in Figure 1, that the

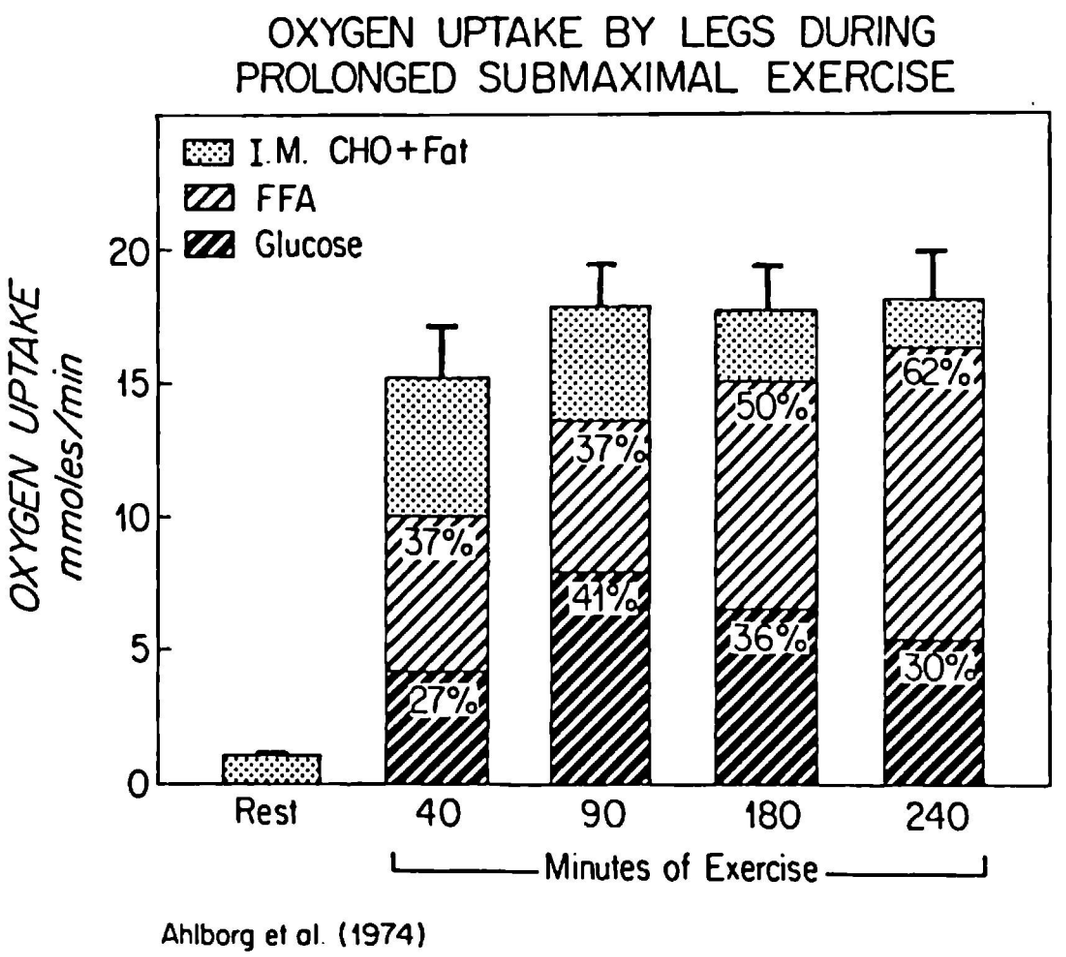


Fig. 1. Leg uptake of oxygen (O_2) and contribution to oxidative metabolism made by substrates at rest and during exercise. The percent values represent proportion of total O_2 uptake accounted for by these substrates. Drawn from Ahlborg et al. (1974).

contribution of blood glucose to total oxidative metabolism by the exercising leg reached a peak of 90 minutes and then declined as exercise continued. On the other hand, the fraction of total metabolism attributed to the uptake of free fatty acids (FFA) exceeded the relative contribution made by glucose as the exercise period continued. The combined uptake of glucose and FFA by the exercising muscle accounted for approximately 65% of the total metabolism at 40 min and by 90 min the contribution approached more than 90%. (See also Felig and Wahren, 1975).

At the time when the utilization of blood-borne glucose is markedly increased, hypoglycemia does not usually occur, due to a balanced increase in the rate of glucose output by the liver (Wahren et al., 1971), which originates via glycogenolysis in the short term, as evidenced by a depletion of liver glycogen stores (Bergstrom and Hultman, 1942), and from increased gluconeogenesis in the longer term (Ahlborg et al., 1974). However, exercise-induced hypoglycemia may occur occasionally in the insulin-dependent diabetic patient undergoing unusually strenuous exercise within 12h of administration of long-acting or intermediate-acting insulin preparations (Felig and Wahren, 1975).

From these various observations, it can be concluded that the quantitatively important components of the pattern of fuel utilization during prolonged periods of mild to moderate exercise involve utilization of muscle glycogen, blood glucose and free fatty acids.

The exercise induced increase in hepatic glucose output is associated with multiple changes in plasma hormone levels (Table 2), including a reduction in insulin and elevations in glucagon, growth hormone, glucocorticoids and catecholamines. The extent of these changes in hormonal levels are complex and depend upon the intensity of exercise, degree of training and the nutritional, metabolic and health state of the subject. Nevertheless, these hormonal changes serve to modulate the alterations in hepatic glucose output in response to exercise (e.g. Felig and Wahren, 1979) as well as the enhanced lipolysis and fatty acid oxidation.

Muscle Protein Metabolism

Because the protein and amino acid metabolism of body

TABLE 2

EXAMPLE OF MULTIPLE HORMONAL RESPONSE TO EXERCISE[1]

Exercise Response (Plasma concentration)	
Norepinephrine	↑
Growth Hormone	↑
Epinephrine	↑
Cortisol	↑
Glucagon	↑
Insulin	↓

Training: Modifies degree of change

Dietary Condition: Modifies degree of change

Health Status: Modifies the responses.

[1]Based on: Hartley et al. (1972a,b); Gyntelberg et al. (1977); Sutton (1978); Bloom et al. (1976); Zinman et al. (1979); and Wirth et al. (1981).

cells and organs is responsive to changes in the availability and source of energy substrates (Munro, 1964; Young et al., 1981) and to alterations in hormonal balance (Munro, 1964), it is important to consider the impact of exercise on protein and amino acid metabolism. First, this should be made in reference to muscle protein metabolism because this is known to be affected by numerous hormones (Young, 1970) and this tissue shows responses *in vitro* to changes in physical activity (reviewed by Young, 1981). Furthermore, a brief discussion of protein and amino acid metabolism in skeletal muscles in relation to exercise is important because it plays an important role in total body protein and amino acid metabolism. For example, in a series of studies in which we have estimated simultaneously rates of muscle protein breakdown and whole body protein breakdown in adult subjects, muscle was found to account for 25-30% of total body protein turnover in young adults, declining to about 20% in elderly subjects (Young and Munro, 1978).

A further indication of the importance of skeletal muscles in whole body protein and amino acid metabolism is revealed by studies of the distribution of enzymes involved in branched chain amino acid oxidation. Specifically, the dehydrogenases of α-keto-isocaproic, and α-keto-isovaleric

acid, the keto acid analogues of leucine and valine, respectively, catalyze the irreversible decarboxylation of the two branched chain amino acids. These enzymes are considered to be the rate limiting enzymes in the pathway of branched chain amino acid oxidation in muscle (Hutson et al., 1978), and Khatra et al., (1977) estimated that of the total body, activity of these enzymes is distributed with about 2/3 associated with the skeletal musculature and 1/3 in the liver in adult humans.

The responsiveness of muscle protein metabolism to physical exercise is indicated from the findings that exercise patterns influence the size and distribution of the different fiber types (Gollnick et al., 1972; Saltin, 1973; Holloszy and Booth, 1976; Costill et al., 1976) and the types of proteins (Holloszy and Booth, 1976), as revealed by measurement of enzyme activities (Table 3) in muscle samples

TABLE 3

FIBER COMPOSITION, AREA AND ENZYME ACTIVITIES IN GASTROCNEMIUS OF ELITE DISTANCE RUNNERS.[1]

Group	% ST[2]	Fiber Area[3]		Enzyme Activity[3]	
		ST	FT	LDH	SDH
Elite Distance	79 ± 3.5	8.3	6.5	746	21.6
Middle Distance	62 ± 2.9	6.4	6.3	788	17.7
Untrained	58 ± 2.5	5.4	4.9	843	6.4

[1] Summarized from Costill et al. (1976).

[2] % of Slow Twitch fibers. ST = Slow Twitch; FT = Fast Twitch.

[3] Values are $\mu^2 \times 10^{-3}$

[4] μmoles/g/min (LDH = lactate dehydrogenase; SDH = succinic dehydrogenase).

_____ = $p < 0.05$ from elite distance runners.

obtained from individuals with differing physical activity patterns. Although such measures of enzyme activity indicate changes in muscle protein metabolism in response to exercise, they give little insight into the biochemical

changes that are responsible for these adaptations.

The effects of exercise on muscle protein metabolism may be explored by various approaches and different models have been used to induce changes in muscle protein mass for this purpose (see Millward, 1980). A summary of some studies, carried out with these various models, concerned with various aspects of muscle protein and amino acid metabolism, is given in Table 4. As shown here the findings

TABLE 4

SOME OBSERVATIONS RELATING TO PROTEIN SYNTHESIS DURING MUSCULAR HYPERTROPHY

Process	Author
Amino Acid Transport	
↑ AIB Accumulation (Tenotomy)	Goldberg et al. (1974)
↑ AIB Accumulation (Stimulation *in vitro*)	Goldberg et al. (1974)
↑ AIB Accumulation (Denervation, diaphragm)	Buse et al. (1975)
Protein Synthesis (*in vitro*, *in vivo*)	
↑ ^{14}C-amino acid incorporation	Laurent & Sparrow (1977)
↑ ^{14}C-amino acid incorporation	Goldberg et al. (1975)
↑ ^{14}C-amino acid incorporation	Laurent et al. (1978)
↑ Ribosome activity	Turner & Manchester (1973)
↑ Cell-sap activity	Turner & Manchester (1973)
↑ Microsomal activity	Hamosh et al. (1967)
Nucleic Acid	
↑ RNA polymerase	Sobel & Kaufman (1970)
↑ ^{3}H-thymidine into DNA	Goldberg et al. (1975)
↑ DNA, RNA content	Various authors

reveal that amino acid transport is enhanced with increased work, and that there is an increased rate of incorporation of labeled amino acids into muscle proteins, including both the sarcoplasmic and fibrillar protein fractions. Furthermore, there are also changes in the metabolism and content of nucleic acids (RNA and DNA) and these favor increased

rates of protein synthesis and growth of muscle with higher work loads. Although the available data are more extensive than indicated here, it is clear that there are a complex series of changes in nucleic acid metabolism and in the protein synthetic machinery of muscle cells. These changes are regulated co-ordinately in response to altered work loads in this organ. However, the signals and primary events that lead to this complex series of changes in muscle protein metabolism remain to be determined (for example, see Young, 1981).

Changes in protein synthesis may also be accompanied by alterations in the rate of protein breakdown and in Table 5 a summary is given of the conclusions by various authors concerning the effects of exercise on protein breakdown. It

TABLE 5

SOME OBSERVATIONS ON THE EFFECTS OF EXERCISE ON PROTEIN BREAKDOWN

Muscle & Condition	Response of Breakdown	Author
Soleus-tenotomy	Reduced[+]	Goldberg (1969)
Soleus-stimulated, stretched	Reduced*	Goldberg (1979)
EDL-Immobilized, lengthened	Increased*	Goldspink (1977)
EDL-Denervated, stretched	Increased*	Goldspink (1978)
Diaphragm-Denerv.	Increased[+]	Turner & Garlick (1974)
ALD (Weighting)	No change[+]	Laurent & Sparrow (1977)
ALD (Weighting)	Increased[+]	Laurent et al. (1978)

[+]*In vivo* measurement. **In vitro* measurement.

is evident that there is little consistency among the various studies; some have concluded that breakdown does not change, others that it is decreased and still others that it is increased. The reasons for these variable conclusions may relate to the use of different models and/or the different methods used to estimate actual breakdown rates.

From these studies it is to be concluded that the rate of protein synthesis is increased, possibly accompanied by changes in protein breakdown, in response to a continuous period of increased muscular work, whether or not an actual hypertrophy of the muscle occurs. It is also evident that the changes in protein metabolism are associated with many of the various phases of amino acid utilization and protein anabolism. Overall these changes favor protein anabolism and, possibly, a more efficient use of dietary derived amino acids for incorporation into muscle proteins. Thus, an increased dietary protein requirement would not be predicted from these biochemical observations, except perhaps in relation to maintenance of a larger muscle mass. An argument against this, and as shown in Table 6, is that Dohm et al. (1977) have concluded that endurance training in rats results in an increased oxidation of leucine in muscle which is paralleled by an enhanced urea N output in trained rats as compared to untrained, pair-fed controls.

TABLE 6

EFFECT OF A SIX-WEEK ENDURANCE TRAINING ON AMINO ACID OXIDATION BY MUSCLE HOMOGENATES IN RATS[1]

Group	Body Wt. (g)	Urea N Excretion ($g/kg^{0.73}/d$)	$^{14}CO_2$ produced (nmol/min/g) from U-^{14}C-Leucine
Untrained	358	0.55	0.21
Pair-fed Untrained	353	0.57	
Trained	328	0.80	0.31

[1]From: Dohm et al. (1977).

In contrast to these extensive, although not entirely consistent, observations on the longer-term effects of repeated exercise on muscle protein and amino acid metabolism, the acute effects of exercise on muscle protein and amino acid metabolism have received less investigation. However, acute changes in physical activity do appear to influence muscle protein and amino acid metabolism. For example, as summarized in Table 7, Dohm et al. (1980) found a reduced rate of muscle protein breakdown when rats were forced to swim for 1h. Furthermore, Booth and Seider (1979) observed

TABLE 7

EFFECTS OF AN ACUTE BOUT OF EXERCISE (1 h swim) ON PROTEIN SYNTHESIS AND BREAKDOWN, USING A PERFUSED HEMICORPUS PREPARATION AND MUSCLE POLYRIBOSOMES[1]

Group	Synthesis		Breakdown
	^{3}H-Tyrosine incorporation[2] (nmole/h/mg protein)	^{14}C-leucine incorporation by polyribosomes (pmole/min/mg RNA)	Rate[3]
Rested	0.32	3.4	8.9
Exercised	0.26	2.5	13.8

[1]Summarized from Dohm et al. (Biochem. J. 188:255 (1980)).

[2]Soluble protein fraction of perfused muscle.

[3]µmol tyrosine release/h per hemicorpus.

an early decrease in protein synthesis when muscular activity was reduced by immobilization of the hind limbs in rats. Thus, muscle protein metabolism is responsive to brief as well as more sustained periods of altered physical activity.

Studies of Protein and Amino Acid Metabolism in Man:

Alterations in protein and amino acid metabolism in the muscles and whole body of rats would imply that exercise also affects the status of tissue and organ protein metabolism in human subjects. In addition to differences in the morphological and enzymatic characteristics of muscle fibers in subjects of varying fitness that were referred to above, studies have been made in intact human subjects of various aspects of protein, amino acid and N metabolism.

By measuring arteriovenous amino acid differences across the skeletal muscles of the leg and the splanchnic bed, Felig, Wahren and colleagues (Felig and Wahren, 1971, 1975; Ahlborg et al., 1974) have found that arterial levels of alanine increase during exercise (Table 8) and that this rise is associated with an increased muscle alanine output and enhanced uptake of this amino acid by the liver (Ahlborg et al., 1974). In contrast, as also shown in Table 8, there is

TABLE 8

ARTERIAL CONCENTRATION AND EXCHANGE OF AMINO ACIDS ACROSS THE LEG AND SPLANCHNIC BED AT THE END OF A 4 h BICYCLE EXERCISE AT ~30% VO_2 max[1]

Amino Acid	Arterial Concentration		Exchange			
	Rest	240min Exercise	Splanchnic		Leg	
			Rest	@240min	Rest	240min Exercise
	---μmol/l---		---μmol/min---			
Glycine	188	160	8.3	31.8*	-8	17.8*
Alanine	192	233	57.6	119.0*	-30.4	-95.4*
Leucine	126	151*	-2.2	-30.2*	-0.8	28.6*
Valine	242	243	-3.2	-31.6*	-0.6	43.4*
Isoleucine	60	81*	-1.0	-17.2*	-0.4	21.8*

[1]Partial summary of data of Ahlborg et al. (1974).

*Significantly different $p < 0.05$ from value at rest.

a selective uptake of branched chain amino acids by the exercising limb and an equivalent output from the splanchnic bed. This implies a possible increase in the rate of oxidation of these branched chain amino acids in the active muscles. Furthermore, because alanine is considered to be a vehicle for nitrogen transport from muscles to liver (e.g. Chochinov et al., 1978), where it may donate its N to urea (Lund, 1981), acute exercise would be expected to lead an increased rate of urea formation. This possibility will be discussed further below because of the implications for changes in the N balance and protein requirement.

There have been relatively few studies designed to quantify dynamic aspects of whole body amino acid metabolism in relation to exercise. Therefore, we have begun to explore this problem with the aid of stable isotope probes (e.g. Young and Bier, 1981a). Aspects of whole body amino acid metabolism are being examined in adult subjects while at rest and in response to a 2 h bicycle ergometer ride at an energy level equivalent to 55% of the $\dot{V}O_2$ max and our preliminary findings reveal a number of important points as follows: free amino acid levels in venous plasma showed little change in response to the exercise, although fatty acid and glycerol levels, reflective of increased adipose tissue lipolysis, rose during this time (Table 9). However, because plasma amino acid levels represent the balance between their rates of inflow and outflow in the circulation, measurements of these levels fail to indicate the possible changes in amino acid metabolism that occur during exercise. Therefore, using a 1-^{13}C-leucine as a stable isotope probe and applying the model described by Waterlow and colleagues (Waterlow, 1967; Waterlow et al., 1978), that we have used in previous studies on the adaptations of whole body amino acid metabolism to dietary factors (Young and Bier, 1981a, 1981b), we examined whole body leucine kinetics before and during a 2h period of moderate exercise. Our initial findings are summarized in Table 10 and they indicate that the rate of leucine oxidation is markedly increased during exercise in these adult subjects. This change in leucine oxidation, as determined in both trained and untrained subjects who had received only a small breakfast before exercise, was associated with a reduced rate of leucine incorporation into body proteins and a reduction in leucine flux, the latter indicative of a decline in the rate of total body protein breakdown. Using a similar approach, Rennie and co-workers (1981) have also observed an increased rate

TABLE 9

SELECTED PLASMA AMINO ACIDS AND BLOOD METABOLITES IN RELATION TO AN ACUTE PERIOD OF EXERCISE IN ADULT MEN[1]

Metabolite	Condition		Post-Exercise (15 min)
	Rest	Exercise (at 120 min)	
Amino Acids (mM)			
Alanine	410	384	325[b]
Glutamine	594	638	569[b]
Leucine	126	135	134
Isoleucine	65	61[a]	62[b]
Threonine	161	144[a]	129[b]
Urea (mg/dl)	16	15	16
Free fatty acid (mM)	0.42	1.47[a]	2.49[b]
Glycerol (mM)	0.11	0.44[a]	0.36[b]

[1]Unpublished data of Wright et al. (1981). Exercise was a bicycle ergometer ride for 2h at 55% VO_2 max.

[a]Significantly different from value at rest.

[b]Significantly different from value at 120' exercise.

of whole body leucine oxidation although they did not find a reduction in total body protein breakdown. These investigators have concluded, however, that the rate of muscle protein breakdown is reduced during exercise (Millward et al., 1981).

Relation of Changes in Metabolism to Nutritional Requirements

In view of the enhanced rate of leucine oxidation in exercised subjects ,it is instructive to consider how this response relates to the substantial increase in total energy expenditure under these conditions. Thus, although the oxidation of leucine and probably other amino acids (e.g.White and Brooks, 1981) is increased with exercise, we have calculated that the contribution made by total amino acid catabolism to the total energy expenditure may actually be lower,

TABLE 10

PARAMETERS OF WHOLE BODY LEUCINE KINETICS IN SUBJECTS AT REST AND DURING 2 h EXERCISE AT 55% $\dot{V}O_2$ max[1]

Parameters	Condition		P
	Rest	Exercise	
Leucine Flux	120.4±6.2(15)[2]	97.0±7.13(15)	< 0.001
Leucine Oxidation	14.8±1.3(8)	46.1±9.7(8)	< 0.01
Leucine Incorporation into protein	113.2±5.4(8)	58.2±9.5(8)	< 0.01

[1]Unpublished data of Wright, Evans, Phinney and Young (1981).
[2]Values are $\mu mole.kg^{-1}h^{-1}$. Mean ± SEM. Number of subjects in parentheses.

in relative terms, during exercise than at rest (Table 11). These data are entirely consistent with the notion that carbohydrate and fats account for the major contribution to the rise in oxidative catabolism associated with exercise, as discussed above.

On the other hand, the rise in leucine oxidation may have considerable significance for the economy of N metabolism and the requirements for protein and indispensable amino acids. This possibility is further underscored when it is considered that a major source of the N of the alanine liberated at an increased rate from exercised muscle (Ahlborg et al., 1974) might arise from leucine (e.g. Goldberg and Chang, 1978) and that the alanine nitrogen is subsequently transferred to urea via urea enzyme cycle activity in the liver. An evaluation of this scheme requires direct estimates of urea synthesis in the exercised subject and these have not yet been performed. However, recent studies, expecially those of Lemon and Mullin (1980) showing plasma urea changes during exercise (Fig. 2) are highly suggestive of enhanced rates of urea formation during exercise and, furthermore, that a prior period of low dietary carbohydrate intake accentuates the change in

TABLE 11

CONTRIBUTION OF PROTEIN OXIDATION[a] TO TOTAL ENERGY EXPENDITURE[b] (%) AT REST AND DURING 2 HOURS OF EXERCISE AT 55% VO_2 max[1]

Subjects	No.	Pre-Exercise	During Exercise
Untrained	3	14.1	4.8
Trained	5	12.2	2.9

[1]Unpublished data of Wright et al. (1981).

[a]Based upon leucine content in whole body protein of 590 μmol g and mean values for leucine oxidation of 14.8 $\mu mol.kg^{-1} h^{-1}$ (pre-exercise) and 46.1 $\mu mol.kg^{-1}h^{-1}$ (during exercise).

[b]Total energy expenditure derived from indirect calorimetry using measured values of VO_2 and "R" during a 2 h period.

plasma urea. The findings of Refsun and Stromme (1974) and those of other investigators, reviewed by Lemon and Nagle (1981), further suggest an enhanced output of urinary urea during brief or prolonged periods of physical activity. Thus, it would be instructive to quantify directly the rate of urea production, using ^{15}N or ^{13}C urea, during exercise in adult subjects in an attempt to improve our understanding of the relationships between the changes in interorgan amino acid flow, discussed earlier, and urea metabolism during and immediately following periods of exercise of varying intensity and duration.

Because urea accounts for the major proportion of total urinary N excretion in well-nourished subjects, changes in urea production with exercise should be reflected by changes in body N balance. Indeed, there is evidence that the latter becomes more negative when moderate exercise is required in healthy men receiving a generous intake of protein and adequate energy (Gontzea et al., 1974; 1975) (e.g. Fig. 3). Hence, it can be suggested that moderate to heavy exercise might increase the requirement for total N, at least during the initial weeks of a program of moderate physical activity. This increased requirement appears even more likely if the increased losses of N via sweat are also taken into account (e.g. Lemon and Mullin, 1980).

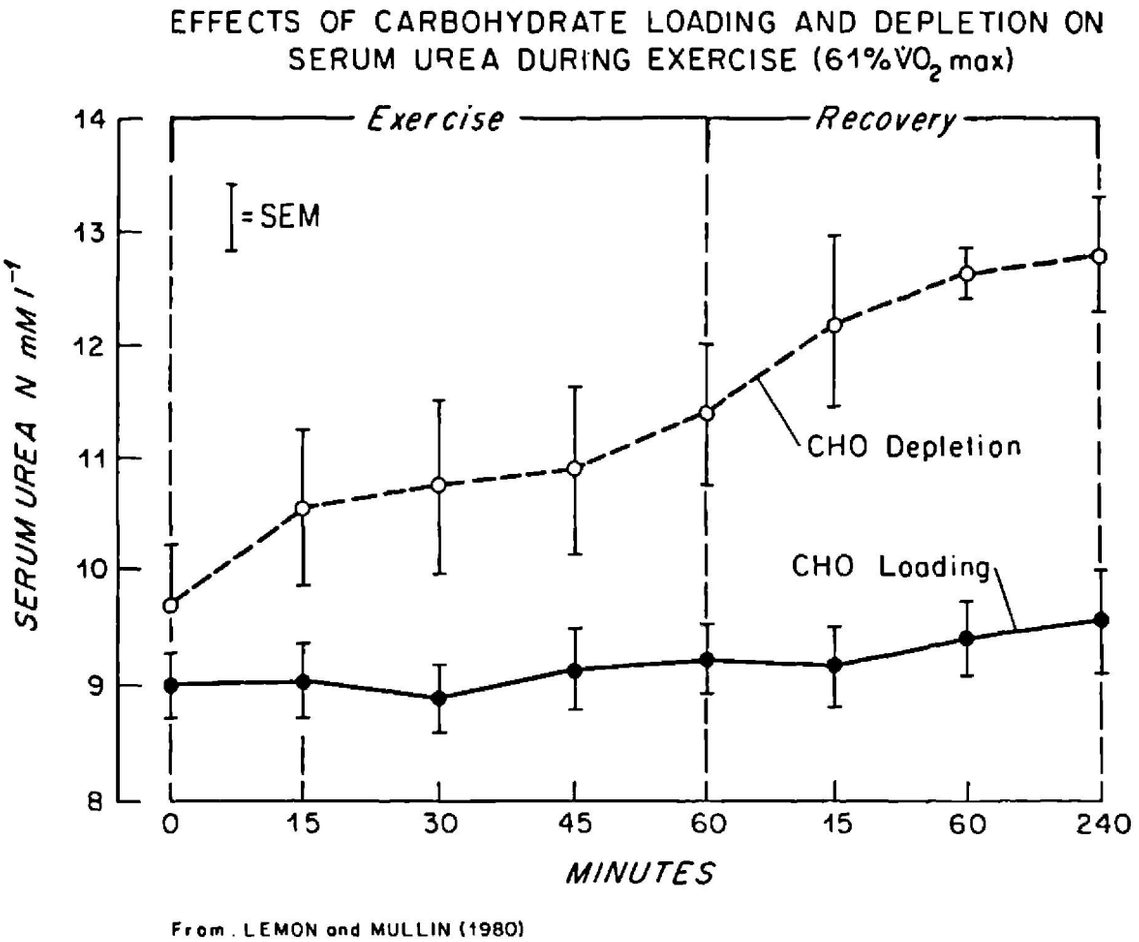
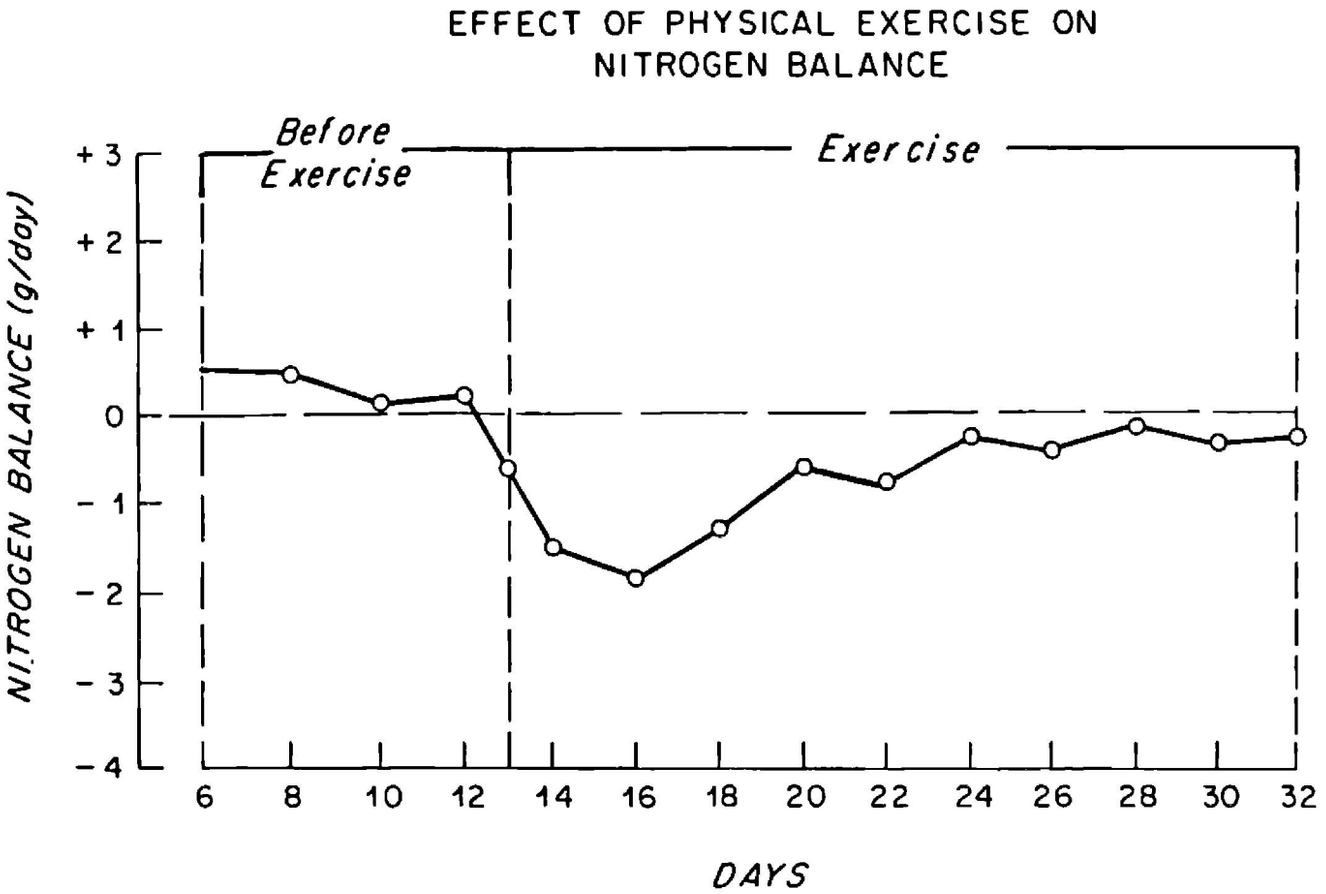


Fig. 2. Change in serum urea concentration during and following recovery from exercise (for 60 min at 61% $\dot{V}_{O_2}$ max on a bicycle ergometer) in adult male subjects who had received previously a high carbohydrate diet (CHO-loaded) for 3 days or who were carbohydrate depleted. Drawn from Lemon and Mullin (1980).

There have been an insufficient number of studies to examine this issue in much greater depth but we have shown, as depicted in Figure 4, that a period of training of isometric exercise in healthy adult men results in a reduction in body potassium, and probably body cell mass, when the test subjects consume a diet approximating the FAO/WHO (1973) dietary protein allowance. In contrast these changes did not occur when subjects were first adapted to a diet providing a more generous intake of 1 g egg protein/kg/day (Torun et al., 1977). Furthermore, a change in protein requirement as a consequence of exercise is also suggested by the data of Yoshimura et al. (1980). These investigators have shown that during training to strenuous physical exercise, the content of hemoglobin in circulating blood de-



From GONTZEA *et al* (1975)

Fig. 3. Mean nitrogen balance for 12 healthy young men before and during a 3-week period of increased physical activity (9.9 Kcal/min for 6 of each 20 min periods per day). Subjects received 1 g protein/kg/day (35% from animal origen). Drawn from Gontzea et al. (1975).

creased when subjects received a diet containing about 1.3 to 1.5 g protein/kg/day, but that this did not occur when the level of protein intake was 2.5 g/kg/day. These observations were interpreted by Yoshimura et al. (1980) to indicate that a high intake protein is required during the course of physical training.

In spite of the early work suggesting the lack of an effect of physical exercise per se on the protein requirement of the host (see FAO/WHO, 1973),the more recent studies referred to here indicate that intermittent bouts of exercise disturb the nitrogen metabolism of the host and that the biochemical observations suggest it is likely that the requirement for total nitrogen and/or for specific dispensable amino acids is increased above that of the sedentary

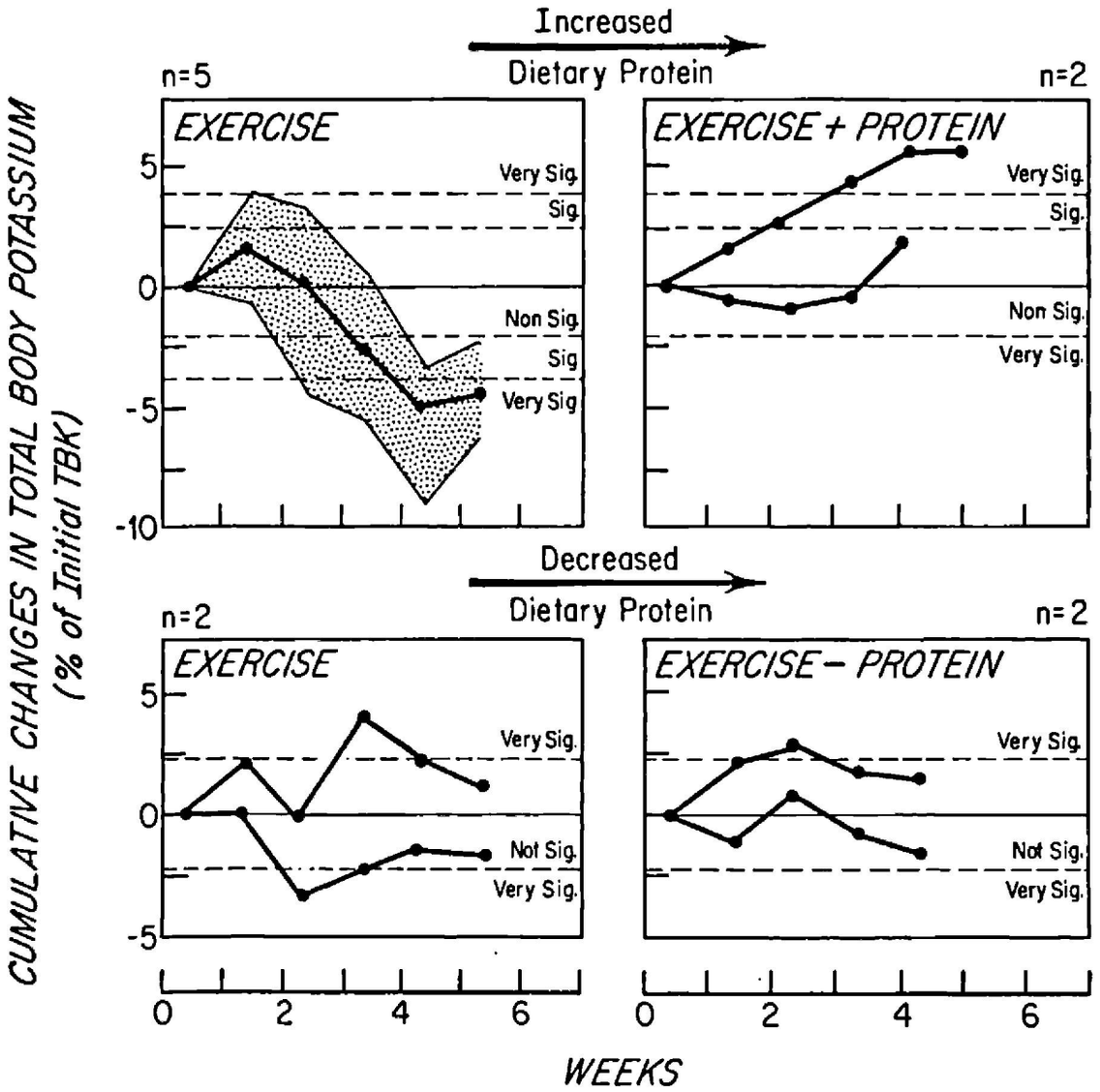


Fig. 4. Weekly mean cumulative changes in total body potassium (TBK) in young men, receiving 0.5 or 1.0 g egg protein/kg/day, while performing a 75 min isometric exercise program daily for 4 to 6 weeks. Drawn from Torun et al., (1977).

individual. This possibility can be examined further in reference to our findings on the rate of whole body leucine oxidation during exercise. Thus, as shown in Table 12, the oxidation of leucine during two hours of moderate exercise on a bicycle ergometer represents an amount equivalent to the upper range of the estimated dietary requirement for this amino acid (FAO/WHO, 1973). Recent studies from our laboratory have shown that the requirement for leucine may

TABLE 12

LEUCINE OXIDATION[1] DURING EXERCISE: ITS RELATIONSHIP TO REQUIREMENT

Status	Rate	Total Quantity
Rest: 2 hrs (recumbent)		
Leucine Oxidation	14.8μmol.kg^{-1}h^{-1}	2087μmol = 274 mg
Leucine Requirement	14.0 mg.kg^{-1}d^{-1}	987 mg
Oxidation: Percent of Requirement		28
Exercise: 2 hrs (55% $\dot{V}O_2$ max)		
Leucine Oxidation	46.1 μmol.kg^{-1}h^{-1}	6500μmol = 853 mg
Leucine Requirement		987 mg
Oxidation: Percent of Requirement		86

[1]Untrained subjects (mean wt. 70.5 kg).

[2]FAO/WHO (1973); WHO Tech. Rept. Ser. No. 522, World Health Organization, Geneva, Switzerland.

be estimated from the rate of whole body leucine (Young and Bier, 1981a,b). Hence, from the results of our recent studies, and assuming that there is not an adaptive reduction in the rate of leucine oxidation during the post-exercise period, in comparison with that for non-exercised subjects, the minimum physiological requirement for this amino acid would be higher for physically active than for sedentary subjects. Of course, another possibility that must be considered in the interpretation of these data is that the rate of leucine oxidation during exercise may be determined, in part, by the previous dietary intake level of leucine. It is possible that subjects who had been adapted to a lower

protein or essential amino acid intake may not show the marked increase in leucine oxidation that was observed in our subjects who had received a generous protein intake for a number of days prior to the exercise test. Furthermore, because leucine oxidation rates, during both the post-absorptive and absorptive phases of amino acid metabolism, fall when the intake of dietary leucine or protein is lowered (Motil et al., 1981), it would also be of interest to determine whether a period of exercise induces a significant increase in leucine oxidation in subjects adapted to a diet that provides leucine at levels approximating current estimates of the requirement for this amino acid in adults. If an increase in leucine oxidation was observed in trained subjects under these dietary conditions, this would provide convincing evidence that the physiological requirement for this amino acid is determined, in part, by physical activity per se.

Finally, it is important to emphasize that the metabolism of leucine is closely associated with the skeletal muscles (e.g. Miller, 1962). Although it is tempting to interpret a change in leucine oxidation during exercise as indicative of a general increase in the oxidation of indispensable (essential) amino acids, it will be important to determine directly whether exercise alters significantly the rate of oxidation of amino acids that are predominantly catabolized in the liver, such as lysine (Hutzler and Dancis, 1975) and tyrosine (Miller, 1962).

Comment on Chronic Patterns of Physical Activity.

In the foregoing section we have considered changes in human body protein and amino acid metabolism that occur in response to brief periods of exercise. We have argued that the metabolic findings suggest increased amino acid requirements in subjects who are physically active. Here, the effects of more continuous patterns of physical activity should also be mentioned.

Studies with animal models, reviewed above, show that continuous periods of work induce muscular hypertrophy and that there is an overall anabolic effect on body protein metabolism and this is accompanied by an improvement in somatic growth (e.g. Boreer, 1980). In contrast, muscle

atrophy is a characteristic of hypokinesia, arising from restricted movement (e.g. Booth, 1977) and the findings of Musacchia et al. (1980) (Figure 5), based on measurement of

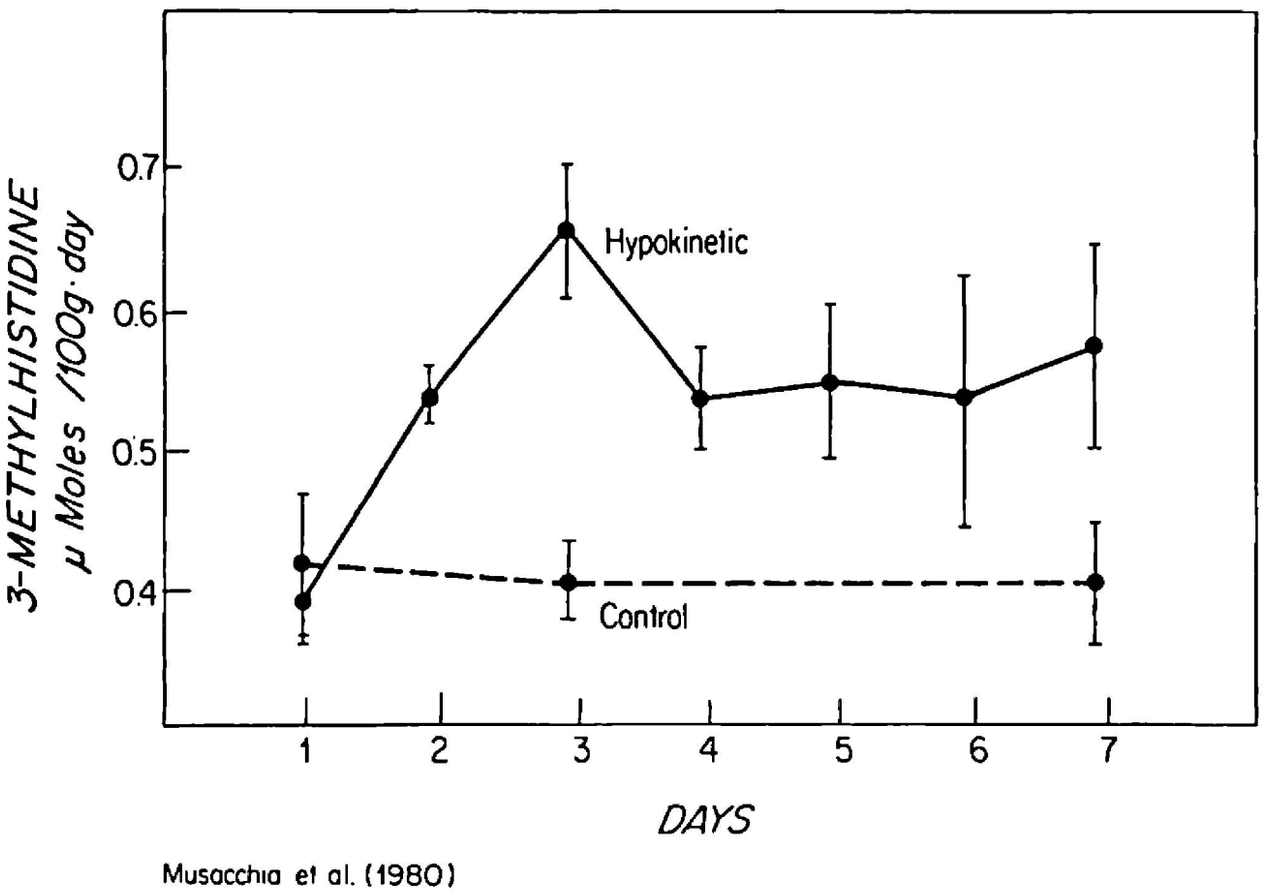


Fig. 5. Change in urinary 3-methylhistidine excretion during 1 week of hypokinesia in young rats (170-190 g body weight). Drawn from Musacchia et al. (1980).

the output of N^{τ}-methylhistidine (3-methylhistidine) in the urine suggest, that with the loss of muscle mass and increased excretion of urea, there is an increased rate of muscle protein catabolism in hypokinetic rats. Thus between these extremes in muscular activity there is a pattern of physical activity that is consistent with and necessary for maintenance of an adequate state of body protein and amino acid metabolism and function. Although this pattern cannot be defined in precise quantitative terms, studies carried out at INCAP by B. Torun and F. Viteri (manuscript in preparation) in young children recovering from protein-energy malnutrition reveal the beneficial effects of con-

tinued mild exercise on the utilization of dietary protein.

In these studies a group of children, aged 2-4y, under treatment for protein-energy malnutrition, was stimulated to be more physically active through a daily program of games that required mild to moderate levels of energy expenditure. Measurements were made of growth and of body energy and metabolic nitrogen balances and results compared with those obtained in a similar group of children treated in the traditional manner at INCAP. A partial summary of these data is given in Table 13 and the changes in linear growth

TABLE 13

ENERGY AND NITROGEN BALANCES AND CREATININE EXCRETION DURING RECOVERY FROM PROTEIN-ENERGY MALNUTRITON, IN CHILDREN DURING VARIOUS PHYSICAL ACTIVITIES[1]

	Group	
	Active	Control
Energy Balance ($kcal\ kg^{-1}day^{-1}$)		
Net intake	119 ± 4[2]	120 ± 3
Expenditure	94 ± 9**	74 ± 8
Retention	26 ± 9**	46 ± 8
Retention per g weight gain	5.0 ± 3.3**	9.3 ± 2.9
Nitrogen Balance ($mg\ kg^{-1}day^{-1}$)		
Intake	398 ± 8	402 ± 11
Retention	145 ± 37	139 ± 30
Creatinine (mg/day)		
Increment in six weeks	41.7 ± 13.4	31.0 ± 11.6

[1]Unpublished data of Torun and Viteri (INCAP, 1981).

[2]Mean ± SD: = 66-67 (active) and 54-63 (control)

**Significantly different from control group ($p < 0.01$).

for the two groups during the course of the study are illustrated in Figure 6. These balance and anthropometric data

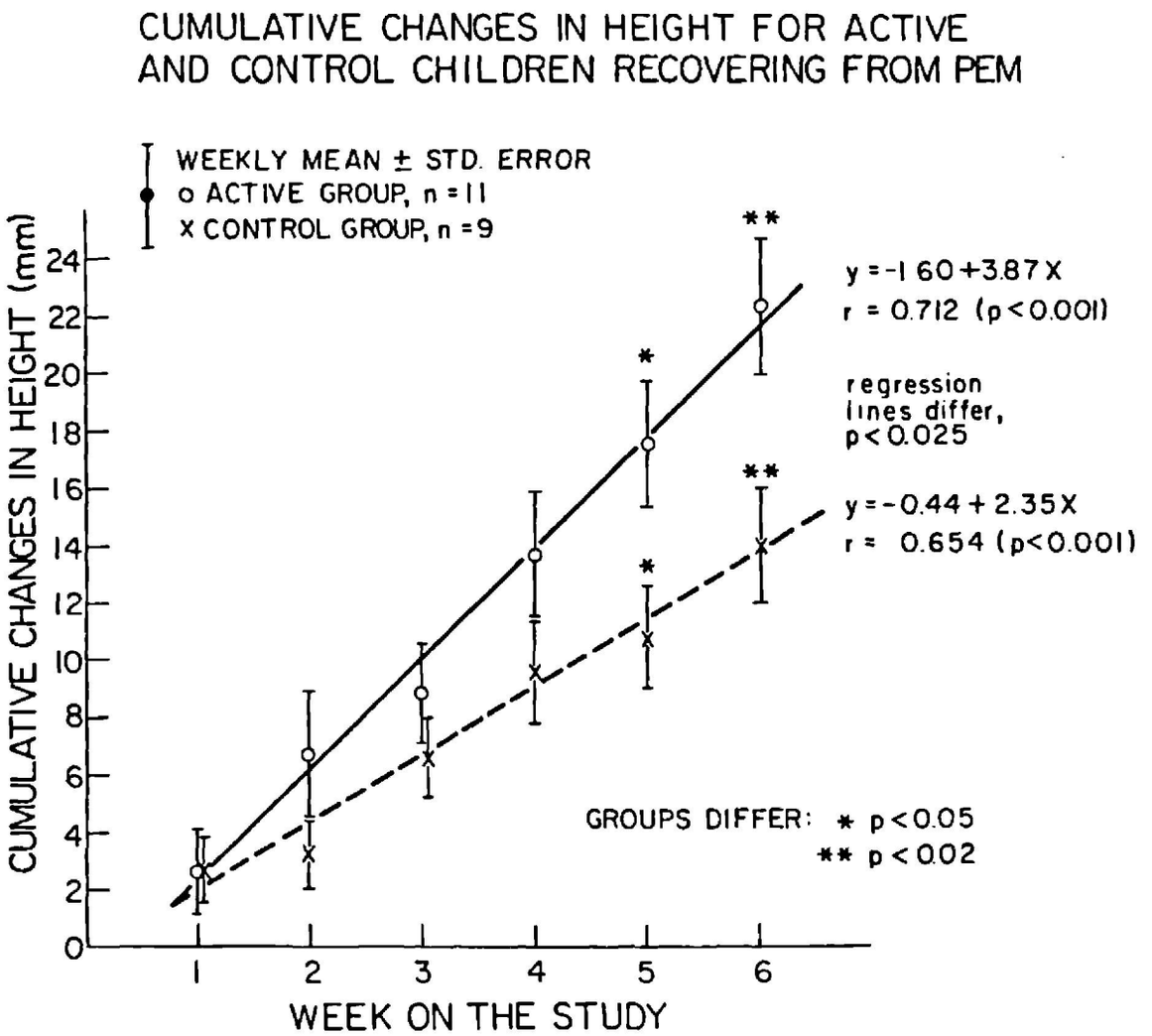


Fig. 6. Linear growth in a group of physically active children, as compared with a control group, during recovery from protein-energy malnutrition (PEM). Unpublished data of B. Torun and F. Viteri (INCAP).

indicate that the more active children grew better in height and in lean body mass. Thus, the utilization of dietary protein and energy for growth was more efficient in the more active children. From these results it is to be concluded that moderate systemic exercise had a growth-enhancing effect and a favorable impact on the utilization of dietary protein. Furthermore, it seems reasonable to expect that this would also apply to well-nourished subjects, both

children and adults.

SUMMARY AND CONCLUSIONS

In this brief and selective review we have discussed recent observations that concern the relationships between physical activity and protein and amino acid metabolism, with particular reference to the requirement for dietary protein. The major focus of our attention has been given to the effects of infrequent, moderate to heavy, exercise on human protein and amino acid metabolism. The metabolic picture that is now emerging leads to the strong speculation that moderate and heavy exercise in adult subjects results in an increase in the minimum physiologic requirement for specific indispensable amino acids and/or total protein. This contrasts with the prevailing view that physical activity per se does not result in an increased need for dietary protein. Because heavy manual labor is characteristic of many of the populations in the developing regions of the world and also because of the growing interest by the public in the United States and other technically advanced nations in physical exercise as a means of improving health and well-being, it would be prudent to undertake a more careful and comprehensive exploration of the effects of physical activity, of various types, intensity and duration, on the amino acid and protein needs of human subjects of all ages.

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