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The effects of dietary neurotransmitter precursors on human behavior[1-3]

Harris R Lieberman, PhD, Suzanne Corkin, PhD, Bonnie J Spring, PhD, Richard J Wurtman, MD, and John H Growdon, MD

ABSTRACT The neurotransmitter precursors tryptophan and tyrosine are present in a variety of foods. In order to document possible effects of tryptophan and tyrosine on human behavior, single oral doses of these substances and matched placebos were administered to 20 men in a double-blind, crossover study. Various tests of mood state and performance were then administered. Tryptophan increased subjective fatigue and decreased self-ratings of vigor and alertness, but did not impair performance on any of the tests. Tyrosine produced no effects in our young population compared with placebo, but did decrease reaction time relative to tryptophan. It may be concluded that tryptophan has significant sedative-like properties, but unlike other sedatives may not impair performance. *Am J Clin Nutr* 1985;42:366-370.

KEY WORDS Tryptophan, tyrosine, neurotransmitter precursors, mood, performance

Introduction

Consumption of certain foods and food constituents can influence the rates at which neurons synthesize and release specific neurotransmitters (1). Dietary substances can alter brain neurotransmission by changing the central nervous system (CNS) concentration of the substrates used for the synthesis of neurotransmitters. Tryptophan and tyrosine are dietary amino acids and also neurotransmitter precursors known to influence the availability of their neurotransmitters. Ingestion of tryptophan increases the CNS concentration of serotonin and its release from brain neurons. Similarly, increased tyrosine availability can enhance the release of catecholamines when cells are firing frequently (1). Since ingestion of both of these precursors may influence the activity of specific neural systems, it is possible that the consumption of tryptophan and tyrosine may also modify the behavioral functions associated with these neurotransmitter systems. For example, it has been reported that ingestion of tryptophan induces drowsiness (2, 3) and decreases the time required for humans to fall asleep (4, 5). These findings are consistent with many animal studies demonstrating that increases in serotoninergic activity are involved in the induction and maintenance of sleep (6). Less is known about the behavioral effects of tyrosine, although when administered to mice it has been reported to have stimulant-like effects (7). It has also been reported that tyrosine may reduce the behavioral effects of acute stress (8).

Although tryptophan and tyrosine are naturally occurring constituents of many foods and have been shown to modify brain composition in animals (1), there have been few investigations of their behavioral effects on waking human subjects. We therefore administered single doses of tryptophan and

[1] From the Department of Psychology and Clinical Research Center (HRL, SC), Massachusetts Institute of Technology, Cambridge, MA, the Department of Psychology (BJS), Harvard University, Cambridge, MA, the Department of Nutrition and Food Science (RJW), Massachusetts Institute of Technology, Cambridge, MA and the Department of Neurology (JHG), Massachusetts General Hospital, Boston, MA.

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[3] Address reprint requests to: Harris R Lieberman, PhD, Department of Psychology, E10-130d, Massachusetts Institute of Technology, Cambridge, MA 02139.

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tyrosine to 20 men, and measured their mood and sensorimotor performance under drug and placebo conditions.

Methods

Subjects

Twenty healthy male subjects, aged 18 to 45 (mean age = 24), participated in the study.[4] They were recruited locally by sign-up sheets and word-of-mouth. The study was approved by the institutional Committee on the Use of Humans as Experimental Subjects.

Experimental design

Tryptophan (50 mg/kg) and tyrosine (100 mg/kg), in pill form, were each administered to all subjects. A double-blind, placebo-controlled, crossover design was employed. After one practice session, each subject ingested one of the two amino acids or one of the two placebos for each of the remaining four sessions. The placebos each were matched in appearance to one of the amino acids. The order of substance ingestion for each subject was systematically varied by use of the Latin-square design. The subject fasted for 12 h before each session, and then, at 0700, ingested the substance designated for that session. Testing began 2 h later.

Two self-report mood questionnaires and four tests of performance were administered.

Visual Analogue Mood Scale (VAMS). The VAMS is a self-report mood questionnaire that yields three factor-analytically derived mood categories: Alert, Sad, and Calm (9). Each of 32 adjectives was rated by the subject by moving a pointer along a horizontal line presented on a cathode ray tube (CRT). The absence of a particular mood was indicated by placing the pointer on the extreme left of the line, and the maximum by placing it on the right.

Profile of Mood States (POMS). The POMS is a self-report mood questionnaire that yields 6 factors: Tension-Anxiety, Depression-Dejection, Anger-Hostility, Vigor-Activity, Fatigue-Inertia, and Confusion-Bewilderment (10). The test consists of 65 adjectives each of which must be rated on a 5-point scale.

Simple Auditory Reaction Time. In this microcomputer-administered test, the subject responded, as rapidly as possible, to the onset of a 75 dB, 1900 Hz tone. After five warmup trials, 125 test trials were presented. A visual cue, presented on a CRT, indicated the start of a trial.

Two-Choice Visual Reaction Time. In this test, the subject was required to discriminate between two slightly different letter-like symbols, which were presented tachistoscopically on a CRT screen by a microcomputer. The stimulus duration was either 54 or 72 ms. To decrease the discriminability of the two stimuli and therefore difficulty of the test, a masking stimulus appeared after each trial. The brief duration of the stimuli, and their small size, required sustained vigilance by the subject.

Grooved Pegboard Test. For this test the subject was required to insert, as rapidly as possible, a series of 25 pegs into randomly oriented holes on a board. Since both the pegs and board are grooved, each peg must be properly oriented to be inserted. The test is more difficult than many other pegboard tests because the holes are slanted.

Thurstone Tapping Test. This is a test of motor speed and coordination (11, 12). In the first part of the test, the subject held a metal stylus in one hand and tapped, as rapidly as possible in a specific sequence, the sectors of a 13 cm circle divided into 4 quadrants. In the second stage of the test, the subject used both hands, simultaneously tapping different patterns with each.

Results

The data from all tests were analyzed by the Latin-square analysis of variance (ANOVA). The two within-subjects main factors in this analysis were substance and test session order. The between-subject variable was order of substance administration. A posteriori comparisons, when appropriate, were made with a two-tailed Neuman-Keuls statistic.

VAMS. The analysis of variance performed on the Alert scale of the VAMS detected a significant main effect for both substance ($p < 0.001$) and test session order ($p < 0.01$). The substance effect was attributable to tryptophan, which on a posteriori testing was found to significantly decrease the Alertness scale as compared to either placebo or tyrosine ($p < 0.01$, **Fig 1**). The other two VAMS scales, Calm and Sad, were not significantly altered by either substance.

POMS. The Fatigue-Inertia and Vigor-Activity subscales of the POMS were significantly altered by substance administration. On a posteriori testing, tryptophan was found to significantly increase the Fatigue-Inertia scale ($p < 0.05$), and decrease the Vigor-Activity scale ($p < 0.01$), when compared to either its placebo or tyrosine (**Fig 2**). Significant effects of test session order were also detected by these two subscales. The other POMS scales yielded no significant findings.

Simple Auditory Reaction Time. This was the only performance test where a significant effect attributable to substance was observed. Tryptophan significantly increased RT when compared to tyrosine ($p < 0.05$ on the post-hoc test), but neither amino acid differed

[4] Data from only 16 subjects is reported for the RT tasks due to a procedural error resulting in the loss of data from the first four subjects.

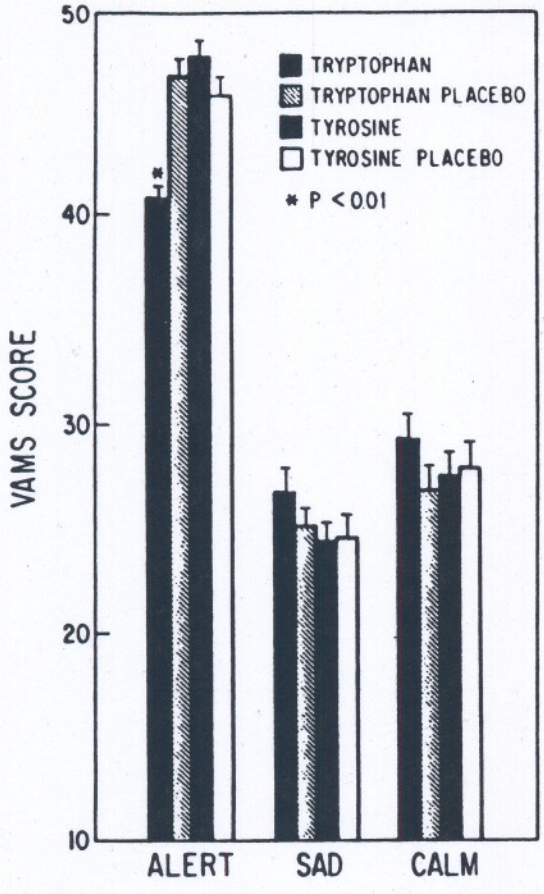

FIG 1. The effects of tryptophan, tyrosine, and their respective placebos on three scales of VAMS self-report mood questionnaire (mean ± SEM).

significantly from its respective placebo. There was also no significant difference between the two placebos; therefore, this performance difference cannot be attributed to a placebo effect.

Two-Choice Visual Reaction Time. Analyses of variance were performed for each of the two stimulus durations presented. Neither amino acid had any effect on two-choice reaction time.

Grooved Pegboard Test. Separate analyses of variance were performed on time for completion and number of pegs dropped. There were no significant effects of substance.

Thurstone Tapping Test. Two analyses of variance were performed on the number of taps per condition (unimanual or bimanual). The substances did not alter performance on this task.

Discussion

The observation of increased drowsiness resulting from tryptophan ingestion is consistent with other reports indicating that this dietary constituent has hypnotic properties (2, 4, 5). We have found that when tryptophan is administered without the other LNAA's present in protein that suppress its uptake into the brain, it has considerable psychopharmacological activity with respect to human mood. Tyrosine, however, when given in a single oral dose, appears to be less potent, at least with regard to the limited number of behavioral parameters we assessed. This finding is not surprising since neurons can become unresponsive to additional tyrosine if their firing frequency slows (1).

The sedative-like effects of tryptophan on human mood are consistent with considerable neurochemical and behavioral evidence that serotoninergic neurons participate in the induction and regulation of sleep. Lesions of serotoninergic neurons reduce time spent sleeping, and various drugs that inhibit serotoninergic neurotransmission also reduce sleep (6).

The finding that tryptophan increased simple RT compared to tyrosine may indicate that these substances have antagonistic properties. There are at least two possible explanations for this result. Ingestion of tyrosine, which competes with tryptophan for uptake across the blood-brain barrier, may decrease brain tryptophan (1). Alternatively, tyrosine by acting on catecholaminergic neurons may itself improve performance in a manner similar to the positive effect of L-dopa administration in patients with Parkinsonism. Tyrosine has in fact been reported to have behavioral effects in animals similar to those resulting from administration of stimulants such as amphetamine and caffeine (7) and to reverse the effects of acute stress (8). It has also been reported to be useful in the treatment of human depression (13).

Because tryptophan induces drowsiness but does not impair performance, at least on the tests we administered, it is a good candidate

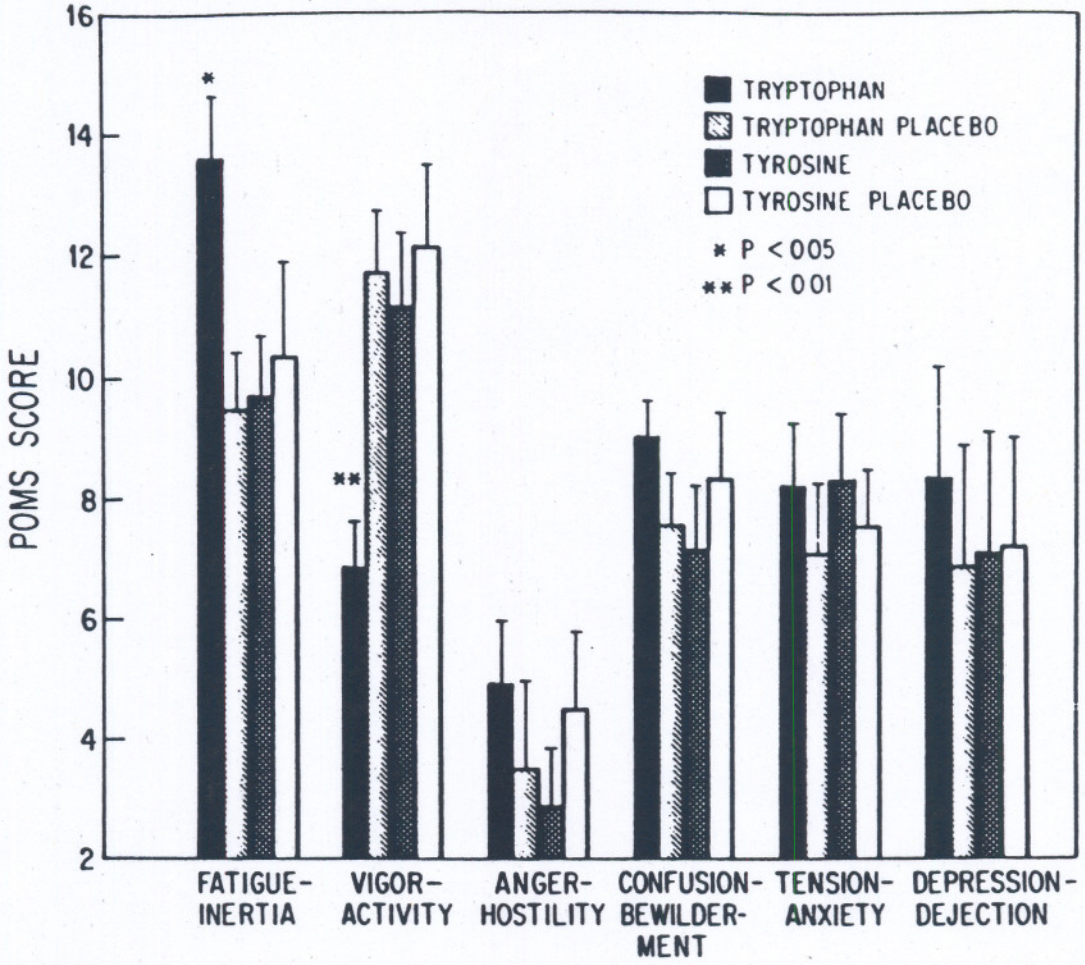

FIG 2. The effects of tryptophan, tyrosine, and their respective placebos on the six subscales of the POMS self-report mood questionnaire (mean ± SEM).

for evaluation as a mild hypnotic. Most prescription drugs currently used as hypnotics, such as the benzodiazepines and barbiturates, impair performance not only immediately after administration but also the next day (14). Further experimentation will be required to confirm the sparing of performance noted after tryptophan administration, especially since there is no consensus as to which tests are most appropriate to use in assessing performance (14). Since tryptophan has been shown to reduce sleep latency in the dose we administered (4), it may be preferable to such drugs, particularly if a less potent hypnotic would be sufficient. Regardless of the possible clinical application of tryptophan, this study confirms that administration of a normal dietary constituent, tryptophan, can significantly modify human behavior.

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