

Tyrosine improves cognitive performance and reduces blood pressure in cadets after one week of a combat training course

J. B. Deijen,^{1*} C. J. E. Wientjes,² H. F. M. Vullings,³ P. A. Cloin¹ and J. J. Langefeld²

¹Department of Clinical Neuropsychology, Vrije Universiteit, Amsterdam, The Netherlands; ²TNO Institute for Human Factors, Soesterberg, The Netherlands; ³Royal Netherlands Army, Department of Behavioral Sciences, Den Haag, The Netherlands

[Received 15 April 1998; Revised 19 November 1998; Accepted 22 November 1998]

ABSTRACT: The effects of the amino acid tyrosine on cognitive task performance were studied on a group of 21 cadets during a demanding military combat training course. In addition, the effects on mood, blood pressure and the norepinephrine metabolite MHPG were determined. Ten subjects received five daily doses of a protein-rich drink containing 2 g tyrosine, and 11 subjects received a carbohydrate rich drink with the same amount of calories (255 kcal). Assessments were made both immediately prior to the combat course and on the 6th day of the course. The group supplied with the tyrosine-rich drink performed better on a memory and a tracking task than the group supplied with the carbohydrate-rich drink. In addition, the supplementation of tyrosine decreased systolic blood pressure. No effects on mood were found. These findings suggest that supplementation with tyrosine may, under operational circumstances characterized by psychosocial and physical stress, reduce the effects of stress and fatigue on cognitive task performance. © 1999 Elsevier Science Inc.

KEY WORDS: Tyrosine, Cognitive performance, Stress, Blood pressure, Mood, Combat course.

INTRODUCTION

Psychosocial and physical stress are known to increase the release of both peripheral and central (brain) norepinephrine (NE) [16,29]. Peripheral and central release of catecholamines are controlled by two separate systems, because peripherally released catecholamines cannot pass the blood—brain barrier. In the frontal cortex, the transmission of noradrenergic neurons is increased by stressful events [16,21]. Noradrenergic projections from the locus coeruleus (LC), which show an increased electrical activity during stress, provide a main innervation to the frontal cortex [1,31]. The activity of noradrenergic neurons in the LC plays an important role in attention processes, alertness, motor activity and the regulation of emotional processes [28]. In animal studies, stress-induced depletion of brain NE was followed by reduced explorative and motor behavior and by behavioral depression [22,41]. Also in humans central NE has been found to be important in maintaining atten-

tion. A clonidine-induced inhibition of NE release resulted in an increase in the number of lapses of attention in healthy males, which was reversed by the antagonist idazoxan [34].

With respect to dopamine (DA), a variety of tasks, including active avoidance, passive avoidance and the radial-arm maze, have been used in experimental animals to show the involvement of DA systems in learning and memory. Systemic DA receptor blockade impaired learning in different tasks suggesting the role of DA blockade in producing learning deficits [6,7,24]. Neurotoxic depletion of catecholamines (CA) in the prefrontal cortex of young adult monkeys produced impairment of spatial memory that was reversed by treatment with the DA agonists L-dopa and apomorphine [12]. With respect to humans, some investigators found an increased incidence of dementia in patients with Parkinson's (PD) disease, a syndrome characterized by atrophy and degeneration of DA neurons [18,42]. The existence of a deficit in visuospatial working memory in PD also indicates the involvement of DA in intellectual functioning [10]. However, in animal studies, where the concentration of NE and DA was measured after stress induction, no changes in the concentration DA was found [41]. Therefore, considerably more severe stress seems to be required to alter DA levels in the brain than NE levels. The release of DA may be more related to coping behaviors than to the uncontrollability of the stressor, which appears to be the crucial determinant of the NE response [22].

The large neutral amino acid L-tyrosine, which is the precursor of NE and DA, has been found to enhance NE synthesis [23] and may thus prevent stress-induced NE depletion in the animal brain. In mice, brain tyrosine was found to reach its maximum concentration 1 h after oral ingestion and returned to baseline level after 4 h [39]. In addition, in rats receiving a tyrosine-rich diet, neither NE depletion nor behavioral impairment was found after stress induction [11,22]. Similar results have been found in humans. Young men who were exposed to cold and hypoxia exhibited fewer stress symptoms, such as headache, tension and fatigue, and showed fewer psychomotor impairments after being supplemented with 100 mg/kg tyrosine [5]. In a more recent human study,

* Address for correspondence: Dr. J. B. Deijen, Department of Clinical Neuropsychology, Free University, De Boelelaan 1111, 1081 HV Amsterdam, The Netherlands. Fax: +31-20-4448832; E-mail: jb.deijen@psy.vu.nl

Shurtleff, Thomas, Schrot, Kowalski, and Harford [33] found that the administration of 150 mg/kg tyrosine prevented the cold-induced (4°C) impairment of short-term memory that was observed in a placebo group. Positive effects of L-tyrosine on mental performance in human subjects were also found in a study from Deijen and Orlebeke [15]. The supplementation of 100 mg/kg L-tyrosine in healthy subjects improved the mental performance under stress (noise of 90 dB) as compared to a placebo condition. In addition, L-tyrosine decreased diastolic blood pressure (DBP) 15 min after ingestion. This was consistent with the blood-pressure-reducing effects found in animals [37,43]. Hence, laboratory studies strongly suggest that supplementation with tyrosine may serve to reduce the cognitive, behavioral and physiological effects of exposure to stress.

Also, protein-containing diets that provide tyrosine have been found to increase the plasma tyrosine/large neutral amino acids (LNAA) ratio and brain tyrosine levels. Plasma tyrosine concentration, expressed relative to the plasma concentrations of the same transport competitive amino acid (tyrosine/LNAA), reflects the amount of tyrosine available to the brain for catecholamine (CA) synthesis. The acute consumption of a high-protein meal was found to almost double the serum tyrosine level and tyrosine ratio in rats [19,20]. In humans, plasma tyrosine levels and the plasma tyrosine ratio were measured in subjects who consumed a protein-rich diet. Plasma tyrosine levels rose significantly during the day when the diet was consumed [26]. In another study oral protein (albumin) was found to increase the ratio in plasma of tyrosine to other LNAA in healthy fasting females by 20–60% [27]. Finally, a protein breakfast was found to cause a significant rise in cerebrospinal fluid tyrosine in patients who were suffering from normal pressure hydrocephalus [38].

The present study was designed to determine whether the administration of L-tyrosine would also be effective in reducing the effects of “real-life” stress. The study was carried out with a group of cadets of the military academy who had to complete a combat training course as part of their training program. As this course involved psychologically, as well as physically highly demanding conditions (including sustained operations and sleep loss), it was considered to be an appropriate environment to study the stress-reducing properties of L-tyrosine. The study focussed specifically on the effects of L-tyrosine on cognitive functioning after stress-induction. We hypothesized that supplementation with tyrosine would reduce the stress-induced cognitive, psychomotor and mood impairments and would lower blood pressure.

MATERIALS AND METHODS

Subjects

Thirty-two cadets of the Royal Military Academy (Koninklijke Militaire Academie; KMA) volunteered to participate in the study. Sixteen subjects were randomly assigned to the tyrosine group, and the remaining 16 subjects were assigned to the placebo group. In the course of the study, 11 subjects dropped out due to injuries, leaving 21 subjects for analysis. This left 10 subjects belonging to the tyrosine group and 11 subjects to the placebo group. The tyrosine group included one female and nine males, aged between 19 and 26 years (mean age \pm SD = 22.8 \pm 2.7). The placebo group consisted only of males, aged between 18 and 27 years (mean \pm SD = 21.4 \pm 2.8).

As an incentive each participant received \$30.00 at the end of the study. The study protocol was approved by the Medical Ethical Committee of the Free University Hospital, and all subjects gave their written consent to participate.

Apparatus

Computer tasks. The tasks were carried out with the use of eight personal computer systems, supplied with a timer, response system (TNO-TM), an analogue/digital (A/D) conversion card (Data Translation DT 2808), a response panel and a joystick (Taskomat, TNO Institute for Human Factors, Soesterberg, The Netherlands).

Four tasks from the Taskomat battery [9] were administered: a Memory Comparison Task (MCT), a Tracking Task (TT), a Continuous Memory Task (CMT) and a Double Task (DT).

The MCT assesses the speed and quality of short-term memory comparisons. During the MCT, stimuli appeared one at a time on the display. The stimuli, which comprised 1, 2 or 4 letters, are monitored for the occurrence of one of four prespecified target letters. Subjects are required to respond accordingly by pressing a “yes” (target present) or a “no” (target absent) key as fast as possible. After an incorrect response, the word “incorrect” is shown on the screen. The time interval between response and next stimulus was 500 ms. If a 1,000-ms deadline had elapsed without response, the next stimulus was presented and a response omission recorded. In this study the test duration was 8 min. The performance measures were the number of correct and incorrect responses.

The TT assesses perceptual-motor skill. On the display, a track moves upwards in a variable direction. The subject has to manipulate a gateway, which can be moved horizontally using a joystick, so that the track goes through the middle of the gateway. Subjects can anticipate the movements of the track with a “preview time” of 2,400 ms. The TT was presented for 7 min (14 intervals of 30 s). The performance measure was the root mean square (RMS) of the distance between the track and the middle of the gateway. This measure was computed for each individual at 30-s intervals as well as for the whole task.

In the CMT, 1, 2 or 4 letters are presented on the display at each trial. The subject is required to press a button when one out of four prespecified target letters is presented. Additionally, the subject has to count the number of times each of the four targets is presented. The duration of the task was 7 min. Performance measures were the number of correct responses and the number of incorrect counts.

During the DT, both the TT and the CMT are presented simultaneously. The DT was presented for 7 min (14 intervals of 30 s).

While performing the TT and the DT, subjects frequently had lapses of attention as a result of exhaustion. During such periods, the variability of the RMS values was not associated with variability of task performance but with the position of the joystick (i.e., the position of the gateway with respect to the track). Consequently, the RMS did not always reflect task performance. To solve this problem, the task-interruption time was determined. The task-interruption time reflects the percentage of the time on task that the joystick is not moved. Task-interruption time was determined for each subject by a combination of judgement and counting the number of periods that the RMS exceeded a cutoff value of 50. The choice for this cutoff value was based on the observation that a failure to move the joystick almost invariably yielded mean RMS values $>$ 50 [8].

Mood questionnaires. The Profile of Mood States (POMS) [25,32] is a questionnaire consisting of the subscales Depression, Anger, Fatigue, Vigor and Tension. The shortened Dutch version of 32 items was used [40]. Responses are made by choosing from five response alternatives.

The State-Trait Anxiety Inventory (STAI) [30,35] consists of a “state anxiety” and a “trait anxiety” scale. State anxiety refers to

situational anxiety. Trait anxiety is considered a relatively stable personality characteristic. Because the present study focusses specifically on changes in the state of the subjects, only state anxiety was assessed. Subjects were instructed to choose from four response alternatives.

Procedure

Prior to the study, all cadets participating in the combat training course were informed about the goal and procedure of the study. Following this, volunteers were invited to participate in the study. Two weeks before commencement of the combat training course, all subjects practiced the computer tasks. This practice session was held in a classroom of the KMA. In this session, shortened versions of all tests were presented.

The pretest, which was also held in a classroom of the KMA, took place 1 week prior to the combat training course. The whole test session lasted 45 min. The presentation of the performance tests was as follows: MCT (8 min), TT (7 min), CMT (7 min) and DT (7 min). In addition to the computer tests, blood pressure was determined and urine samples were collected to determine MHPG. At the end of the practice session, subjects received the POMS and the STAI. They were asked to send their completed questionnaires to the first author in a stamped addressed envelope, before the start of the combat training course.

On days 2–5 of the combat training course, the drinks containing tyrosine and the placebo drinks were ingested between 0700 and 0800 h. On day 6 (the posttest) the drinks were ingested between 0200 and 0300 h. The drinks were supplied by the commanders. This procedure made it possible to control compliance.

The posttest took place on day 6 of the first week of the combat training course, between 0500 and 0800 h. A classroom in the barracks, located near the training ground, served as the testing room. The protocol was similar to that used in the pretest, with the exception that the subjects completed the questionnaires immediately after having performed the computer tests. As in the pretest session, blood pressure was assessed and urine samples collected to determine the brain metabolite of NE, MHPG. The measurement of blood pressure was carried out by experimenters who were unaware of the group to which subjects had been assigned.

Combat Training Course

The combat training course aims to increase stress tolerance and improve operational effectiveness. During the 2-week training course, the cadets have to endure a number of highly physically demanding and emotionally stressful conditions, including sleep deprivation and food rationing. During the whole course the subjects' diet was restricted and controlled. The last meal before the posttest on day 6 was provided between 1900 and 2000 h (i.e., about 10 to 12 h before the last test and 6 to 8 h before the last experimental drink). In the combat training course, the limits of physical endurance are reached, and psychological stress is induced by the unpredictability of the demanded activities.

Supplementation

L-tyrosine was supplied in a 500-ml drink, consisting of orange juice in which 70 g of the diet powder PROTIFAR (Nutricia, Zoetermeer, The Netherlands) was dissolved. This amount of PROTIFAR contains 42 g of proteins, including 2 g of tyrosine. In addition to tyrosine, 70 g PROTIFAR contains the following: alaline (1.5 g), arginine (1.5 g), aspartic acid (3.4 g), cysteine (0.4 g), glutamic acid (9.5 g), glycine (0.8 g), histidine (1.3 g), isoleucine (4.3 g), leucine (4.3 g), lysine (3.7 g), methionine (1.1 g), phenylalanine (2.1 g), proline (4.2 g), serine (2.6 g), threonine

(1.9), tryptophan (0.6 g) and valine (2.7 g). The placebo group received a 500-ml mixture of orange juice, in which 67 g of FANTOMALT (Nutricia) was dissolved. FANTOMALT is a diet powder consisting of 95% carbohydrates but contains no protein. Both drinks contained the same amount of calories (255 kcal). Subjects were required to take one drink daily for a period of 5 days.

The containers with the drinks were handed out by the group commander. The containers were marked with a yellow or green spot: which color each subject received was noted on a list given to the commander. The commanders were not aware of which color corresponded to the respective treatments.

It must be stressed that L-tyrosine was not supplemented in pure form but in protein-rich powder, and the placebo was not a real placebo administration. PROTIFAR contains, in addition to tyrosine, other amino acids that are not precursors of NE. FANTOMALT does not contain any amino acids and is therefore assumed not to influence NE synthesis. As a consequence of dose and dosage form restrictions imposed by the army's medical supervisor, only administrations of tyrosine as naturally occurring in food were permitted. A second restriction in the present study was that we were not allowed to obtain plasma amino acid levels after the subjects had consumed the test diets. The army's medical supervisor decided that it was ethically unjustified to obtain blood samples from the volunteers. Permission was given only for the collection of urine samples, because this is a noninvasive procedure.

Data Analysis

With respect to the MCT, the number of correct and incorrect responses was averaged across all trials and blocks, resulting in a correct and an incorrect score for each subject. The RMS tracking scores during the TT and the DT were computed for each of the fourteen 30-s intervals and were averaged across the entire task, with the exception of the first and last interval. After the squared interval values had been averaged, the root of the average was computed. The performance on the CMT could not be assessed. However, as a consequence of the extreme degree of fatigue, most of the subjects were unable to retain the target letters during the task, which made it impossible to determine the quality of the task performance.

Possible differences in treatment outcome between placebo and tyrosine groups were assessed by one-way Analyses of Covariance (ANCOVA) where group was the independent factor and pretest score served as the covariate. The RMS tracking scores during the 14 subsequent intervals were analyzed by means of ANCOVAs where group was the independent factor and interval was the repeated measurement factor. Owing to the absence of any variance in task-interruption time values at the pretest, only the task-interruption time values of the posttest were analyzed using one-way Analyses of Variance.

In other studies tyrosine supplementation has been found to decrease blood pressure and improve psychomotor performance [15,33,37,43]. Therefore, statistical tests were one-tailed, except for the 14 repeated RMS scores, the MHPG data and the scores from the questionnaires for which no hypothesis had been formulated.

RESULTS

Perceptual-motor Tasks

The number of correct responses on the MCT was significantly higher at the posttest in the tyrosine group than in the placebo group ($F(1,18) = 4.11, p < 0.05$). In contrast, the number of

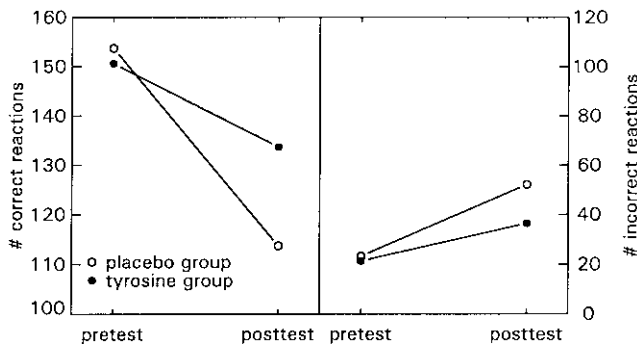


FIG. 1. Memory comparison task: mean number of correct and incorrect reactions of the placebo ($n = 11$) and tyrosine ($n = 10$) groups during pretest and posttest.

incorrect responses observed in the tyrosine and placebo groups was not significantly different (see Fig. 1).

In addition, the tyrosine group had a better RMS tracking score on the TT at the posttest than the placebo group ($F(1,18) = 6.14, p < 0.05$) (see Fig. 2). The mean RMS values for the 14 separate intervals of the TT in the tyrosine and placebo groups are shown in Fig. 3. The ANCOVA indicated an interaction between Groups and Intervals ($F(13,234) = 1.64, p = 0.08$). This result suggests that the tyrosine group performed increasingly better on the TT than the placebo group. The percentages of task interruption times are depicted in Fig. 4. The ANCOVA showed that the posttest task-interruption time value of the tyrosine group was lower than that of the placebo group ($F(1,18) = 5.10, p < 0.05$). This result indicates that the tyrosine group had fewer lapses of attention during the posttest. With respect to the DT, the mean RMS tracking scores at the posttest were not significantly different between the two groups (see Fig. 2). In contrast, for the separate RMS interval values a significant interaction was found between Groups and Intervals ($F(13,234) = 2.16, p < 0.05$), indicating an improving performance for the tyrosine group over time (Fig. 3). The task-interruption time values of the DT in both experimental groups are shown in Fig. 4. The posttest task-interruption time tended to be higher in the placebo group than in the tyrosine group ($F(1,19) = 2.78, p = 0.06$).

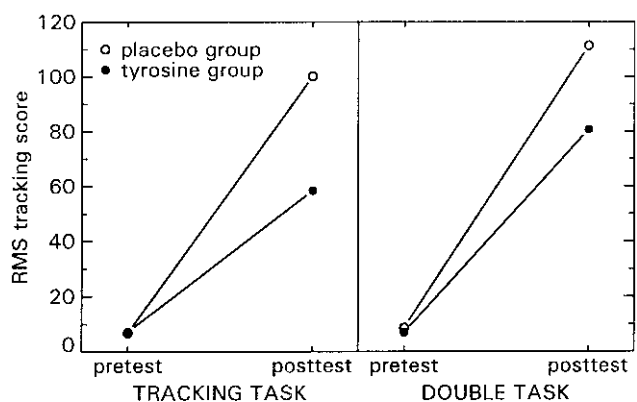


FIG. 2. Tracking task and double task: mean root mean square (RMS) tracking scores of the placebo ($n = 11$) and tyrosine ($n = 10$) groups during pretest and posttest.

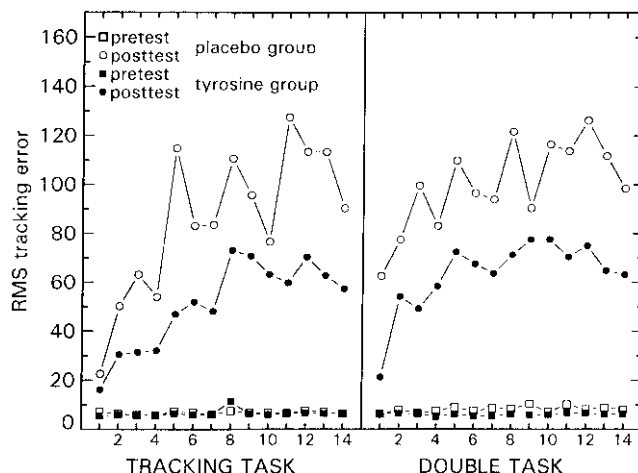


FIG. 3. Tracking task and double task: mean root mean square (RMS) tracking scores for each period of the placebo ($n = 11$) and tyrosine ($n = 10$) groups during pretest and posttest.

Questionnaires

The mean scores on the POMS scales, including the results of the ANCOVAs, are summarized in Table 1. At the posttest session, there were no differences in the scores between the tyrosine and placebo groups on any of the scales. Similarly, with respect to the state anxiety scores on the STAI, no significant group differences were found (see Table 2).

Disregarding group differences, significant changes in a number of scores on the POMS and the STAI across test days were found. The fatigue was significantly higher and the vigor score significantly lower at the posttest than at the pretest (fatigue, pretest: 3.9 ± 3.0 ; posttest: 14.3 ± 5.2 ; $t(12) = -7.82, p < 0.001$; vigor, pretest: 12.5 ± 4.6 ; posttest: 8.1 ± 4.7 ; $t(12) = 4.34, p = 0.001$). Also the tension and anxiety scores were significantly higher at the posttest than at the pretest (tension, pretest: 2.6 ± 2.9 ; posttest: 5.1 ± 2.1 ; $t(12) = -2.65, p = 0.02$; anxiety, pretest: 29.9 ± 9.8 ; posttest: 41.6 ± 8.3 ; $t(12) = -3.88, p = 0.002$).

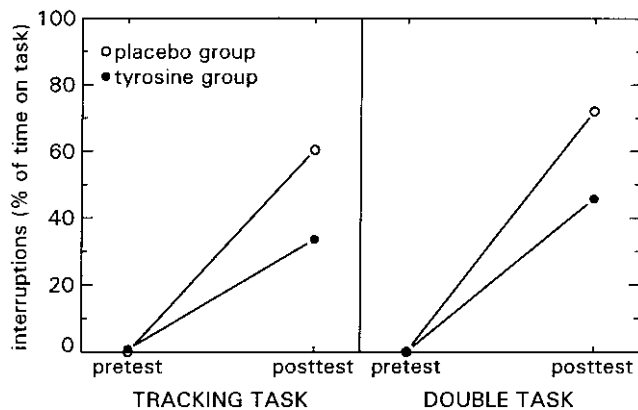


FIG. 4. Tracking task and double task: mean percentage of task interruption time of the placebo ($n = 11$) and tyrosine ($n = 10$) groups during pretest and posttest.

TABLE 1

RESULTS OF ANCOVAS ON THE POMS SCORES OF THE PLACEBO ($n = 7$) AND TYROSINE ($n = 6$) GROUPS AT PRETEST AND POSTTEST

Subscale	Group	Pretest	Posttest	ANCOVA (two-tailed)
Depression	Placebo	0.28	2.14	n.s.
	Tyrosine	3.33	2.50	
Fatigue	Placebo	3.71	14.00	n.s.
	Tyrosine	4.17	14.67	
Vigor	Placebo	14.43	8.71	n.s.
	Tyrosine	10.33	7.33	
Anger	Placebo	2.71	6.00	n.s.
	Tyrosine	5.67	6.67	
Tension	Placebo	2.42	5.71	n.s.
	Tyrosine	2.83	4.50	

Physiological and Biochemical Assessments

With respect to DBP, no significant differences at the posttest were found. However, the tyrosine group had a lower systolic blood pressure (SBP) than the placebo group on the posttest (see Table 3). The posttest MHPG assessments for the two groups were not significantly different. This applies to the MHPG-creatinine ratio as well as to MHPG itself (see Table 4).

DISCUSSION

The aim of the present study was to investigate whether supplementation with a drink containing tyrosine during a highly demanding combat training course would reduce the negative effects of stress and fatigue on cognitive performance and emotional well-being. In addition, the effects of tyrosine on blood pressure and on the concentration of the NA metabolite MHPG were assessed. During the posttest, which took place 6 days after the start of the combat course and 5 days after tyrosine supplementation began, the tyrosine group was found to perform better than the placebo group on several tests, specifically an MCT and a TT. Only in the DT was there no significant difference between groups at the posttest on the RMS tracking score; however, the direction of the difference between means was similar to that found for the TT. The lack of a significantly better DT tracking performance in the tyrosine group may be due to the time of presentation (last task) and to the complexity of the DT. These factors may have reduced the motivation of the subjects to perform well, resulting in increased error variances.

The present findings support the notion that the supplementation of tyrosine may reduce the cognitive effects of psychosocial stress and fatigue. The cognitive performance in the tyrosine group was higher than in the placebo group on an MCT and a TT. With

TABLE 2

RESULTS OF ANCOVAS ON STATE ANXIETY SCORES OF THE PLACEBO ($n = 7$) AND TYROSINE ($n = 6$) GROUPS AT PRETEST AND POSTTEST

Scale	Group	Pretest	Posttest	ANCOVA (two-tailed)
State anxiety	Placebo	24.14	40.57	n.s.
	Tyrosine	36.67	42.83	

TABLE 3

RESULTS OF ANCOVAS ON BLOOD PRESSURE VALUES OF THE PLACEBO ($n = 11$) AND TYROSINE ($n = 10$) GROUPS AT PRETEST AND POSTTEST

Subscale	Group	Pretest	Posttest	ANCOVA (one-tailed)
Systolic blood pressure	Placebo	139.73	132.83	$p < 0.05$
	Tyrosine	136.20	122.10	
Diastolic blood pressure	Placebo	72.73	72.00	n.s.
	Tyrosine	70.20	68.20	

respect to the TT, differences between groups increased as the task continued. In addition, the percentage of time that the subjects were not able to perform the TT, probably due to attentional lapses, was larger in the placebo group. The results can be explained by the action of tyrosine, which prevents the depletion of NA in the brain [5,15,33].

However, the possible influence of tyrosine on noradrenergic brain activity could not directly be demonstrated by a difference in the MHPG assessments in urine. As 60% of the MHPG concentration is of central origin, a larger MHPG concentration in the tyrosine group than in the placebo group would have been indicative of a tyrosine-induced increase in NE metabolism in the brain. The presence of other amino acids in the protein-rich mixture, which contained 2 g tyrosine instead of administration of pure tyrosine (e.g., in the form of tablets) prevents a definitive conclusion of the effects of tyrosine on noradrenergic brain activity from being made. Also, it must be pointed out that the drink had a lower dose of tyrosine than the standard administered dose of 100–150 mg/kg (i.e., ± 6 –12 g) [5,15,33].

The plasma ratio of a specific amino acid to the other LNAAs is crucial for reaching the brain. Therefore, the LNAAs that were present in high quantities in the mixture compete with tyrosine for passage across the blood—brain barrier. These LNAAs were (iso)leucine, phenylalanine and valine. Although it can be assumed that these amino acids may have an additional influence on brain functioning, the lower blood pressure that was found in the tyrosine group is likely to be the consequence of tyrosine. Moreover, stress-induced depletion of NE can be counteracted only by a precursor of NE (i.e., tyrosine). Therefore, it seems quite likely that the availability of L-tyrosine played an important role in the improvement of cognitive performance. The activity of the other amino acids may have had an additional influence on brain functioning. Because the tyrosine-rich drink was also rich in calories, the placebo had to contain an equivalent number of calories. Therefore it was

TABLE 4

RESULTS OF ANCOVAS ON MHPG VALUES OF THE PLACEBO ($n = 10$) AND TYROSINE ($n = 9$) GROUPS AT PRETEST AND POSTTEST

Subscale	Group	Pretest	Posttest	ANCOVA (two-tailed)
MHPG/creatinine ratio	Placebo	0.138	0.179	n.s.
	Tyrosine	0.138	0.166	
MHPG	Placebo	2.144	2.370	n.s.
	Tyrosine	1.493	1.992	

decided to supplement the placebo with a drink consisting of carbohydrates with the same number of calories as the tyrosine-rich drink. Although not a real placebo, we assumed that this drink, which does not affect NE synthesis, would have no effect on cognitive functioning. Only possible effects on physical performance could be expected. However, some investigators believe that carbohydrate consumption may result in a relative increase in the LNAA TRP, which may be followed by an increased serotonin synthesis and release. This may adversely affect cognitive function [23]. Based on animal studies, a 50–100% increase in plasma TRP/NAA is assumed to be sufficient to cause significant changes in brain 5-hydroxytryptamine (5-HT) synthesis in humans [2]. The data relating brain serotonin and carbohydrate meals are based on rats and not on humans [44]. Indeed, it is well established that carbohydrate meals raise brain tryptophan and serotonin in rats with empty stomachs. The effect that carbohydrate ingestion has on the synthesis and release of serotonin may only apply to fasting organisms that consume a single meal of carbohydrates to ensure that blood insulin levels are low before carbohydrate consumption [17]. In humans the changes that occur in the plasma tryptophan ratio are much smaller than those that occur in rats, and they may be too small to influence brain serotonin significantly [44]. The results of several studies on plasma amino acid responses indicate that carbohydrate meals do not alter TRP/NAA ratio or 5-HT synthesis in humans [3,4,38]. A review on animal and human studies concludes that, owing to the limited data available on humans, any effects of carbohydrate meals on human brain serotonin are likely to be negligible [44]. Regarding dietary effects on behavioral measures, several studies [13,14,36] did not find any significant effects of high carbohydrate meals on mood and performance. After *post-hoc* splitting of sexes, Spring et al. [36] found only that women were more sleepy and tense and men were less sleepy and more calm after a carbohydrate meal than after a protein meal. These studies support the notion that the placebo drink did not impair cognitive function.

Overall, the present findings support the notion that tyrosine has a stress-reducing effect, although it is possible that amino acids other than tyrosine may have contributed to this effect. The tyrosine-rich drink influenced the performance on the MCT in terms of reaction times and number of incorrect responses. Task interruption periods were not observed during the MCT. Tyrosine administration improved tracking performance (TT) and reduced the number and duration of task interruptions.

The present study also partially confirms the finding by Deijen and Orlebeke that tyrosine reduces blood pressure [15]. In contrast to the reduction in DBP found by Deijen and Orlebeke, the present findings indicate a tyrosine-induced reduction in SBP. This reduction in SBP may either reflect a direct influence of tyrosine on the blood pressure regulation as a result of changes in central NE levels [43] or be due to the indirect consequences of stress reduction.

Tyrosine administration was not found to affect mood state in the present study. However, only 13 of the 21 subjects returned the questionnaires. Therefore, no definite conclusion can be drawn concerning findings of the questionnaires, except that the combat training course significantly increased fatigue, tension and anxiety.

The present results support the notion that tyrosine administration may also reduce the negative effects of “real-life” stress on cognitive performance under operational conditions. However, more human studies on the effects of “pure tyrosine” supplementation on mental functioning under stress are needed to provide further evidence for this claim.

ACKNOWLEDGEMENT

This study was performed by order of the Department of Behavioral Sciences of the Royal Netherlands Army.

REFERENCES

1. Abercrombie, E. D.; Jacobs, B. L. Single-unit response of noradrenergic neurons in the locus coeruleus of freely-moving cats: Acutely presented stressful and nonstressful stimuli. *J. Neuroscience* 7:2837; 1987.
2. Ashley, D. V. M. Factors affecting the selection of protein and carbohydrate from a dietary choice. *Nutr. Res.* 5:555–571; 1985.
3. Ashley, D. V. M.; Barclay, D. V.; Chauffard, F. A.; Moennoz, D.; Leathwood, P. D. Plasma amino acid responses in humans to evening meals of different composition. *Am. J. Clin. Nutr.* 36:143–153; 1982.
4. Ashley, D. V.; Leathwood, P. D. Meals which may influence brain serotonin metabolism in man. *Int. J. Vit. Nutr. Res.* 53:222; 1983.
5. Banderet, L. E.; Lieberman, H. R. Treatment with tyrosine, a neurotransmitter precursor, reduces environmental stress in humans. *Brain Res. Bull.* 22:759–762; 1989.
6. Beatty, W. W.; Rush, R. A. Spatial working memory in rats: Effects of monoaminergic antagonists. *Pharmacol. Biochem. Behav.* 18:7–12; 1983.
7. Beninger, R. J. Dissociating the effects of altered dopaminergic function on performance and learning. *Brain Res. Bull.* 23:365–371; 1989.
8. Bles, W.; De Graaf, B.; Keuning, J. A.; Ooms, J.; De Vries, M. H.; Wientjes, C. J. E. Experiments on motion sickness aboard the M. V. “Zeevakkel” (Report IZF 1991 A-24). Soesterberg, The Netherlands: TNO Institute for Perception; 1991.
9. Boer, L. C.; Gaillard, A. W. K.; Jorna, P. G. A. M. De Taskomat-een batterij van informatieverwerkingstaken (Report IZF 1987-2). Soesterberg, The Netherlands: TNO Institute for Perception; 1987.
10. Bradley, V. A.; Welch, J. L.; Dick, D. J. Visuospatial working memory in Parkinson’s disease. *J. Neurol. Neurosurg. Psychiat.* 52:1228–1235; 1989.
11. Brady, K.; Brown, J. W.; Thurmond, J. B. Behavioral and neurochemical effects of dietary tyrosine in young and aged mice following cold-swim stress. *Pharmacol. Biochem. Behav.* 12:667–674; 1980.
12. Brozoski, T. J.; Brown, R. M.; Rosvold, H. E.; Goldman, P. S. Cognitive deficit caused by regional depletion of dopamine in prefrontal cortex of rhesus monkey. *Science* 205:929–932; 1979.
13. Christensen, L.; Redig, C. Effect of meal composition on mood. *Behav. Neurosci.* 107:346–353; 1993.
14. Deijen, J. B.; Heemstra, M. L.; Orlebeke, J. F. Dietary effects on mood and performance. *J. Psychiat. Res.* 23:275–283; 1989.
15. Deijen, J. B.; Orlebeke, J. F. Effect of tyrosine on cognitive function and blood pressure under stress. *Brain Res. Bull.* 33:319–323; 1994.
16. Dimsdale, J. E.; Moss, J. Plasma catecholamines in stress and exercise. *JAMA* 243:340–342; 1980.
17. Fernstrom, J. D. Carbohydrate ingestion and brain serotonin synthesis: Relevance to a putative control loop for regulating carbohydrate ingestion, and effects of aspartame consumption. *Appetite* 11:35–41; 1988.
18. Gibb, W. R. G. Dementia and Parkinson’s disease. *Br. J. Psychiat.* 154:596–614; 1989.
19. Gibson, C. J. Dietary control of retinal dopamine synthesis. *Brain Res.* 382:195–198; 1986.
20. Gibson, C. J. Alterations in retinal tyrosine and dopamine levels in rats consuming protein or tyrosine-supplemented diets. *J. Neurochem.* 50:1769–1774; 1988.
21. Glavin, G. B. Stress and brain noradrenaline: A review. *Behav. Neurosci. Rev.* 9:233; 1985.
22. Lehnert, H.; Reinstein, D. K.; Strowbridge, B. W.; Wurtman, R. J. Neurochemical and behavioral consequences of acute uncontrollable stress: Effects of dietary tyrosine. *Brain Res.* 303:215–223; 1984.
23. Lehnert, H.; Wurtman, R. J. Amino acid control of neurotransmitter synthesis and release: Physiological and clinical implications. *Psychother. Psychosom.* 60:18–32; 1993.

24. Levin, E. D.; Galen, D.; Ellison, G. D. Chronic haloperidol effects on radial arm maze performance and oral movements in rats. *Pharmacol. Biochem. Behav.* 26:1–6; 1987.
25. McNair, D. M.; Lorr, M.; Droppleman, L. F. *Manual of the Profile of Mood States*. San Diego: Educational and Industrial Testing Service; 1981.
26. Melamed, E.; Glaser, B.; Growdon, J. H.; Wurtman, R. J. Plasma tyrosine in normal humans: Effects of oral tyrosine and protein-containing meals. *J. Neural. Transm.* 47:299–306; 1980.
27. Moller, S. E. Effect of various oral protein doses on plasma neutral amino acid levels. *J. Neural. Transm.* 61:183–191; 1985.
28. Murphy, D. L.; Redmond, D. E. The catecholamines: Possible role in affect, mood and emotional behavior in man and animals. In: Freidhoff, A. J., ed. *Catecholamines and behavior*. New York: Plenum Press; 1975:73–117.
29. Odink, J.; Wientjes, C. J. E.; Thissen, J. T. N. M.; Beek, E. J. van der; Kramer, F. M. Type A behavior, borderline hyperventilation and psychological, psychosomatic and neuroendocrine responses to mental task load. *Biol. Psychol.* 25:107–118; 1987.
30. Ploeg, H. M. van der; Defares, P. B.; Spielberger, C. D. Handleiding bij de Zelf-Beoordelings Vragenlijst ZBV: Een Nederlandstalige bewerking van de Spielberger State-Trait Anxiety Inventory. Lisse: Swets & Zeitlinger BV; 1980.
31. Rossetti, Z. L.; Portas, C.; Pani, L.; Carboni, S.; Gessa, G. L. Stress increases noradrenaline release in the rat frontal cortex: Prevention by diazepam. *Eur. J. Pharmacol.* 176:229–231; 1990.
32. Shacham, S. A shortened version of the Profile of Mood States. *J. Pers. Assess.* 47:305–306; 1983.
33. Shurtleff, D.; Thomas, J. R.; Schrot, J.; Kowalski, K.; Harford, R. Tyrosine reverses a cold-induced working memory deficit in humans. *Pharmacol. Biochem. Behav.* 47:935–941; 1994.
34. Smith, A.; Nutt, D. Noradrenaline and attention lapses. *Nature* 380: 291; 1996.
35. Spielberger, C. D. *Test manual for the State-Trait Anxiety Inventory—STAI form Y*. Palo Alto, CA: Consulting Psychologists Press; 1980.
36. Spring, B.; Maller, O.; Wurtman, J.; Digman, L.; Cozolino, L. Effects of protein and carbohydrate meals on mood and performance: Interactions with sex and age. *J. Psychiat. Res.* 17:155–167; 1983.
37. Sved, J. D.; Fernstrom, J. D.; Wurtman, R. J. Tyrosine administration reduces blood pressure and enhances brain norepinephrine release in spontaneously hypertensive rats. *Proc. Natl. Acad. Sci. USA* 76:3511–3514; 1979.
38. Teff, K. L.; Young, S. N.; Marchand, L.; Botez, M. I. Acute effect of protein or carbohydrate breakfasts on human cerebrospinal fluid monoamine precursor and metabolite levels. *J. Neurochem.* 52:235–241; 1989.
39. Topall, G.; Laborit, H. Brain tyrosine increases after treating with prodrugs: Comparison with tyrosine. *J. Pharm. Pharmacol.* 41:789–791; 1989.
40. Wald, F. D. M.; Mellenbergh, G. J. De verkorte versie van de Nederlandse vertaling van de Profile of Mood States (POMS). *Ned. Tijdschr. Psychol.* 45:86–90; 1990.
41. Weiss, J. M. Stress-induced depression: Critical neurochemical and electrophysiological changes. In: Madden, J., ed. *Neurobiology of learning, emotion and affect*, vol IV. New York: Raven Press; 1991: 123–154.
42. Whitehouse, P. J. Clinical and neurochemical consequences of neuronal loss in the nucleus basalis of Meynert in Parkinson's disease and Alzheimer's disease. In: Yahr, M. D.; Bergman, K. J., eds. *Advances in neurology*. New York: Raven Press; 1986:393–397.
43. Yamori, Y.; Fujiwara, M.; Horie, R.; Lovenberg, W. The hypotensive effect of centrally administered tyrosine. *Eur. J. Pharmacol.* 68:201–204; 1980.
44. Young, S. N. Some effects of dietary components (amino acids, carbohydrate, folic acid) on brain serotonin synthesis, mood and behavior. *Can. J. Physiol. Pharmacol.* 69:893–903; 1991.