

# The Role of Protein and Amino Acids in Sustaining and Enhancing Performance

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## Amino Acid and Protein Requirements: Cognitive Performance, Stress, and Brain Function

*Harris R. Lieberman*<sup>1</sup>

### INTRODUCTION

This chapter addresses amino acid and protein requirements and brain function. A particular focus will be the possibility that central demands for amino acids may modify nutritional requirements when individuals are exposed to extreme environments and other stressors associated with combat and high-intensity military or civilian occupations.

To function adequately, the central nervous system (CNS) requires a number of amino acids found in protein foods. Amino acids such as tryptophan, tyrosine, histidine, and arginine are used by the brain for the synthesis of various neurotransmitters and neuromodulators (Betz et al., 1994). To date, CNS requirements for specific amino acids have not been systematically investigated, perhaps because it has been assumed that brain requirements for precursor amino acids were not critical. Furthermore, appropriate methods of determining

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whether adequate levels of particular precursors are provided to the CNS by the diet do not exist. Although little information on CNS requirements of specific amino acids is available, results from several lines of related research suggest that the peripheral concentration of particular amino acids can be a factor in the regulation of central neurotransmission, cognitive performance, and mood state. For example, if the amino acid tryptophan is either artificially elevated or lowered, changes in brain function and behavior can occur (Young, 1996). Even in normal humans, acute tryptophan depletion produces transient alterations in mood state (presumably by reducing the CNS concentration of serotonin), in particular increased subjective depression and increased aggression (Young, 1996). In contrast, administration of single doses of pure tryptophan to humans increases sleepiness and may reduce pain sensitivity (Hartmann, 1986; Lieberman et al., 1985). These changes are consistent with the various functions attributed to serotonin in the CNS.

CNS requirements for specific amino acids during periods of undernutrition or when individuals are exposed to highly stressful conditions may be particularly critical. For example, among moderately undernourished, but not highly stressed soldiers participating in a field test of an energy deficient ration, decrements in tryptophan were associated with impaired cognitive performance (Lieberman et al., 1997). Furthermore, a series of studies suggests that supplemental administration of tyrosine increases brain catecholaminergic neurotransmission and has beneficial effects on various behavioral parameters associated with resistance to stress (for a recent review, see Lieberman, 1994). Tyrosine is one of the dietary precursors for the synthesis of the catecholamines, dopamine and norepinephrine. The beneficial neurochemical and behavioral consequences of supplemental tyrosine administration are most readily observed when humans and other animals are exposed to various environmental and psychological stressors (Wurtman et al., 1981).

#### **The Blood-Brain Barrier: A Key Determinant of Brain Nutritional Status**

Unlike most other organs, the brain is isolated from the general circulation by the blood-brain barrier (BBB). The nature of the barrier is determined by the special properties of the cerebral vasculature, specifically the epithelial cells of the brain capillaries, which selectively prevent the transport of various substances into the brain (Betz et al., 1994; Pardridge 1977). In general, lipophilic compounds typically can passively cross the BBB, but water soluble compounds, such as amino acids, cannot. The BBB, therefore, must contain special mechanisms for selectively transporting key water soluble compounds, such as essential amino acids, into the brain (Pardridge, 1977; Betz et al., 1994). The special status of the brain with regard to its accessibility to nutritional and other systemic metabolic factors has profound implications for the determination of the nutritional requirements of the CNS. For example, in the

periphery, a variety of substances can be used as energy substrates, but the brain must rely almost exclusively on glucose (Pardridge, 1977). In examining the brain's requirements for protein and amino acids, it is essential to keep in mind that many substrates available to other organ systems are not available to the brain as a consequence of the BBB's "protection" of the brain. The protected status of the brain could have important implications under conditions of metabolic stress induced by undernutrition, exposure to adverse environmental conditions, or severe physical stress. It is possible that under such conditions, brain nutrient requirements relative to other organ systems may be proportionally much greater.

Although the brain is protected by the BBB, it still requires a number of substrates for adequate function. The importance of various amino acids as precursors for key brain neurotransmitters is well established, and transport mechanisms exist to provide these to the brain. At least three active transport mechanisms convey amino acids into the brain (Betz et al., 1994). Separate mechanisms exist for transport of the large neutral amino acids (LNAA), basic, and acidic amino acids across the BBB. However, small neutral amino acids like glycine and alanine appear to be actively pumped out of the brain (Betz et al., 1994). These three mechanisms and some of the amino acids that they transport are presented in Table 14-1.

Because whole classes of amino acids are actively transported by amino acid-specific carrier mechanisms, compounds from the same class of amino acids actually compete for transport into the brain (Pardridge, 1977). The functional implication of this unique characteristic of the BBB is that the amino acid composition of food is of greater consequence to the brain than perhaps any other organ system. Unlike other organ systems, the brain cannot simply absorb the nutrients it requires from the general circulation but rather only receives those nutrients that are transported across the BBB.

Several of the amino acids that are transported across the BBB and, in some instances, compete for access to the brain, are precursors of important brain neurotransmitters as shown in Table 14-2. There is evidence that most of the

TABLE 14-1 CNS Amino Acid Transport Mechanisms

Large Neutral	Basic	Acidic
Leucine	Lysine	Glutamate
Phenylalanine	Arginine	Aspartate
Tryptophan	Ornithine	
Valine		
Isoleucine		

neurotransmitters listed in Table 14-2 are, under certain conditions, precursor sensitive; therefore, as the peripheral concentration of any of the precursors varies, there could be consequences with regard to brain metabolism, function, and behavior (for a recent review see Young, 1996).

As shown in Table 14-3, these neurotransmitters have a variety of important functions in the brain, regulating or modulating a variety of key CNS functions. Of course, the precise relationship between a neurotransmitter and the behavior of an organism is difficult to summarize and is usually the subject of considerable controversy. Clearly, the functions outlined in Table 14-3 are not only critical in a general way for maintaining the normal behavioral status of an organism, but are also closely related to the ability of that organism to function in stressful conditions. In single nonphysiologic doses, or when administered in special diets, all of the amino acid precursors of the transmitter systems shown in Table 14-3 have been found to alter brain activity.

This chapter will focus on the large neutral amino acids (LNAAs), tryptophan and tyrosine, because the data on the effects of these neurotransmitter precursors on brain chemistry and behavior is most convincing. Perhaps one of the most critical issues (and most difficult to answer currently) is: Under what, if any, physiological situations will nutrient availability from food affect brain function?

**TABLE 14-2** Amino Acids and Their Neurotransmitter/Neuromodulator Products

Amino Acid	Product
Tryptophan	Serotonin
	Melatonin*
Tyrosine/phenylalanine	Dopamine
	Norepinephrine
	Epinephrine
Histidine	Histamine
Arginine	Nitric Oxide
Threonine (etc.)	Glycine

\* Melatonin is not believed to be a neurotransmitter but is a behaviorally active metabolite of tryptophan synthesized by the pineal gland. There is evidence that administration of tryptophan increases the release of melatonin in humans (Hajak et al., 1991).

**TABLE 14-3** Putative Functions of Various Neurotransmitter Systems (with Amino Acid Precursors)

Serotonin	Mood, pain, food intake, arousal
Dopamine	Motor function, mood, arousal
Norepinephrine	Arousal, attention, anxiety
Histamine	Food intake, arousal, Thermoregulation
Nitric oxide	Arousal, anxiety, memory
Glycine	Motor function

### TRYPTOPHAN

Tryptophan is the rarest of the essential amino acids found in food and, as noted above, is the precursor of serotonin. Evidence from a number of animal studies suggests strongly that changes in the protein: carbohydrate ratio of food consumed can alter brain serotonin. As the proportion of carbohydrate relative to protein increases, so does the level of brain serotonin. Consistent with the functions of serotonin listed in Table 14-3, the availability of tryptophan to the brain can alter behavioral factors such as alertness, level of depression, aggression, and pain sensitivity (for a recent review, see Young, 1996).

The effects of the protein: carbohydrate ratio of meals on brain serotonin is well documented, although the physiologic relevance of the relationship is controversial. The association between protein and carbohydrate intake and brain serotonin concentration was first observed by Fernstrom and Wurtman (1971). Subsequently, numerous animal studies have appeared that confirm and extend the initial observation. A recent paper by Fernstrom and Fernstrom (1995a) carefully documented the effects of meals that varied in protein:carbohydrate ratio on serotonin concentration in several brain regions in the rat. It was clearly demonstrated that as the concentration of protein in the test meals increased, brain concentration of serotonin fell parametrically. In both the hypothalamus and cortex, the highest levels of serotonin were observed following a pure carbohydrate meal. The authors noted that variation in hypothalamic serotonin induced by meals differing in protein: carbohydrate ratio could play a role in regulating food intake since the hypothalamus performs a critical role in appetite regulation. However, the functional significance of cortical changes is difficult to explain.

The phenomenon of peripheral modulation of brain serotonin occurs as a consequence of both the previously noted competition of the LNAA for transport across the BBB and the selective uptake by muscle of the branched-

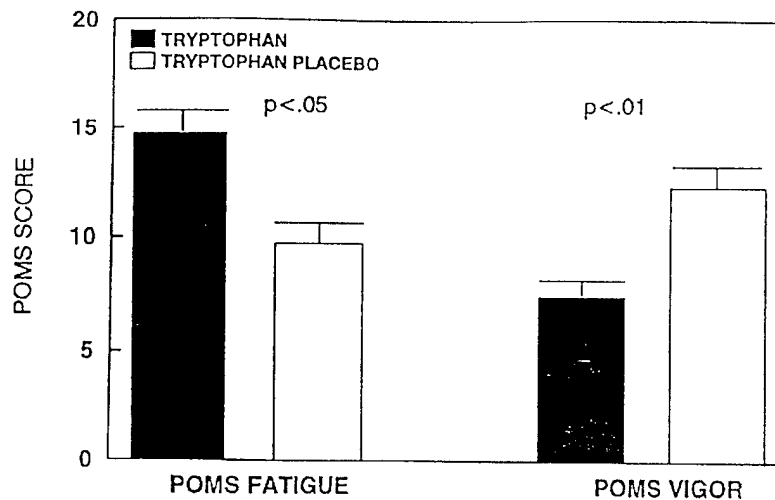
chain amino acids following a carbohydrate meal. Following consumption of carbohydrate, which elicits the secretion of insulin, the concentration of the branched-chain amino acids in the plasma falls as they move into muscle, while tryptophan levels remain relatively unchanged. Therefore, since more tryptophan is available for transport by the LNAA carrier mechanism, tryptophan transport to the brain increases and more tryptophan is available for the synthesis of serotonin. In humans, it has been established that changes in the protein:carbohydrate ratio of foods can alter plasma tryptophan levels in the same way as in experimental animals (Lieberman et al., 1986a).

To date, an association of changes in protein and carbohydrate intake with changes in behavior has not been clearly established, but several behavioral functions have been shown to be sensitive to substantial changes in plasma tryptophan levels. When tryptophan is administered in pure form or in higher than physiologic concentrations in meals, or is artificially lowered by administering tryptophan-free meals, substantial changes in a variety of behavioral parameters can be observed. One of the most frequently documented effects of tryptophan administration is an increase in self-reported mental fatigue. Tryptophan's effects on arousal and alertness appear to be similar to those produced by mild over-the-counter sedatives such as antihistamines. These effects have been documented with self-reported mood questionnaires (Figure 14-1) and by polysomnography (Hartmann and Greenwald, 1984; Lieberman et al., 1985). The hypnotic-like effects observed in humans after tryptophan administration are consistent with reports implicating brain serotonin neurons in the regulation of alertness. Although tryptophan is clearly not as potent as prescription hypnotic drugs, it was sold as an over-the-counter, natural sleep aid until several years ago. It was withdrawn from the market when a large number of cases of a rare disease called eosinophilia-myalgia syndrome (EMS) were seen in individuals who were taking it. The exact cause of the disease has never been conclusively demonstrated, although it has been suggested that a contaminant was present in the tryptophan produced by one manufacturer.

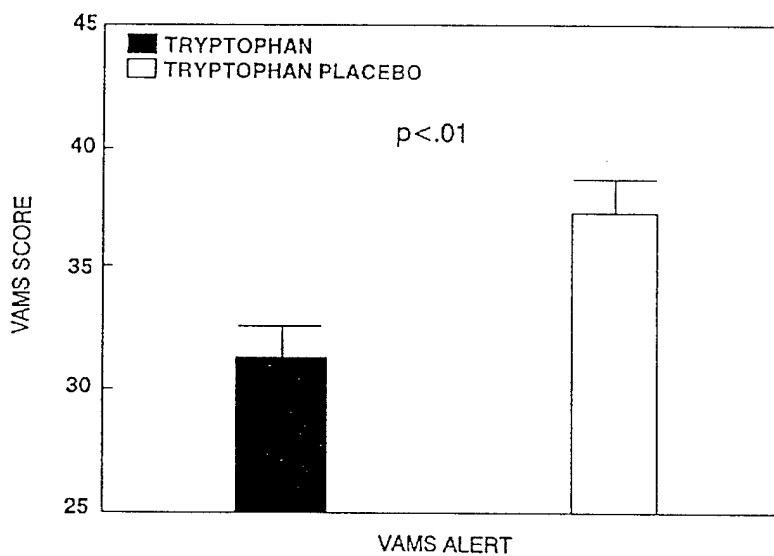
Another well-established effect of tryptophan relates to the role of serotonin in the regulation of mood, in particular, level of depression. Most antidepressant drugs increase serotonergic neurotransmission, although many have other central effects as well. Consistent with this role of serotonin in the brain, it appears that single meals that are deficient in tryptophan have substantial acute effects on self-reported level of depression. A series of studies have been conducted in several laboratories to examine the effects of specially formulated tryptophan-free meals on mood state. These studies have consistently observed substantial increases in depression when these low-tryptophan meals are ingested (Young, 1996) when measured with standard self-reported mood questionnaires in normal individuals, as shown in Figure 14-2 (Smith et al., 1987), and in individuals suffering from various clinical syndromes associated with high levels of depression.



Panel A



Panel B



**FIGURE 14-1** Effects of a single dose of tryptophan (50 mg/kg) on the self-reported fatigue, vigor, and alertness of healthy volunteers as assessed with the Profile of Mood States (POMS) Questionnaire (Panel A) and Visual Analog Mood Scale (VAMS) (Panel B). SOURCE: Adapted from Lieberman et al. (1986).

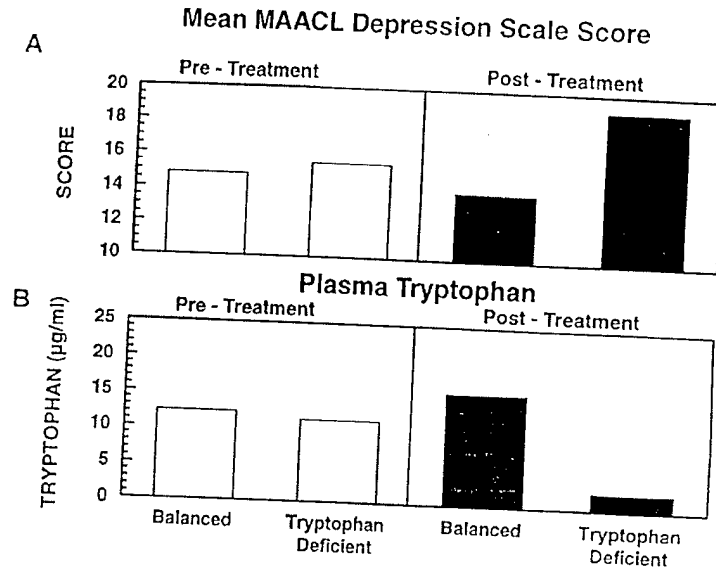


FIGURE 14-2 Effects of a single tryptophan deficient meal on self-reported depression and plasma tryptophan levels of healthy volunteers. SOURCE: Adapted from Smith et al. (1987).

Tryptophan-deficient meals also affect the level of aggression displayed by normal volunteers. When normal individuals are classified as belonging to a high-aggressive personality type based on standardized personality questionnaires, administration of tryptophan-deficient meals increases not only aggressive mood state, but also the level of aggressive behavior overtly displayed (Figure 14-3) (Cleare and Bond, 1995). Administration of a high-tryptophan meal to such individuals decreases aggressive mood and behavior (Cleare and Bond, 1994).

Tryptophan has also been reported to decrease pain sensitivity in animal models, normal humans, and patients suffering from certain clinical conditions where pain is present (Lieberman et al., 1983; Seltzer et al., 1983). The changes in aggression and pain induced by artificially altering plasma levels of tryptophan are consistent with data implicating serotonin in the regulation of aggression and pain sensitivity.

Overall, there is little doubt that substantial variations in plasma tryptophan levels can have a major impact on the behavior of humans and other animals. However, it should be noted that the doses of tryptophan that have been shown to be unequivocally psychoactive may produce changes in brain tryptophan that are larger than those produced by any food that increases or decreases brain serotonin. Currently, the smallest change in levels of plasma or brain tryptophan that will have an impact on brain function or behavior is unknown. Therefore, it

is not currently possible to determine whether nutritional requirements for tryptophan are in any way related to brain demands for this amino acid.

### TYROSINE

Another amino acid that has been extensively examined for behavioral effects is tyrosine, the precursor of three neurotransmitters: norepinephrine, dopamine, and epinephrine (see Table 14-2). Tyrosine is not typically considered to be an essential amino acid since it can be synthesized by humans from phenylalanine; however, it has been suggested by some investigators that the brain may not be able to synthesize sufficient tyrosine from phenylalanine to meet its needs (Pardridge, 1977). Tyrosine is generally found in larger quantities than tryptophan in most protein foods. Since tyrosine is a LNAA, it competes with tryptophan and the other LNAAs for transport across the BBB.

#### High Trait Aggressive Subjects

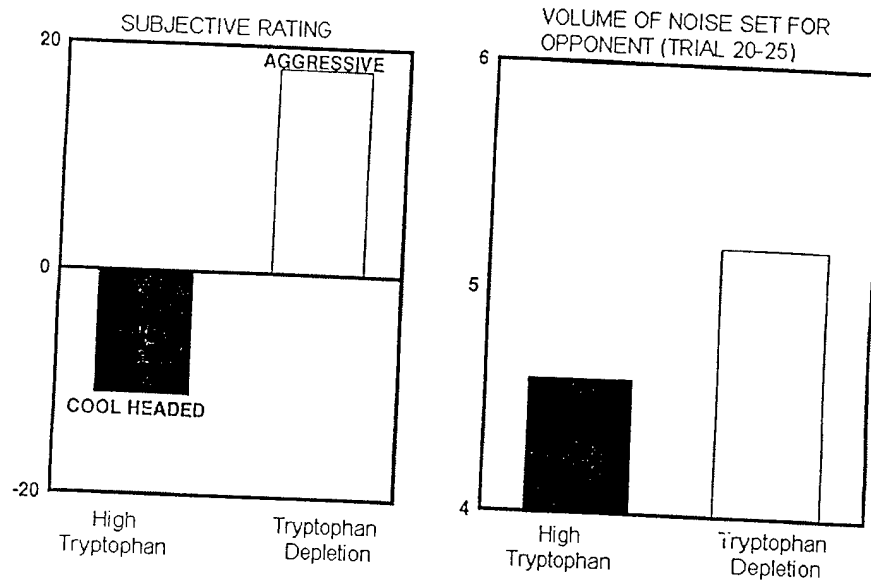


FIGURE 14-3 Effects of tryptophan-depleted and -supplemented meals on subjective and objective measures of aggression among normal, high-trait aggressive volunteers. On the left, the effects of such meals on a bipolar scale measuring aggression/cool headedness are plotted. On the right, an objective measure of aggression, (willingness of the tested individual to deliver aversive [noise] stimuli to another individual) is plotted. SOURCE: Adapted from Cleare and Bond (1995).

Under certain conditions, it appears that administration of tyrosine can affect brain neurotransmission. Specifically, it has been hypothesized that when central catecholaminergic neurons are very active (as occurs during exposure to acute stress), they will become precursor sensitive (Wurtman et al., 1981). Although these neurons are not normally believed to be affected by the availability of tyrosine, they may require additional tyrosine to function optimally when they are firing frequently (Lieberman, 1994; Wurtman et al., 1981). Norepinephrine is believed to play a critical role in the response of the brain to acute stress. Exposure to heat, cold, cardiovascular stressors, and electric shock all produce significant increases in brain catecholaminergic activity (Stone, 1975). Central noradrenergic neurons seem to be critical for regulating key behavioral parameters such as attention, arousal level, and mood state (Lieberman, 1994). Although norepinephrine appears to be particularly critical for the brain's response to stress, another brain catecholamine, dopamine, also appears to be involved in certain aspects of the acute response to various stressors.

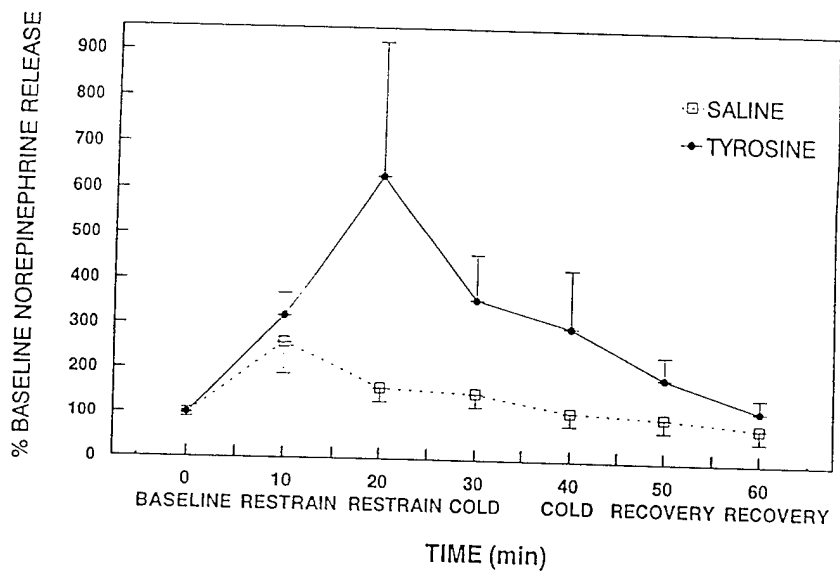


FIGURE 14-4 Effect of immobilization stress alone and in combination with cold stress on hippocampal norepinephrine release in tyrosine- (400 mg/kg) and placebo-treated rats. Testing conditions, in 10-min intervals, are specified on the x-axis. SOURCE: Adapted from Lieberman and Shukitt-Hale (1996).

The neurochemical consequences of exposure to stress and the effects of supplemental tyrosine under such conditions have been examined in animal models. Two recent studies examined the effects of a combination of cold and restraint stress on release of norepinephrine in the rat hippocampus (Luo et al., 1993; and Shukitt-Hale, 1996). The technique of microdialysis was used to assess norepinephrine release since it permits continuous assessment of neurotransmitter release *in vivo* from a specific brain region (Ungerstedt et al., 1982). Immediately prior to exposure to the stressors, some animals received an intraperitoneal injection of 400 mg/kg of tyrosine while others received a placebo injection. Figure 14-4 illustrates the effects of stress and supplemental tyrosine under these conditions. The combination of cold and restraint stress substantially increased the release of norepinephrine in the hippocampus over baseline levels; when animals were pretreated with tyrosine, the magnitude of the increase was substantially amplified (Lieberman and Shukitt-Hale, 1996). To evaluate the hypothesis that supplemental tyrosine can prevent some adverse behavioral and physiological effects of exposure to various acute stressors, a number of animal and human studies have been conducted (for reviews, see Lieberman, 1994; Owasoyo et al., 1992; Salter, 1989). In general, the results of these studies suggest that tyrosine administration, particularly when the stress is severe, will have beneficial effects on the ability of the organism to function adequately.

In some of the initial studies, rats were exposed to foot shock, and their spontaneous behavior was assessed (Lehnert et al., 1984a; Lehnert et al., 1984b). In these studies, rats that were pretreated with tyrosine were more active and appeared to be less debilitated following exposure to the stressor. In other animal studies in which high doses of tyrosine were administered, learning and memory, as well as other aspects of performance in the cold and under high-altitude conditions, were improved (Ahlers, et al., 1994; Rauch and Lieberman, 1990; Shukitt-Hale et al., 1996; Shurtleff et al., 1993). In addition, tyrosine has been shown to have beneficial effects in animals exposed to heat stress by reducing immobility, the dependent measure in the Porsolt swim test (Yeghiayan, *in press*; Figure 14-5). In human studies, tyrosine has been found to have positive effects on cognitive performance during exposure to a combination of cold and high-altitude stress as well as cold stress alone (Banderet and Lieberman, 1989; Shurtleff et al., 1994). Tyrosine also appears to enhance performance of individuals exposed to psychological stress (Figure 14-6) (Deijen and Orlebeke, 1994). These human studies are consistent with neurochemical and behavioral studies of animals that also suggest that tyrosine has beneficial effects on the ability of animals to cope with acute stress and can improve performance on tasks requiring attention and learning. Although not directly addressing the issue of dietary requirements for tyrosine, these studies indicate that there may be an increased CNS requirement for this amino acid during periods of intense stress.

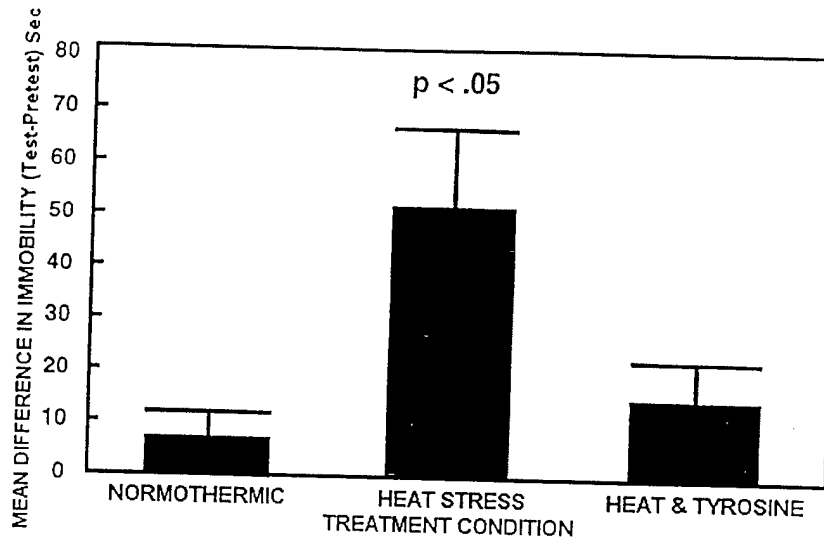


FIGURE 14-5 Effect of heat stress and tyrosine on performance of rats in the Porsolt swim test. Increased immobility (mean difference in immobility) indicates inability of the animal to respond appropriately to the heat stressor. SOURCE: Adapted from Yeghiayan, in press.

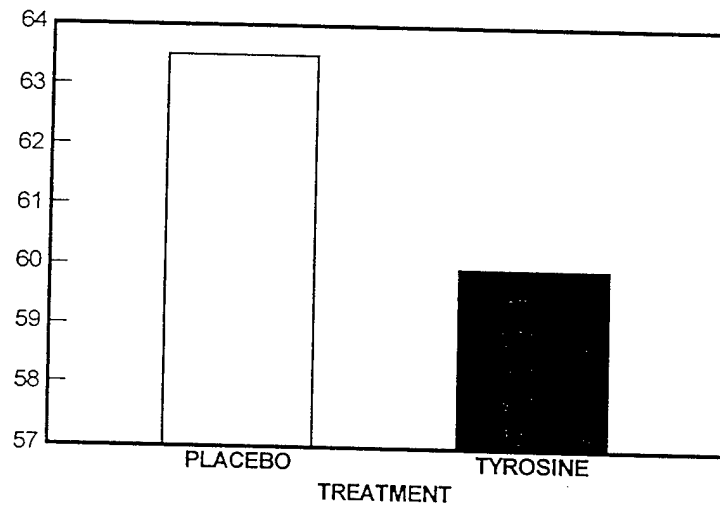


FIGURE 14-6 Performance on a stressful test of attention and memory (Stroop Task) in humans treated with placebo or 100 mg/kg of tyrosine. SOURCE: Adapted from Deijen and Orlebeke (1994).

### CHANGES IN AMINO ACIDS DURING FIELD STUDIES: UNDERNUTRITION AND MENTAL PERFORMANCE

Several years ago, as part of a U.S. Army Research Institute of Environmental Medicine (USARIEM) field study of an experimental lightweight ration, the relationship between plasma amino acid levels and mental performance was assessed. The light weight ration tested, termed the Ration, LightWeight-30 (RLW-30), was intended to be the sole source of nutrition for soldiers operating without logistical support for up to 30 days (Askew et al., 1987). The ration was nutritionally balanced but calorie energy deficient since it provided only 2,000 kcal of energy per day. In this study, which was conducted under temperate climatic conditions, the RLW-30 was compared with the standard Army field ration—the Meal, Ready-to- Eat (MRE-Version VI). The macronutrient intake of soldiers consuming the two types of rations, as well as the actual mean daily energy expenditure of the soldiers in each group can be found in Table 14-4. The individuals receiving the RLW-30 ration had a substantial daily energy deficit of over 1,300 kcal, while the control group's energy intake was only several hundred kcal below their daily energy expenditure level. At the start and conclusion of the study, two standard tests of cognitive performance previously shown to be sensitive to the effects of nutritional parameters (simple visual reaction time and four-choice visual reaction time) were administered to the soldiers. In addition, on the same day that performance was assessed, blood samples were drawn and plasma amino acids determined. Plasma levels of both tryptophan and tyrosine were reduced substantially (Figures 14-7 and 14-8) over the course of the study among the soldiers consuming the RLW-30 ration. To ascertain whether changes in plasma levels of either tryptophan or tyrosine were related to behavioral function during this field study, changes in the ratio of tryptophan and tyrosine to the other

**TABLE 14-4** Mean Daily Nutrient Intakes of the Standard Field Ration and Lightweight Ration Groups for 30 Days of a Field Study

Nutrient	Standard Field Ration Group (+SEM)	Lightweight Ration Group (+SEM)
Energy, kcal	2,782 ± 42	1,946 ± 15
Protein, g	112 ± 2	64 ± 1
Carbohydrate, g	318 ± 6	197 ± 2
Fat, g	119 ± 2	100 ± 1
Energy Expenditure (kcal)	3,250	3,275

SOURCE: Adapted from Askew et al., 1987.

LNAAs were computed and correlated with changes in performance. Plasma ratios are believed to be a better indicator of transport of amino acids across the BBB than absolute levels of an amino acid because of the previously noted competition of similar amino acids for a common carrier (Pardridge, 1977). There were significant correlations between both types of performance and the tryptophan to other LNAAs ratio but not the tyrosine ratio (Figure 14-9) (Lieberman et al., 1997). This indicates that under conditions of undernutrition, tryptophan may be the best indicator of changes in mental performance. Therefore, maintaining adequate tryptophan levels may be particularly important when the optimal amino acid content of field rations is under consideration. This is consistent with the data discussed above, indicating that decrements in plasma tryptophan induced by administration of a single tryptophan-deficient meal can substantially increase depression and aggression and alter arousal in normal volunteers (Cleare and Bond, 1995; Smith et al., 1987). Although a significant correlation between tyrosine levels and performance was not observed during this field study, the research was conducted in a relatively nonstressful environment, not under conditions where the influence of tyrosine on central catecholamines is likely to be important.

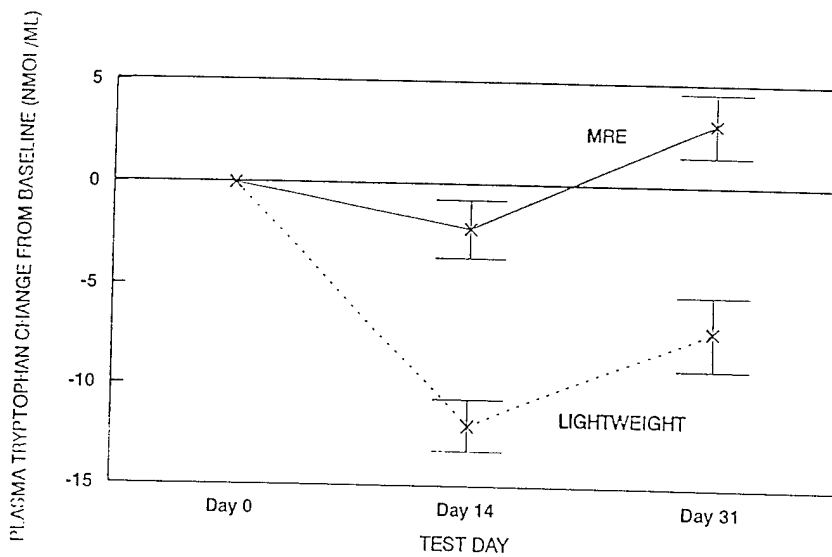


FIGURE 14-7 Plasma tryptophan levels in soldiers consuming either a lightweight ration or standard field rations (the MRE) over the course of a 31-day field study conducted in a temperate climate. SOURCE: Adapted from Lieberman et al., 1997.



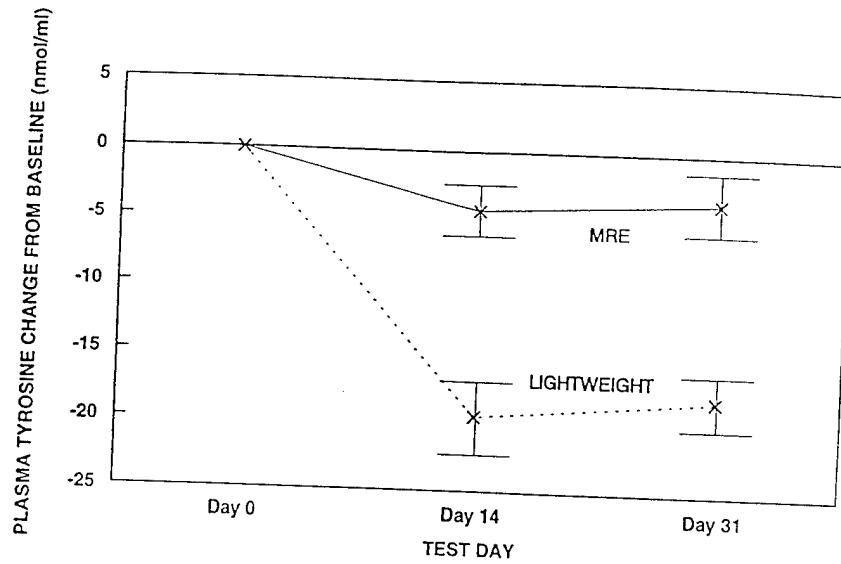


FIGURE 14-8 Plasma tyrosine levels in soldiers consuming either a lightweight ration or standard field rations (the MRE) over the course of a 31-day field study conducted in a temperate climate. SOURCE: Adapted from Lieberman et al., 1997.

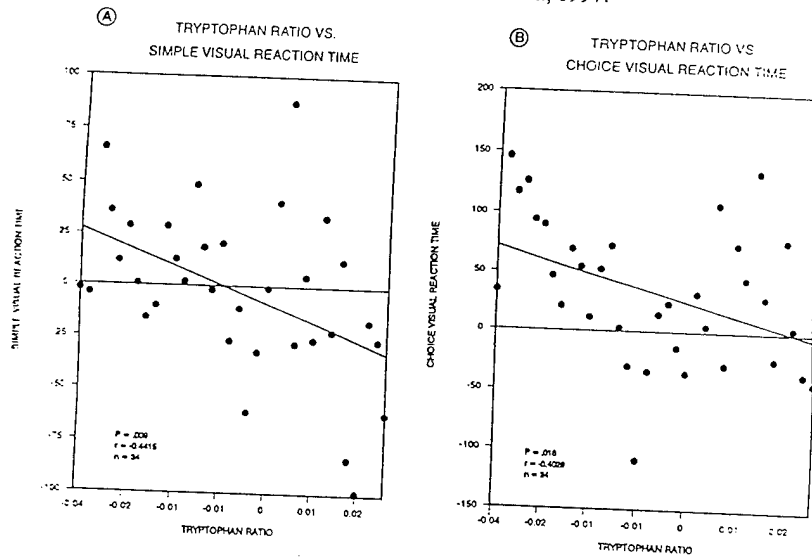


FIGURE 14-9 Relationship between changes in plasma: tryptophan ratio and two tests of cognitive performance in soldiers consuming either a lightweight ration or standard field rations (the MRE) over the course of a 31-day field study conducted in a temperate climate. Reductions in tryptophan ratio were significantly correlated with degraded performance on both simple (A) and choice (B) visual reaction time tasks. SOURCE: Adapted from Lieberman et al., 1997.

### AUTHOR'S CONCLUSION AND RECOMMENDATIONS

Maintenance of appropriate plasma concentration of at least one amino acid, tryptophan, the precursor of serotonin, is essential for optimal brain function and cognitive performance. Substantial decreases or increases in the typical levels of tryptophan present in the plasma will substantially disrupt normal behavior and brain function. Reduced plasma tryptophan increases depression and aggression, while increases in this amino acid induce drowsiness and decrease pain sensitivity. The optimal range for plasma and brain tryptophan levels has not been established in humans or any other species, nor has the daily requirement for this amino acid been determined with respect to its effects on brain function.

Administration of tyrosine, precursor of the catecholamines including norepinephrine, has been shown to prevent some of the adverse neurochemical and behavioral effects of exposure to acute stress. Optimal plasma and brain levels of this amino acid may be less critical than that of tryptophan, except under stressful conditions. Of course, such conditions are of great relevance to the development of optimal military rations. The possible importance of other amino acids such as histidine, arginine, or threonine to the regulation of behavior is currently not known.

Given the importance of optimal cognitive function to soldiers and the documented relationship between several amino acids and brain function, studies to quantify CNS requirements for specific amino acids under conditions of metabolic, environmental, and psychological stress are required. Such studies could provide the basis for optimizing the amino acid content of field rations intended for use in extremely stressful combat conditions. Development of methods to evaluate CNS requirements for specific amino acids under normal and adverse circumstances is also necessary. Consideration should be given to conducting further animal research using techniques such as microdialysis to assess release of brain transmitters under various environmentally and nutritionally stressful conditions, including undernutrition, thermal stress, hypoxia, and psychological stress.

A recent consensus report by an international working group on protein and amino acid requirements concluded that "Amino acid requirements at all ages require further investigation. Such studies should include consideration of amino acid use for processes other than protein deposition" (Working Group, 1996). Given the importance of the neurotransmitter precursors for the CNS, it is recommended that some of these functional measures be behavioral. Specifically, functional outcome measures based on behavioral and other CNS end points should be considered as potentially critical measures of amino acid and protein requirements, particularly when the amino acid in question is known to affect brain function. When humans are exposed to stressors such as extreme environmental conditions, intense exercise, or psychological stress, the

importance of brain requirements for amino acids may be relatively greater than under optimal physiological conditions.

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### DISCUSSION

ROBERT NESHEIM: I will take one question if anybody has a quick one, and then I think we need to take a break. Yes?

GERALD COMBS: Since tryptophan is the least abundant amino acid in most proteins and would be the most constant, its relationship to total protein would be more nearly the same than any other amino acid. Do you think that might be part of the reason why it was the only one that was correlated with function?

HARRIS LIEBERMAN: It is hard to say, because tryptophan has other unique characteristics. I think the fact that it is precursor dependent with regard to variations in protein to carbohydrate ratio, could also be an important factor. But, yes, it is quite possible. You are right there.