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Effects of 30 days of undernutrition on plasma neurotransmitter precursors, other amino acids, and behavior

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As part of a 30-day field exercise, 17 soldiers consumed a calorie-deficient, lightweight ration (1946 kcal/day) while 17 others consumed a calorie-adequate control ration (2782 kcal/day). Mean energy expenditure for both groups was 3200 to 3300 kcal/day. Plasma amino acid levels were assessed at the start, after 14 days, and at the completion of the study. Behavioral testing was conducted at the start and completion of the study. Alanine, which is used for gluconeogenesis, fell from 389 to 323 nmol/mL over the trial among those who consumed the calorie-deficient diet, whereas it increased in the control group. Plasma tyrosine also fell significantly, from 70 to 52 nmol/mL, as did tryptophan (from 62 to 55 nmol/mL) in the calorie deficient group. The ratio of tyrosine to other large neutral amino acids, an indicator of tyrosine transport to the brain, also fell in the deficient group (from 0.104 to 0.084). At the completion of the study, plasma tryptophan ratio was significantly lower in the calorie deficient group (0.091) compared with the control group (0.103). Decrements in tryptophan, but not tyrosine, ratio were associated with impairments in simple and choice visual reaction time ($r = -0.4415$, $P = 0.009$; $r = -0.4029$, $P = 0.018$, respectively). Therefore, changes in plasma amino acids occurring during a controlled form of undernutrition can be substantial; some of these alterations may be related to the functional consequences of undernutrition. (J. Nutr. Biochem. 8:119–126, 1997.) © *Elsevier Science Inc. 1997*

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Introduction

Substantial reductions in plasma amino acid concentrations have been documented in obese men deprived of all food for long periods of time, and among individuals with severe Kwashiorkor[1] or protein-calorie malnutrition.[2] Low levels of most plasma amino acids have also been observed in obese individuals consuming protein-sparing modified fast diets.[3] Severe long-term starvation appears to reduce plasma concentrations of many amino acids, particularly essential ones, with the severity of the decline related to the degree and duration of the deficient diet.[2,4,5] Less severe forms of malnutrition have more variable effects on amino acid levels, with the nature and extent of the changes related to the type of deficiency.[1,4–6] The behavioral consequences of semistarvation include apathy, irritability, and depression; however, only small decrements in cognitive and psychomotor performance are typically observed.[7,8] The physiologic factors responsible for these behavioral decrements are not known.

We monitored changes in plasma amino acid levels and psychomotor performance as part of a larger field study of soldiers who received either a balanced, but calorie deficient, diet or standard field rations for 30 days.[9] The study was conducted to test a lightweight (0.45 kg/day), compact U.S. military field ration (Ration, Lightweight—30 days) under development. The protype ration provided approximately 2000 kcal/day and was vitamin and mineral fortified. It was formulated to provide the sole source of food for up to 30 days for soldiers operating without logistic support. We examined changes in plasma amino acids and psychomotor performance occurring among the participants in an attempt to document and relate these changes.

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Table 1 Nutrient composition of the FN and LW group diets[1]

Nutrient	FN Group	LW Group
Calories, kcal	4023	1976
Protein, g	151	68
Fat, g	160	103
Carbohydrate, g	495	194
Water, g	498	22
Vitamin A, mcg RE	2040	800
Vitamin D, mcg	NA[2]	14.8
Vitamin E, mg TE	NA[2]	124
Ascorbic acid, mg	317	106
Thiamin (B_1), mg	7.1	2.2
Riboflavin (B_2), mg	3.1	2.1
Niacin, mg NE	38.1	27.0
Vitamin B_6, mg	5.6	2.2
Folacin, mcg	NA[2]	0.4
Vitamin B_{12}, mcg	NA[2]	3.0
Calcium, mg	1057	890
Phosphorous, mg	2039	1248
Magnesium, mg	404	359
Iron, mg	25	19
Zinc, mg	NA[2]	15.4
Iodine, mcg	NA[2]	NA[2]
Sodium, mg	6889	2915
Potassium, mg	4103	1887
Pantothenic acid	NA[2]	5.9
Manganese, mg	NA[2]	2.2
Copper, mg	NA[2]	0.7

[1]Quantities of nutrients are for 1 day's ration.
[2]Nutrient values are not available.

Methods and materials

Subjects

The test subjects were 34 men from a U.S. Army Special Forces Unit based at Fort Devens, MA. They averaged 27 ± 4.7 years of age, 203 ± 7.1 cm in height, and they weighed 77.1 ± 8.3 kg. Their mean body fat, as determined by hydrostatic weighing, was 16 ± 4.5%. They were all in good health as determined by physical examinations, medical histories, and laboratory tests. Before enrollment in the study, subjects were briefed on its purpose, design, and the risks involved. All who participated gave their informed consent to a protocol approved by Human Use Review Committees. The health of each subject was monitored by a physician during the study. Subjects were free to withdraw from the study at any time.

Before the start of the study, two teams of 17 men each were established. One team was designated as an experimental, light-weight (LW) ration group, and the other a fully nourished (FN) group.

Diets and nutrient intake

The LW ration macronutrient composition was 39% carbohydrate, 47% fat and 14% protein (*Table 1*). It consisted mainly of specially formulated high-density, nutrient-rich foods including cereal bars; dehydrated entree bars; beverage bars; bread-like bars; beef jerky; and dairy, dessert, and fruit bars. The FN ration group consumed the standard U.S. military field ration (the Meal Ready to Eat [MRE]) which, for the most part, contained conventional food-stuffs. The macronutrient composition of the MRE, Version VI, ration was 49% carbohydrate, 36% fat, and 15% protein. A detailed description of the macro- and micronutrient composition of the rations is in *Table 1*.[9]

Each day of the study the volunteers recorded all the food they consumed in individual log books. Mean daily calorie and macro-nutrient consumption per subject for the entire 30-day test period were calculated (*Table 2*).[9] An estimate of energy requirements was made from caloric intakes and body weight loss of the soldiers. The energy requirements for the FN group, based upon an average daily caloric intake of 2782 kcal and a 30-day weight loss of 1.8 kg, was 3250 kcal. The estimated daily requirement for the LW group, based upon an average daily caloric intake of 1946 kcal and a 30-day weight loss of 5.13 kg, was 3275 kcal. These estimates of energy expenditure were confirmed by measurements made on a subset of each group using the doubly labeled water method.[10]

Table 2 Thirty-day mean (± SEM) daily nutrient intakes of the FN and LW groups

Nutrient	FN Group	LW Group
Energy, kcal	2782 ± 42	1946 ± 15
Protein, g	112 ± 2	64 ± 1
Carbohydrate, g	318 ± 6	197 ± 2
Fat, g	119 ± 2	100 ± 1

Operational scenario and activity patterns

During the study both groups engaged in similar types of light and moderate physical activity with a few interspersed periods of heavy exertion. All subjects lived out of their packs for the entire time (25 days) they were in the field. However, before and after the field exercise, a total of 5 days were spent in garrison. The field portion of the study was conducted in Northern Vermont during late September and October in temperate climatic conditions. Temperatures during the test usually ranged between 4 to 11°C, although freezing temperatures and snow were occasionally encountered. The test site was in a remote location. The soldiers were not permitted to forage or purchase food. While in garrison, the soldiers were isolated from all possible sources of supplemental food.

To verify that the extent and patterns of activity of the two groups were comparable, a daily log of activities was recorded by a member of each unit. Analysis of these records indicated that the activity patterns of the two groups were similar.

Changes in body composition

Hydrostatic weighing was used to assess body composition of the subjects before and after the field training exercise. Subjects reported to a laboratory for underwater weighing in a well-hydrated, fasted condition. Residual lung volume was estimated using the oxygen rebreathing technique.[11] Seven to ten trials were conducted to obtain an accurate measure of hydrostatic weight.[12] Body density determined from underwater weight was converted into percent body fat using a standard formula.[13] The FN group lost 1.5 ± 1.3 kg of body fat and gained 0.2 ± 1.3 kg of fat free mass. The LW group lost both 2.5 ± 1.4 kg of body fat and 1.5 ± 1.7 kg of fat free mass. When individuals move from indoor living conditions to the field, some loss of body weight is to be expected, even when adequate food supplies are available. However, the loss of a significant amount of fat free mass, which occurred only in the LW group, indicates their diet was calorically inadequate.

Urine ketone levels

Every day, urine samples were tested for ketones with urine dipsticks (N-multistix, Ames Division, Miles Laboratories) on the first void in the morning following an overnight fast. Only small

amounts of ketones were detected in the urine of the FN group (1 to 3 mg/dL per day) as would be anticipated when energy intake and expenditure are in rough balance. However, somewhat higher levels of ketones were present in the LW group, generally 3 to 6 mg/dL per day, suggesting increased use of fat stores.

Plasma amino acid levels

Venous blood samples for determination of amino acid levels were drawn on day 0 (the day before subjects began the diets), day 14, and day 31 at 0600 to 0800 hr after an overnight fast. Plasma was obtained from centrifuged whole blood then frozen and stored at −30°C for later analysis. Plasma amino acid levels were determined in deproteinized samples by HPLC (High Performance Liquid Chromatography)[14] with a fluorometric detector (Beckman HPLC system, Model 334). Tryptophan concentration was determined using the fluorometric technique of Denckla and Dewey[15] as modified by Lehmann.[16] The ratios of tryptophan and tyrosine to the other large neutral amino acids (LNAAs), valine, methionine, leucine, isoleucine, phenylalanine, and tyrosine or tryptophan, were derived.

Reaction time performance tests

Two reaction time tests,[17] shown previously to be sensitive to nutritional variables,[18–20] were administered to assess psychomotor performance. Both tests were presented on portable computers (GRiD Compass II, GRiD Systems Corporation, Mountain View, CA USA) and both measured reaction time in milliseconds. The simple visual reaction time task consisted of 300 trials of a visual cue presented in the center of the computer display; the subject was instructed to respond as quickly as possible using the space bar. Choice visual reaction time measured more sustained performance by presenting a variable visual cue, which randomly appeared in one of four locations on the computer display for 500 trials. The subject was instructed to respond as quickly as possible, but was also required to accurately indicate the location of the variable cue by pressing one of four adjacent cursor keys. Tests were given on day 0 and day 31, in conjunction with blood draws, between 0900 and 1100 hr.

Statistical analyses

Plasma amino acid levels were compared by a two-way ANOVA with repeated measures. Diet (LW versus FN) was a between-subject variable, whereas time of measurement (day 0, 14, or 31) was a within-subject variable. Separate one-way ANOVAs were then used to compare mean plasma amino acid concentration within each diet across time, and within each time between diets. Linear regressions, with changes in amino acid ratios (tryptophan or tyrosine over the sum of the other LNAAs) as predictor variables and changes in reaction time (simple and choice) as dependent measures, were used to determine if precursor availability was related to performance changes over the course of the study.

Results

Substantial alterations in the plasma levels of various amino acids were observed in the LW ration group (*Table 3*). Alanine levels dropped substantially over the course of the

Table 3 Mean (± SEM) plasma amino acid concentrations (nmol/mL) and selected ratios

Amino Acid	FN day 0	FN day 14	FN day 31	LW day 0	LW day 14	LW day 31	ANOVA
			Neutral Amino Acids				
Glycine	238.68 (9.98)	291.21 (8.46)	262.82 (6.29)	235.16 (6.66)	282.13 (10.69)	285.45 (9.72)	T,I
Alanine	340.44 (16.25)	367.64 (12.88)	393.36 (16.33)	389.35 (15.49)	369.69 (10.77)	322.74 (11.01)	I
Valine	253.61 (9.82)	213.59 (5.89)	220.92 (9.04)	282.09 (12.24)	213.86 (4.85)	242.82 (6.16)	D,T
Methionine	26.94 (1.97)	26.62 (0.90)	25.39 (0.83)	26.26 (1.54)	22.95 (0.96)	26.90 (0.98)	—
Isoleucine	72.82 (4.10)	71.39 (2.28)	67.88 (2.55)	78.17 (3.93)	53.28 (1.68)	75.80 (1.90)	T,I
Leucine	144.54 (6.28)	134.04 (2.70)	136.49 (4.15)	159.21 (6.78)	117.06 (2.92)	152.03 (2.96)	T,I
Tyrosine	59.24 (4.10)	54.95 (1.89)	55.75 (2.28)	69.64 (3.91)	50.06 (2.65)	51.51 (1.96)	T,I
Phenylalanine	58.18 (2.26)	56.76 (1.33)	57.24 (1.15)	61.00 (2.11)	50.47 (1.65)	60.76 (1.66)	T,I
Tryptophan	54.38 (2.02)	52.22 (1.42)	57.44 (1.57)	62.35 (2.18)	50.41 (1.25)	55.22 (1.74)	T,I
			Precursor Ratios				
Tryptophan ratio	0.090 (0.004)	0.094 (0.003)	0.103 (0.003)	0.093 (0.003)	0.100 (0.003)	0.091 (0.003)	I
Tyrosine ratio	0.097 (0.005)	0.100 (0.004)	0.097 (0.003)	0.104 (0.005)	0.098 (0.004)	0.084 (0.003)	T,I
			Basic Amino Acids				
Histidine	146.29 (6.39)	131.28 (2.83)	126.66 (5.38)	147.53 (5.10)	139.12 (2.94)	137.50 (2.72)	T
Lysine	200.78 (6.81)	187.04 (9.09)	184.06 (8.02)	201.91 (8.45)	199.49 (7.03)	207.08 (7.14)	—
Arginine	102.61 (5.00)	128.76 (3.53)	123.01 (6.46)	100.40 (3.94)	114.08 (3.00)	112.89 (5.28)	D,T

Significant factors on ANOVA ($P < 0.05$): D = diet; T = time; I = diet × time interaction.

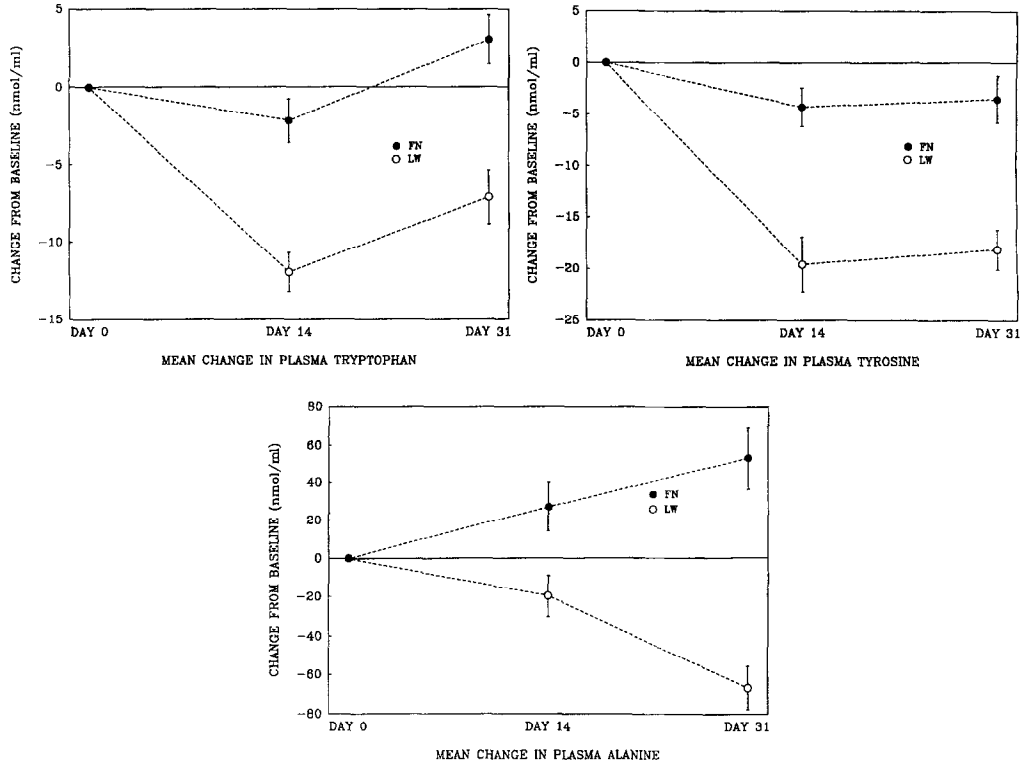

Figure 1 Mean (±SEM) change from baseline of plasma tryptophan, tyrosine, and alanine concentrations in the fully nourished (FN) and lightweight (LW) groups over the course of the study.

study in the LW ration group, but rose consistently in the FN group (*Figure 1*) as demonstrated by a significant diet × time interaction on the overall ANOVA ($F(2, 64) = 10.00$, $P < 0.0002$). The one-way ANOVAs verified this pattern of change. There were significant differences over time for each individual diet ($F(2, 64) = 6.46$, $P = 0.003$ for the LW group; $F(2, 64) = 3.86$, $P = 0.026$ for the FN group) and between diets at day 0 and 31 ($F(1, 32) = 4.74$, $P = 0.037$ and $F(1, 32) = 12.86$, $P = 0.001$, respectively). The change within a group may be the most reliable index of treatment effects for this variable, because there was a significant difference between groups in plasma alanine at the start of the study (*Figure 1*).

There were also significant changes attributable to diet among the straight-chain large neutral amino acids. Plasma tyrosine was stable in the control group, but decreased significantly in the LW ration group (*Figure 1*) as indicated by a statistically significant interaction factor on the two-way ANOVA ($F(2, 64) = 5.24$, $P < 0.01$). The one-way ANOVAs confirmed these findings; plasma tyrosine fell significantly over time in the LW group ($F(2, 64) = 17.74$, $P < 0.0001$), but not in the FN group ($F(2, 64) = 0.96$, $P = 0.39$). There were no significant between-group differences at any of the test times on the one-way ANOVAs. Tryptophan increased by the end of the study in the control subjects, but was lower in the LW group, especially two weeks into the diet (*Figure 1*). There was a main effect of time ($F(2, 64) = 14.32$, $P < 0.0001$) and a significant interaction ($F(2, 64) = 9.06$, $P = 0.0003$) on the two-way ANOVA for tryptophan. The one-way ANOVAs for tryptophan, which examined change over time within each diet group, were also both significant ($F(2, 64) = 3.74$, $P = 0.03$ within the FN group and $F(2, 64) = 19.64$, $P < 0.0001$ within the LW group).

Both tyrosine and tryptophan are neurotransmitter precursors and their transport into the brain depends on their plasma concentration relative to that of the other LNAAs in the plasma.[21] Therefore, the ratios of both tyrosine and tryptophan to the sum of the other LNAAs were derived (*Table 3*). Tyrosine ratio fell over time in the LW ration group and was stable in the control group (*Figure 2*). Tryptophan ratio increased over measurement sessions in the control group and during week two for the LW ration group, but by the end of the study was only marginally lower among soldiers receiving the LW ration (*Figure 2*). Two-way ANOVAs indicated significant interaction effects for both tyrosine and tryptophan ratio and a main effect of time for tyrosine ratio. In the post-hoc ANOVAs, tyrosine ratio fell significantly in the LW ration group ($F(2, 64) = 12.36$, $P < 0.0001$), but not among the FN group ($F(2, 64) = 0.27$, $P = 0.76$). When contrasts were conducted at each time there was only a significant difference between diets for tyrosine ratio at the final period ($F(1, 32) = 8.55$, $P = 0.01$). Tryptophan ratios varied significantly over time ($F(2, 64) = 6.28$, $P = 0.005$) within the FN group and the LW group ($F(2, 64) = 3.24$, $P = 0.05$). When comparisons were made at each time between the diet groups for tryptophan ratio, the only significant difference was at the final period ($F(1, 32) = 8.75$, $P = 0.01$), with tryptophan ratio lower in the LW group.

Another straight-chain LNAA, phenylalanine, was un-

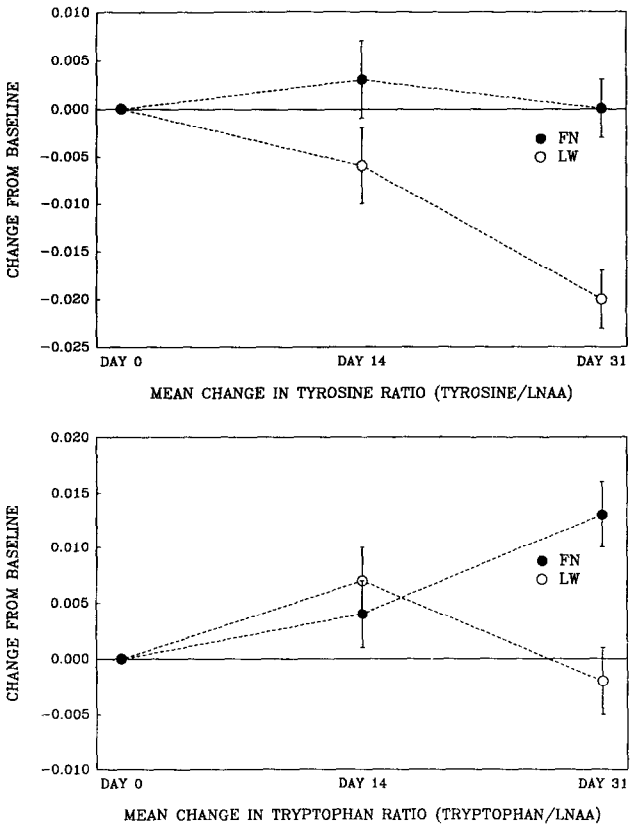

Figure 2 Mean (±SEM) change from baseline of plasma tyrosine ratio and tryptophan ratio in the fully nourished (FN) and lightweight (LW) groups over the course of the study.

changed in the control group, but declined after two weeks of consumption of the LW diet and then returned to baseline levels at the conclusion of the study. Plasma methionine was unchanged among both groups of soldiers (*Table 3*).

There was no consistent pattern of change among the branched chain LNAAs (*Table 3*). Valine tended to fall over time regardless of diet, whereas leucine fell after 2 weeks in both groups, but recovered in the LW ration group. Isoleucine fell after 2 weeks on the LW ration and then recovered at the conclusion of the study; it changed little in the control group.

Among the basic amino acids there were few consistent changes attributable to the LW ration. Arginine appeared to increase in the FN group, while histidine fell in both groups (*Table 3*).

To determine whether changes in plasma precursor ratios were related to changes in psychomotor performance over the course of the study, linear regression was employed using difference scores (day 0 vs. day 31, see group means below) for the behavioral and biochemical variables of interest. Decrements in tryptophan were significantly associated with impairments in simple ($r = -0.4415$, $P = 0.009$, *Figure 3*) and choice visual reaction time ($r = -0.4029$, $P = 0.018$, *Figure 4*). Performance was most impaired among those individuals whose tryptophan ratio decreased most. Changes in plasma tyrosine ratio did not predict decrements in performance ($r = 0.1407$, $P = 0.427$ for simple reaction time; $r = 0.0826$, $P = 0.642$

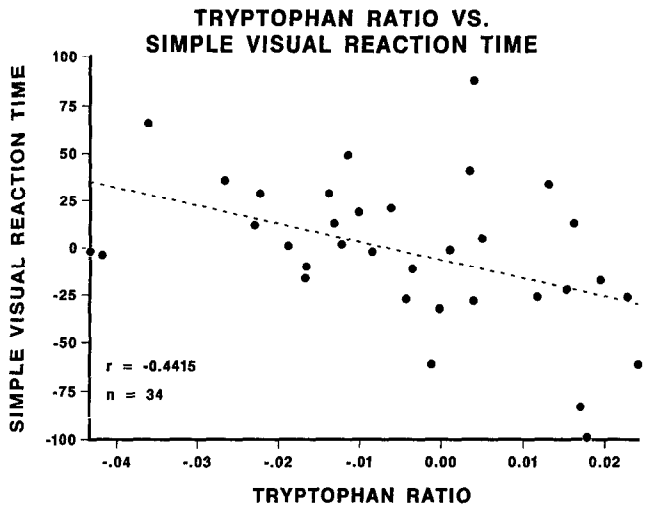

Figure 3 Changes in tryptophan ratio versus simple visual reaction time (msec).

for choice visual reaction time). Additionally, changes in individual plasma tryptophan ratios did not significantly correlate with changes in plasma tyrosine ratios ($r = -0.1939$). There were no significant changes in either reaction time measure as a function of differences in diet, per se.[9] Simple reaction time decreased pre to post in the FN group (379.00 ± 11.74 vs. 372.65 ± 11.26) and increased in the LW group (365.76 ± 9.93 vs. 376.24 ± 7.46), while choice visual reaction time decreased in both groups (FN, 608.65 ± 17.09 vs. 564.35 ± 15.99; LW, 576.31 ± 13.87 vs. 560.19 ± 12.26); the differences in diet were not significant.

Discussion

Among all the amino acids assayed, the largest proportional decline occurred for plasma tyrosine in the LW ration group. After only 2 weeks on this diet, tyrosine had fallen by 28% and at the end of the study it remained 26% below

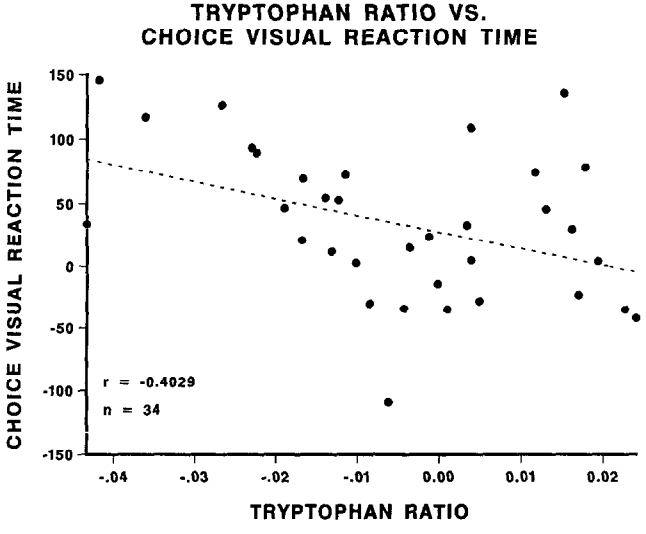

Figure 4 Changes in tryptophan ratio versus choice visual reaction time (msec).

baseline. The tyrosine/LNAA ratio fell by 19% by the end of the study in this group, although it was largely unchanged (6% below baseline) two weeks after the field test began. Because the LNAAs compete for access to the brain, tyrosine ratio may be a better predictor of the availability of tyrosine to the brain than plasma tyrosine.[21–23] Consequently, the different patterns of decline in tyrosine concentration and ratio observed suggest that peripheral consequences of reduced tyrosine availability would be apparent before any central nervous system deficits are observed.

Metabolites of tyrosine such as dopamine, norepinephrine, epinephrine, and thyroid hormones have a variety of peripheral functions. Under certain conditions tyrosine availability has been shown to influence the rate of synthesis of some of these substances. In animals, exogenous administration of tyrosine increases excretion of dopamine, norepinephrine, and epinephrine,[24,25] and alters cardiac excitability, blood pressure, and corticosterone levels.[26–31] Tyrosine pretreatment increases pulse pressure when humans are exposed to acute cardiovascular stress.[32] Whether the decrement in plasma tyrosine induced by the LW diet was of sufficient magnitude to have functional consequences is not known. At the completion of the study there were somewhat larger decrements in aerobic capacity as well as isokinetic muscle strength and endurance in the LW group compared to the FN group.[9] These could be related to diminished peripheral catecholamine availability. Other nutritional or non-nutritional factors could also account for these changes. For example, the decrement in plasma tryptophan observed in the LW group could be related to their lower physical performance, because tryptophan administration to healthy individuals has been reported to improve treadmill endurance time.[33] It should be noted that the relationship between changes in plasma amino acid levels and behavior is controversial. However, most of the studies that have been conducted[23,31,34] have only employed manipulations that produce acute changes in amino acid levels. The relationship between chronic changes in amino acid levels and objectively assessed performance has rarely been evaluated.

The substantial decrement in tyrosine/LNAA ratio and tyrosine that occurred by the end of the study may have also had adverse central consequences. Under certain conditions, tyrosine availability can be rate-limiting for brain dopamine and norepinephrine synthesis.[35] By the end of the study, decrements in certain behavioral parameters were also observed among some soldiers consuming the LW ration.[9] In particular, increased levels of a variety of somatic symptoms such as fatigue, dizziness, tremor, and weakness were often reported. In addition, the LW subjects were less willing to engage in self-initiated behavioral tasks. Because central catecholaminergic pathways, particularly those that contain norepinephrine, appear to play a key role in the ability of animals to respond to certain external stressors,[36–39] the reduced availability of tyrosine to the brain may have accounted for the adverse behavioral changes produced by consumption of the LW diet. Administration of supplemental tyrosine to humans may restore behavioral and neurophysiologic functions impaired by exposure to acutely stressful conditions.[40–42] However, levels of stress and anxiety, as assessed by standardized questionnaires, were not greatly elevated among the volunteers in this study. It has been suggested that the apathy and depression observed in individuals suffering from chronic protein-energy malnutrition may be attributable to effects on the brain of low plasma tyrosine levels.[6] However, because such individuals also have exceedingly low plasma tryptophan levels, decrements in serotoninergic neurotransmission also could contribute to their behavioral symptoms, as discussed later. Numerous other metabolic abnormalities are present during chronic malnutrition, so factors other than decrements in tyrosine or tryptophan availability may account for the behavioral changes observed in such individuals. For instance, decreased blood glucose levels[43] or increases in urinary ketones[44] have also been shown to produce adverse changes in behavior.

In this study, the overall mean plasma ratio of the neurotransmitter precursor tryptophan to the other LNAAs did not significantly decline over time as a consequence of consumption of the LW diet. However, by the end of the study, the tryptophan ratio was significantly lower and absolute levels of tryptophan fell considerably in those consuming the LW diet compared with the control group. Therefore, changes in the availability of tryptophan (the precursor of serotonin) to the brain also should be considered as potentially responsible for the adverse behavioral changes we observed. Brain serotonin levels are readily affected by the peripheral availability of tryptophan.[22,23] It was the change in plasma tryptophan ratio, not tyrosine, which was related to the change in psychomotor performance, assessed by simple and choice reaction time tasks, observed in this study. Whether such effects are directly attributable to changes in plasma tryptophan ratio, and consequently reduced brain serotonin synthesis, cannot be determined from this study. However, in healthy, fully nourished men, reduction in the availability of tryptophan produced by a single tryptophan deficient diet significantly increased depression and impaired performance.[45] Because serotoninergic neurons may be more sensitive to variations in their precursor availability than catecholaminergic neurons,[23] decrements in tryptophan may be more likely to be responsible for the behavioral deficits seen in undernutrition than reductions in tyrosine availability.

Another amino acid that significantly declined in the LW group was alanine, down 17% from baseline by day 31. This decrease is consistent with the role this amino acid is known to play in gluconeogenesis.[2] Alternatively, alanine may be lower due to reduced levels of pyruvate or glutamate, because pyruvate is transaminated using glutamate to form alanine de novo.[46] Alanine accounts for a substantial proportion of the total glucose output attributable to amino acid metabolism. However, because 75% of glucose output is normally derived from glycogenolysis, alanine only becomes an important source of glucose when glycogen stores are depleted—as apparently occurred among the LW ration group. By the end of the study, those soldiers had lost 1.5 kg of their fat free body mass (2.3% of their total body mass). They also had elevated urine ketone levels as early as 5 days into the study, although they were never severely ketotic. A decrease in plasma alanine is observed in prolonged fasting and the more severe stages of Kwashiorkor.[1,2] Alanine is also substantially reduced 26 and 40 days after obese

individuals are placed on pure protein, semistarvation diets.[3] The increase in plasma alanine observed in the FN control group may be attributable to their much smaller, but consistent, daily energy deficit (468 kcal/day). Over the course of the 30-day trial, the FN group lost a small, but significant, amount of body weight (1.8 kg on average), mostly as fat, and their energy consumption was several hundred calories per day less than their actual energy expenditure. In study after study conducted by laboratories in a number of countries, it has been observed that food consumption in the field does not meet energy requirements; the underlying causes for this are not well understood.[47] However, unlike the LW group, they did not use lean body mass to maintain gluconeogenesis. Antener et al.[6] observed greatly increased plasma alanine levels among healthy subsistence farmers in Zaire who consumed diets that were marginally deficient in calories and protein but contained adequate amounts of carbohydrate.

In conclusion, changes in plasma amino acids occurring during a controlled form of undernutrition can be substantial. Some of these alterations, such as reduced availability of tyrosine and tryptophan, may be related to the functional consequences of undernutrition. Reduced physical ability, as well as the alterations in behavior and performance observed in undernourished individuals, could be associated with such deficiencies. Other changes, notably reductions in plasma alanine levels, appear to be associated with using lean body mass for maintenance of glucose homeostasis. It should be noted that the diets differed in two important respects; first, in the total calorie intake and second, in the macronutrient content. Therefore, it is not possible to say to what extent the differences in plasma amino acid levels were caused by limited energy intake or to the different macronutrient composition of the diets. However, the greater part of the effects seen were probably because of lower calorie intake.

Acknowledgments

The views, opinions, and/or findings contained in this report are those of the authors and should not be construed as an official Department of the Army position, policy, or decision, unless so designated by other official documentation.

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