

Tyrosine Improves Working Memory in a Multitasking Environment

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THOMAS, J. T., P. A. LOCKWOOD, A. SINGH AND P. A. DEUSTER. *Tyrosine improves working memory in a multitasking environment*. PHARMACOL BIOCHEM BEHAV 64(3) 495–500, 1999.—Previous studies indicate that tyrosine may prove useful in promoting improved performance in situations in which performance is compromised by stress. To extend the generality of previous tyrosine findings, the present study examined the effects of tyrosine ingestion on performance during both a Multiple Task and a Simple Task battery. The multiple task battery was designed to measure working memory, arithmetic skills, and visual and auditory monitoring simultaneously, whereas the simple task battery measured only working memory and visual monitoring. Ten men and 10 women subjects underwent these batteries 1 h after ingesting 150 mg/kg of l-tyrosine or placebo. Administration of tyrosine significantly enhanced accuracy and decreased frequency of list retrieval on the working memory task during the multiple task battery compared with placebo. However, tyrosine induced no significant changes in performance on the arithmetic, visual, or auditory tasks during the Multiple Task, or modified any performance measures during the Simple Task battery. Blood levels of ACTH and cortisol were not, but heart rate and blood pressure were significantly increased during the performance tasks. The present results indicate that tyrosine may sustain working memory when competing requirements to perform other tasks simultaneously degrade performance, and that supplemental tyrosine may be appropriate for maintaining performance when mild to severe decrements are anticipated. © 1999 Elsevier Science Inc.

Tyrosine Working memory Performance Catecholamines Stress

TYROSINE, a large neutral amino acid normally present in protein foods, is a precursor of the catecholamine (CA) neurotransmitters, dopamine, norepinephrine, and epinephrine (2,6,20,24,25). Tyrosine hydroxylase (TH) serves as the rate-limiting enzymatic step in the CA biosynthetic pathways (6–8,20,21). Synthesis and metabolism of the tyrosine-dependent neurotransmitters affect a variety of central and peripheral functions. In particular, dopamine neurons projecting to the mesoprefrontal cortex are thought to be involved in working memory and the stress response (20,21). Neurochemical changes in specific brain structures during exposure to certain stressors include an increase in turnover and a decrease in the absolute levels of CA (2,6,7,20,21,25). Acute exposure to stressful events, in addition to CA changes, is also associated with behavioral and cognitive changes (2–4,9–15). In animals, changes include a decrease in environmental exploration and interaction (20) and impairments in working memory (13,14).

In humans, working memory impairments (12) and attentional narrowing (3,4) have been observed during stressful conditions.

Importantly, administration of tyrosine has been shown to improve performance on a variety of tasks and diminish behavioral deficits associated with stressful conditions (1–4,9–15,22,23). For example, tyrosine has been shown to improve cold-induced decrements in working memory in both animals (14) and humans (12,15); improve subject performance on stress-sensitive attention tasks (3); improve attentional focus in the presence of a distractor (3); and attenuate performance decrements and adverse mood states associated with acute exposure to cold and hypoxia (2–4,10,13). However, to date, no studies have been reported that suggest that tyrosine may affect performance under conditions of minimal to mild stress.

Because supplemental tyrosine administration has been shown to improve the performance of simple tasks in the pres-

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ence of moderately stressful distracting stimuli (3), it is possible that performance of more complicated tasks or multiple tasks simultaneously, that may induce minimal stress, could also be enhanced by supplemental tyrosine. One such multiple task cognitive battery, the SYNWORK (5), was created by the Office of Military Performance Assessment Technology in response to a need for a performance test with a complexity between typical performance assessment batteries and complex task-specific simulators. Performance assessment batteries have tended to focus on only one aspect of performance at a time (i.e., memory, reaction time), and therefore, have not provided information about interactive task performance in more dynamic and complex situations.

The purpose of the present study was to examine the potential effects of tyrosine administration on a test battery designed to measure working memory, visual and auditory monitoring, and arithmetic skill performance simultaneously in a multiple task environment. Additionally, the effects of tyrosine administration on performance during a modified, more simple version of SYNWORK, which involved only two tasks—working memory and visual monitoring—were examined for comparison.

METHOD

Subjects

Ten men and 10 women subjects were recruited from active duty personnel and government civilians in the Washington, DC metropolitan area. Subjects were healthy, nonsmokers, free of any regular medications or drugs, and had 20/20 or corrected 20/20 vision. The subjects averaged 28.8 ± 0.7 (mean \pm SEM) years of age (range = 20–38), 176.0 ± 2.1 cm of height (range = 157.5–203.0), and 75.0 ± 2.6 kg (range = 46.5–104) of weight. The nature and risks of the study were explained and each subject signed an Informed Consent form, medical history form, and received a physical examination. This study was approved by the Committee for the Protection of Human Subjects of the Naval Medical Research Institute and the Institutional Review Board of the Uniformed Services University of the Health Sciences.

Testing

Testing was conducted in a sound-proof room utilizing a computer with a color display monitor to present stimuli and record responses. Subjects were familiarized with the tasks during six practice sessions completed on 6 different days; each practice session lasted 30 min. Within 1 week after completing the final practice session, subjects began the first test session. At the beginning of each test session the subject was weighed, seated, and then a catheter was placed in the brachial vein of the nondominant arm. The subject remained sitting quietly in the soundproof room for 15 min, after which blood pressure and pulse rate were recorded and a blood sample was obtained.

Using a crossover double-blind procedure, the subject then ingested a mixture of 150 mg/kg l-crystalline tyrosine with 70 g applesauce or a placebo (7 g microcrystalline cellulose with applesauce). Sixty minutes postingestion, the subject began the tasks. The subjects were exposed to two different tasks. One task consisted of the complete SYNWORK battery (Multiple Tasks), which contained four simultaneous subtasks), and the second task was a modified battery that con-

sisted of only two of the subtasks: the Sternberg Memory task and the Visual Monitoring task (Simple Task Battery). The Multiple and Simple Task versions of the battery were enforced for 15 min each, for a total of 30 min. As the tasks were counterbalanced to control for order effects, half of the subjects completed the Multiple Task battery first, followed by the Simple Task battery, while the other half completed the tasks in the opposite order. For the second test session, the subject ingested the mixture not consumed during the first test session, and completed the attention tasks in the same order as during the first testing session. The two testing sessions were separated by no more than 1 week.

Blood samples were drawn, and blood pressure and pulse rates were recorded at –5, 60, 90, and 150 min relative to substance ingestion. Additionally, blood pressure and pulse rates were recorded at 10-min intervals during execution of the performance battery.

Performance Tests

Multiple Task Battery: SYNWORK. The Multiple Task battery consisted of four simultaneously occurring tasks on which performance was evaluated based on accumulated points. Table 1 provides an overview of the data gathered from each task relative to the performance measures. For the four tasks, the computer screen was separated into four quadrants. The Sternberg Memory Task (SMT) was presented in the upper left quadrant; an arithmetic task in the upper right quadrant; a visual monitoring task (VMT) in the lower left quadrant; and an auditory monitoring task in the lower right quadrant.

TABLE 1
PERFORMANCE INFORMATION EXTRACTED FROM
MULTITASKING BATTERY

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| 1. Sternberg Memory Task (SMT) |
| a. Percentage of correct answers |
| b. Mean reaction time latency for correct responses |
| c. Mean reaction time latency for incorrect responses |
| d. Mean reaction time latency for correct and incorrect responses combined |
| e. Number of times master list of letters was retrieved |
| 2. Arithmetic Task |
| a. Number of problems attempted |
| b. Number of correct answers |
| c. Percentage of correct answers (number of correct answers divided by the number attempted) |
| d. Mean reaction time latency for correct responses |
| e. Mean reaction time latency for incorrect responses |
| f. Mean reaction time latency for correct and incorrect responses combined |
| 3. Cursor Reset Task |
| a. Number of times subject reset the cursor back to the center |
| b. Number of times subject allowed cursor to reach the end point (lapses) |
| 4. Tone Detection |
| a. Number of positive tones detected |
| b. Number of times subject incorrectly perceived that a high pitched tone had occurred |
| c. Percentage of high tones correctly detected |
| d. Overall percentage of tones detected |
| e. Mean reaction time detection latency for all tones combined |
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The SMT used in the present study is a procedural version designed to assess working memory (17–19). The task consisted of a list of eight randomly selected letters displayed in a box in the top portion of the quadrant; these letters were visible for 5 s, after which they were replaced by the words “RETRIEVE LIST.” At the beginning of each trial, a sample letter was displayed in a box in the center of the quadrant. The subject was required to indicate whether the letter in the center of the screen matched one of the letters in the original list by clicking the mouse on either the “YES” or “NO” box at the bottom of the window. After a response occurred, the sample letter disappeared and a new letter was displayed every 15 s. If the response was correct, 10 points were added to the score. If the response was incorrect or not obtained within 15 s, 10 points were deducted from the score. The total number of letters presented during this test was approximately 60.

Number problems were presented for the arithmetic task; each problem contained three numbers less than 1000 that were to be added together. Four boxes, one for each numeric column in the solution of the problem, were located below the three numbers to be added. The subject’s task was to adjust the answer by clicking a “+” or “–” sign located below each character of the answer. When completed, the subject clicked a box at the bottom of the quadrant labeled “DONE,” resulting in the presentation of a new problem. Ten points were added to the subject’s total score for each correct response, and 10 points were subtracted for each incorrect response.

For the visual monitoring task (VMT), there was a pointer that moved from the center of a graduated scale, 201 pixels in length, toward either end at a fixed rate of 50 ms per pixel. Clicking the mouse on the “RESET” box at the top of the screen reset the pointer to the center of the scale. The subject’s task was to prevent the pointer from reaching the end of the scale. The number of points awarded for each reset were proportional to the distance of the pointer from the center at the time of reset. Subjects could receive as few as one point for resets that occurred when the pointer was within 10% of the center and as many as 10 points when the pointer was within 10% of the end of the scale. Ten points were subtracted per second if the pointer reached the end of the scale and was not reset within 2 s. To maximize the number of points received, the subject should have attempted to reset the cursor at the point furthest from the center, but before the pointer reached the end of the scale.

During the auditory monitoring task, a brief low (931 Hz) or high (1234 Hz) tone was presented every 5 s; high tones occurred 20% of the time. The subject’s task was to click on a box at the top of the quadrant labeled “HIGH SOUND REPORT” each time a high tone was presented; no response was required after the presentation of a low tone. The subject was awarded 10 points for each correct response and penalized 10 points for each error.

Simple Task Battery: Simplified Sternberg Memory Task/Visual Monitoring Task. To measure working memory and visual monitoring performance during a simpler task, the SMT and VMT were isolated from the SYNWORK battery and presented simultaneously. The SMT was presented in the upper half and the VMT was presented in the lower half of the computer monitor. The parameters for the SMT were similar to those for the Multiple Task battery except that the random appearance of each letter occurred every 10 s instead of every 15 s. Thus, the total number of letters presented during this test was approximately 90. In addition, the pointer on the VMT moved at 500 ms per pixel instead of the 50 ms speed as in the complete SYNWORK battery.

Blood Sample Collections and Analyses

Blood samples were collected with syringes and immediately transferred to appropriate tubes: chilled EDTA tubes (1.6 mg EDTA/ml blood) for ACTH and cortisol analyses; room temperature EDTA tubes for the determination of hemoglobin (Hb) and hematocrit (Hct) levels; and chilled tubes containing heparin (15 IU Heparin/ml) and sodium fluoride (1 mg fluoride) for measuring plasma glucose and lactate. Tubes for ACTH and cortisol were placed on ice until plasma was separated by centrifugation at 8–10°C at 3000 rpm for 15 min; these samples were stored at –50°C until assayed. Blood samples for Hb and Hct were assayed immediately, and plasma samples for glucose and lactate were refrigerated and assayed within 24 h.

Lactate and glucose concentrations were determined in duplicate (YSI Select 2700 Analyzer, Yellow Springs Instrument Co., Inc., Yellow Springs, OH). Hb and Hct were determined in triplicate by the cyanomethemoglobin and microcapillary methods, respectively. Plasma cortisol was measured by radioimmunoassay (RIA) (Diagnostic Products Corporation, Webster, TX). Plasma ACTH concentrations were assayed by a two-site immunoradiometric assay (IRMA) (Nichols Institute Diagnostics, San Juan Capistrano, CA). Detection limits of the assays were 8.3 nmol/l for cortisol and 0.22 pmol/l for ACTH. The intraassay coefficients of variation (CV) for cortisol and ACTH were less than 6 and 8%, respectively. The interassay CVs were less than 10 and 15% for cortisol and ACTH, respectively. All samples from a single subject were analyzed in one assay to eliminate interassay variations, and all values were within the linear range of the standard curve.

Data Analyses

Data were analyzed as a factorial design with repeated measures; the factors considered were treatment, gender, and time. A multivariate general linear model was used. When significant effects were detected by MANOVA, Duncan’s multiple range test was used to identify differences across time and treatments. Significance was set at the 0.05 level (see Table 1 for a description of the dependent measures that were extracted from the SYNWORK battery). Data are presented as the mean (\pm SEM).

RESULTS

Performance on Simple and Multiple Task Batteries

Figure 1 presents total points accumulated on the Multiple and Simple Task batteries under tyrosine and placebo conditions. Overall, more points were accumulated during the Simple Task compared to the Multiple Task battery. No significant main effect of tyrosine was obtained on total points accumulated, but a trend toward greater point accumulation under tyrosine was noted for the Multiple Task battery. Inspection of the SMT data indicated an effect of tyrosine on working memory when simultaneous attention to multiple tasks was required. Table 2 compares the results of the SMT during the Multiple and Simple Task batteries. Subjects performed at a higher level on the SMT working memory task when it was paired only with the VMT. Importantly, although working memory performance was reduced when the Multiple Task battery was enforced, subjects obtained a significantly higher percentage of correct responses on the SMT under tyrosine compared with placebo conditions (Table 2).

TABLE 2
COMPARISON BETWEEN THE MULTIPLE AND SIMPLE TASK BATTERIES FOR
PERFORMANCE MEASURES ON THE STERNBERG MEMORY TASK

Performance Measure	Complex Task		Complex Task	
	Placebo	Tyrosine	Placebo	Tyrosine
Correct (%)	83.7 ± 2.3	87.2 ± 2.6*	94.4 ± 1.3	94.6 ± 1.7
List retrieval (number)	1.9 ± 0.5	0.8 ± 0.2*	1.1 ± 0.4	0.7 ± 0.3
Correct latency (s)	3.1 ± 0.2	3.2 ± 0.2	1.3 ± 0.1	1.3 ± 0.1
Error latency (s)	3.5 ± 0.2	3.3 ± 0.4	1.7 ± 0.1	1.4 ± 0.2
Average latency (s)	3.3 ± 0.2	3.2 ± 0.2	1.5 ± 0.1	1.3 ± 0.1

* Significantly different from placebo condition ($p < 0.05$).

Moreover, the number of times subjects had to retrieve the list of letters was significantly less under tyrosine conditions. List retrieval was also lower under tyrosine conditions during the Simple Task battery, but this did not achieve statistical significance ($p = 0.09$). Although correct latency, error latency, and average latency were not altered by tyrosine compared placebo, all aspects of latency were slower for the Multiple as compared to the Simple Task battery. With respect to the VMT, although no effects of tyrosine were observed, the numbers of resets and lapses on the Multiple and Simple Task batteries were consistent with the cursor speed (50 ms vs. 500 ms) and the requirement to attend to other tasks during the Multiple Task battery. The number of lapses on the Multiple Task averaged 0.95 ± 0.4 and 0.89 ± 0.3 times, whereas the number during the Simple Task was only 0.11 ± 0.07 and 0.17 ± 0.09 time, for placebo and tyrosine conditions, respectively.

Table 3 presents the performance data for the Multiple Task battery under conditions of placebo and tyrosine. No other significant main effects due to tyrosine administration were observed for the arithmetic, tone detection, or the cursor

reset task. However, analysis of the data by gender revealed a number of differences with respect to several of the performance tasks. Specifically, women performed at a significantly lower level on the math and tone detection tasks for all measures of performance. For example, the number of arithmetic problems attempted by the men averaged 46.4 ± 3.2 and the average for the women was 32.5 ± 2.9 . The number of tones detected by the men averaged 37.1 ± 2.2 , whereas the number detected by the women was 28.8 ± 2.7 . Similar gender differences were also noted for number and percent correct on the arithmetic and tone detection tasks (data not shown).

In addition to gender effects, significant gender times treatment interactions were observed. For SMT trials on where an incorrect response was recorded, men responded more quickly ($p = 0.038$) during tyrosine (2.7 ± 0.4 s) compared with the placebo condition (3.9 ± 0.4 sec), whereas women responded more slowly during the tyrosine (4.0 ± 0.5 s) compared with placebo (3.2 ± 0.3 s). Furthermore, a significant interaction ($p = 0.007$) was noted for percent correct on the arithmetic task: tyrosine slightly improved performance for the men (placebo: 86.2 ± 1.3 vs. tyrosine: 90.0 ± 1.0), but not the women (placebo: 82.4 ± 4.6 vs. tyrosine: 77.5 ± 5.3).

Endocrine and Physiological Data

The endocrine and physiological data obtained at the various time intervals during the sessions are presented in Table 4. No significant effects were found between tyrosine and placebo treatments for any of the physiological or hormonal data. Although no significant increases over the duration of an experimental session were noted for ACTH and cortisol,

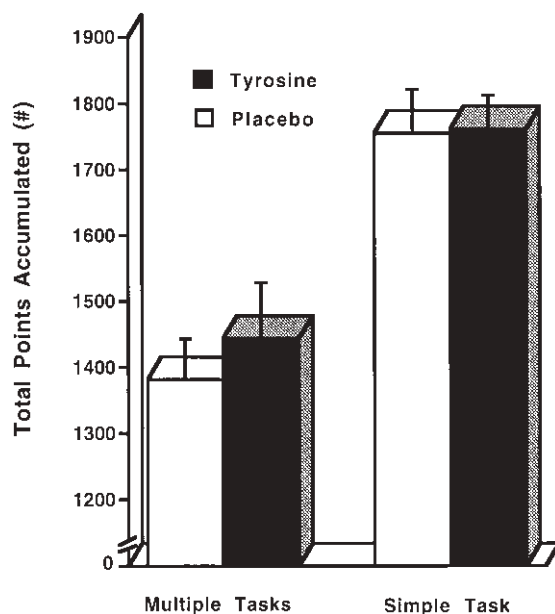


FIG. 1. Mean (\pm SEM) total points accumulated on the Multiple Task and Simple Task batteries under placebo (open bars) and tyrosine (closed bars) conditions. Scores for the Simple Task battery were higher than scores on the Multiple Task battery.

TABLE 3
COMPARISON OF PERFORMANCES MEASURES ON THE
MULTIPLE TASK BATTERY UNDER CONDITIONS OF
PLACEBO AND TYROSINE

	Placebo	Tyrosine
Math task		
Problems attempted (number)	39.1 ± 3.2	41.3 ± 3.8
Correct answers (number)	33.4 ± 2.9	35.5 ± 3.6
Percent correct (%)	84.4 ± 2.3	84.1 ± 2.9
Time/Problem (s)	24.9 ± 2.8	28.1 ± 3.4
Tone task		
Detected (number)	33.1 ± 1.9	33.5 ± 2.0
Detected (%)	78.1 ± 4.9	79.9 ± 4.6
Correct (%)	88.7 ± 3.4	87.3 ± 3.6

TABLE 4
MEAN (\pm SEM) ENDOCRINE AND PHYSIOLOGIC RESPONSES BEFORE, DURING, AND AFTER
THE PERFORMANCE BATTERIES UNDER PLACEBO (P) AND TYROSINE (T) CONDITIONS

Time (min)		-5	60	75	90	150
ACTH (pmol/l)	P	3 \pm 0.5	3 \pm 0.3	ND	4 \pm 0.4	3 \pm 0.4
	T	4 \pm 0.5	3 \pm 0.4	ND	4 \pm 0.6	3 \pm 0.4
Cortisol (nmol/l)	P	391 \pm 46	278 \pm 44	ND	320 \pm 46	331 \pm 44
	T	470 \pm 73	331 \pm 66	ND	398 \pm 66	336 \pm 52
HR (beats/min)*	P	59 \pm 2.0	60 \pm 2.0	67 \pm 2.5	65 \pm 2.0	60 \pm 2.0
	T	59 \pm 2.2	60 \pm 2.5	69 \pm 2.9	64 \pm 2.1	60 \pm 2.4
MAP†	P	84 \pm 1.8	87 \pm 1.7	88 \pm 2.1	87 \pm 2.1	83 \pm 1.6
	T	83 \pm 1.6	87 \pm 1.8	89 \pm 2.1	88 \pm 1.8	84 \pm 1.5

The batteries began at 60 and ended at 90 min.

Values are means \pm SEM; *heart rate (HR) in beats per minute; ND = not determined; †MAP: mean arterial pressure = diastolic pressure + (systolic pressure - diastolic pressure)/3.

significant increases in heart rate and mean arterial pressure were observed.

DISCUSSION

The present findings suggest a unique capability of tyrosine for maintaining working memory under conditions in which physiologic indicators of stress are minimally changed and biochemical indicators are unchanged. Specifically, this study demonstrated that administration of the CA precursor, tyrosine, compared with placebo, served to prevent decrements in working memory, as indicated by performance on the Sternberg Memory Task (SMT), when subjects were required to perform multiple tasks simultaneously. Moreover, retrieval of the list of letters presented during the SMT was significantly less frequent under conditions of tyrosine compared to placebo. In contrast, tyrosine was without significant effect on the SMT when the task was presented in conjunction with only the visual monitoring task. These beneficial effects of tyrosine are consistent with previous research demonstrating that tyrosine improves memory performance under specific experimental or environmental conditions (12,15). However, performance-preserving effects of tyrosine have previously been noted only under conditions of moderate to severe stress.

When CA synthesis and release increase during stressful situations, neurotransmitter depletion may occur in catecholaminergic neurons (2,6-8,20). As such, additional precursor may be required to maintain adequate CA synthesis (6,7). Wurtman et al. (24,25) formulated the hypothesis that tyrosine supplementation should increase CA synthesis and release from catecholaminergic neurons under conditions of stress, because the physiological activity of the neurons were enhanced. In other words, supplemental tyrosine should be effective in situations where dopaminergic/catecholaminergic neurons/receptors are activated, CA synthesis is enhanced, and intraneuronal CA stores are rapidly or chronically depleted (6,20,24,25). Maintaining an adequate supply of tyrosine for CA synthesis may be the biochemical mechanism instrumental in alleviating stress-induced behavioral and cognitive deficits. Based on Wurtman's hypothesis, a number of studies have clearly demonstrated that tyrosine administration improves performance of both animals and humans on a variety of tasks during exposure to specific stressors (2,3,9,12-15). In most cases, performance measures under tyrosine con-

ditions were maintained at prestress levels, whereas in the absence of tyrosine, moderate to severe decrements in performance were noted.

It is important to note that the significant effects of tyrosine in the present study were specifically related to aspects of working memory, including accuracy and the frequency of list retrieval. No significant effects of tyrosine were observed for the arithmetic, auditory, or visual monitoring tasks, and tyrosine did not improve the accuracy of memory performance on the Simple Task battery. These findings are consistent with the notion that tyrosine reversal of stress-induced cognitive performance impairments may be specific to working memory and consistent with previous research on stress-induced changes in working memory performance (12,15). It is possible that these preferential effects of tyrosine on working memory relate to dopamine neurons projecting to the mesoprefrontal cortex. These neurons, thought to be involved in working memory, have unique characteristics that make them highly susceptible to the effects of reductions in precursor availability: a high basal firing rate and rapid neurotransmitter turnover (21). Studies in rats have shown that destruction of the prefrontal cortex, depletion of dopamine, and/or blockade of the dopamine receptors in the mesoprefrontal cortex induce deficits in working memory (21). Moreover, supplemental tyrosine has been shown to increase functional transmitter outflow from mesoprefrontal dopamine neurons under conditions in which the physiological activity of the neurons was selectively enhanced (6,21), and restore depleted levels of both norepinephrine and dopamine in specific brain regions associated with working memory (15,21). Thus, tyrosine's efficacy with respect to working memory may be related to the firing activity of the neurons in the mesoprefrontal cortex and perhaps other catecholaminergic neurons.

We have several lines of evidence that support enhanced neuronal activity. First, the small, but significant changes in heart rate and blood pressure during the Multiple and Simple Task batteries are indicative of sympathetic activation and, hence, mild stress. Moreover, a comparison of the SMT data during the Multiple Task and the Simple Task battery under placebo conditions clearly indicated a lower accuracy on the Multiple Task Battery (multiple: 83.6% vs. simple: 94.6) and increased list retrieval (multiple: 1.9 \pm 0.5 vs. simple: 1.1 \pm 0.4 time). Incorporating the working memory task into a multiple task environment (concurrently with arithmetic, visual, and auditory monitoring tasks) degraded working memory perfor-

mance, and this performance decrement may reflect enhanced physiological activity, and hence, neuronal firing. Finally, although the absence of changes in ACTH and cortisol provide evidence that the HPA axis was not activated, these classic indicators of stress do not necessarily reflect brain activity. Clearly, further work would be required to document an increased neuronal firing.

Although the intention of the study was not to compare men and women, it was necessary to look at possible differences during the analysis phase because tests can be gender biased and tyrosine could exert differential effects. In fact, we did note specific gender differences on two specific performance tasks—the arithmetic and tone detection tasks—even though all subjects had practiced the test and performance results had stabilized. At this point no specific explanations can be offered for the observed results, except that men do tend to outperform women on arithmetic tests (16). It will be important in the future to examine the influence of gender on cognitive function following tyrosine administration.

In summary, this is one of the first indications that tyrosine administration may serve to maintain aspects of performance, specifically, working memory, under conditions of only mild

stress. Administration of tyrosine improved accuracy and reduced the number of times a list of letters was retrieved during a working memory task where working memory was degraded due to the competing requirement of performing other tasks simultaneously. Thus, supplemental tyrosine may be appropriate for maintaining a given level of performance when moderate to severe decrements in performance are anticipated. However, there is no indication that tyrosine has an actual performance enhancing capability, but rather the capability of returning degraded performance close to normal ranges or maintaining prestress performance under stressful scenarios.

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REFERENCES

- Avraham, Y.; Bonne, O.; Berry, E. M.: Behavioral and neurochemical alterations caused by diet restriction—The effect of tyrosine administration in mice. *Brain Res.* 732:133–144; 1996.
- Banderet, L. E.; Lieberman, H. R.: Treatment with tyrosine, a neurotransmitter precursor, reduces environmental stress in humans. *Brain Res. Bull.* 22:759–762; 1989.
- Deijen, J. B.; Orlebeke, J. F.: Effect of tyrosine on cognitive function and blood pressure under stress. *Brain Res. Bull.* 33:319–232; 1994.
- Dollins, A. B.; Krock, L. P.; Storm, W. F.; Wurtman, R. J.; Lieberman, H. R.: L-tyrosine ameliorates some effects of lower body negative pressure stress. *Physiol. Behav.* 57:223–230; 1995.
- Elsmore, T. F.: SYNWORK1: A PC-based tool for assessment of performance in a simulated work environment. *Behav. Res. Methods Instrum. Comput.* 26:421–426; 1994.
- Fernstrom J. D.: Stress and monoamine neurons in the brain. In: Marriott, B. M., ed. *Food components to enhance performance*. Washington, DC: National Academy Press; 1994:161–175.
- Korf, J.; Aghajanian, G. K.; Roth, R. H.: Increased turnover of norepinephrine in the rat cerebral cortex during stress: Role of the locus coeruleus. *Neuropharmacology* 12:933–938; 1973.
- Milner, J. D.; Wurtman, R. J.: Catecholamine synthesis: Physiologic coupling to precursor supply. *Biochem. Pharmacol.* 35:875–881; 1986.
- Neri, D. F.; Wiegmann, D.; Stanny, R. R.; Shappell, S. A.; McCardie, A.; McKay, D. L.: The effects of tyrosine on cognitive performance during extended wakefulness. *Aviat. Space Environ. Med.* 66:313–319; 1995.
- Owasoyo, J. O.; Neri, D. F.; Lamberth, J. G.: Tyrosine and its potential use as a countermeasure to performance decrement in military sustained operations. *Aviat. Space Environ. Med.* 63:364–369; 1992.
- Reinstein, D. K.; Lehnert, H.; Scott, N. A.; Wurtman, R. J.: Tyrosine prevents behavioral and neurochemical correlates of an acute stress in rats. *Life Sci.* 34:2225–2231; 1984.
- Schrot, J.; Thomas, J. R.; Shurtleff, D.: Administration of l-tyrosine prevents cold-induced memory deficits in Naval Special Warfare personnel. Naval Medical Research Institute Technical Report (NMRI 96-11; February, 1996, Bureau of Medicine and Surgery, Department of the Navy.
- Shukitt-Hale, B.; Stillman, M. J.; Lieberman, H. R.: Tyrosine administration prevents hypoxia-induced decrements in learning and memory. *Physiol. Behav.* 59:867–871; 1996.
- Shurtleff, D.; Thomas, J. R.; Ahlers, S. T.; Schrot, J.: Tyrosine ameliorates a cold-induced delayed matching-to-sample performance decrement in rats. *Psychopharmacology (Berlin)* 112:228–232; 1993.
- 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.
- Snow, W. G.; Weinstock, J.: Sex differences among non-brain-damaged adults on the Wechsler Adult Intelligence scales: A review of the literature. *J. Clin. Exp. Neuropsychol.* 12:873–886; 1990.
- Sternberg, S.: High speed scanning in human memory. *Science* 153:652–654; 1966.
- Sternberg, S.: Two operators in character recognition: Some evidence from reaction-time measurement. *Percept. Psychophys.* 2:45–53; 1967.
- Sternberg, S.: Memory-scanning: Mental processes revealed by reaction-time experiments. *Am. Sci.* 57:421–457; 1969.
- Stone, E. A.: Stress and catecholamines. In: Freidhoff, A. J., ed. *Catecholamines and behavior*. New York: Plenum Press; 1975:31–72.
- Tam, S. Y.; Roth, R. H.: Mesoprefrontal dopaminergic neurons: Can tyrosine availability influence their functions? *Biochem. Pharmacol.* 53:441–453; 1997.
- Thomas, J. R.; Ahlers, S. T.; House, J. F.; Schrot, J.: Repeated exposure to moderate cold impairs matching-to-sample performance. *Aviat. Space Environ. Med.* 60:1063–1067; 1989.
- Thomas, J. R.; Ahlers, S. T.; House, J. F.; Schrot, J.; Van Orden, K. F.; Winsborough, M. M.; Hesslink, R. L.; Lewis, S. B.: Adrenergic response to cognitive activity in a cold environment. *J. Appl. Physiol.* 68:962–966; 1990.
- Wurtman, R. J.: Effects of nutrients on neurotransmitter release. In: Marriott, B. M., ed. *Food components to enhance performance*. Washington, DC: National Academy Press; 1994:239–261.
- Wurtman, R. J.; Hefti, F.; Melamed, E.: Precursor control of neurotransmitter synthesis. *Pharmacol. Rev.* 32:315–335; 1981.