MOOD, PERFORMANCE, AND PAIN SENSITIVITY: CHANGES INDUCED BY FOOD CONSTITUENTS

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Summary—We examined the behavioral effects of the dietary constituents tryptophan and tyrosine on human mood, sensorimotor performance and pain sensitivity. Tryptophan and tyrosine are neurotransmitter precursors present in varying amount in protein-containing foods. Tryptophan (50 mg/kg) increased subjective drowsiness and fatigue but unlike many hypnotics did not impair sensorimotor performance. Tryptophan also decreased human pain sensitivity in a manner that was more specific than certain analgesic drugs.

INTRODUCTION

Brain metabolism is known to be sensitive to the consumption of specific dietary constituents and even to the ratio of protein to carbohydrate within a single meal (Fernstrom and Wurtman, 1971; Wurtman et al., 1981).

Diet influences brain neuronal activity by modifying the rate of synthesis and release of specific neurotransmitters. Food constituents that can affect brain function in this way are either precursors used by neurons as a substrate for the synthesis of certain neurotransmitters, or substances that alter the availability of these precursors to the brain. Since distinct types of behaviors are associated with certain neurotransmitter systems, a physiological mechanism exists whereby the behavior of an organism could be directly influenced by diet.

The neurotransmitters characterized by precursor-dependence are acetylcholine, the catecholamines (dopamine and norepinephrine), serotonin, histamine and glycine (Wurtman et al., 1981). Serotonin, dopamine, and norepinephrine metabolism all can be influenced by plasma levels of two large neutral amino acids (LNAA) that are present in protein-containing foods. Tryptophan, one of these amino acids, is the substrate for the synthesis of serotonin; its ingestion has been shown to increase brain levels of this neurotransmitter (Fernstrom and Wurtman, 1971). Tyrosine, another LNAA, is the substrate for dopamine and norepinephrine synthesis. Ingestion of tyrosine can, under certain circumstances, modify dopaminergic and norepinephrinergetic neurotransmission (Wurtman et al., 1981).

If ingestion of these dietary amino acids can modify brain neurotransmission, it is appropriate to determine whether these food constituents also alter behavior. The two experiments described below therefore examined the effects of tryptophan and tyrosine on various aspects of human behavior. The behavioral functions tested were those believed
to be associated with the serotonin, dopamine, and norepinephrine neurotransmitter systems.

The behaviors that have been linked to serotonergic neurotransmission include sleep, feeding, locomotor activity, aggression, and pain sensitivity (Wurtman et al., 1981). The evidence suggesting that serotonergic neurons participate in the regulation of sleep is particularly convincing. In animals, electrolytic lesions of the midbrain raphé, where the cell bodies of many serotonergic neurons reside, greatly reduce time spent sleeping. Systemic administration of p-chlorophenylalanine (PCPA), which inhibits serotonin synthesis, produces an even greater sleep deficit than an electrolytic lesion (McGeer et al., 1978). In humans, administration of tryptophan hastens the onset of sleep (Hartmann and Elion, 1977; Hartmann and Spinweber, 1979) and induces drowsiness (Greenwood et al., 1975; Lieberman et al., 1982). We therefore examined the effect of tryptophan on alertness, as reflected by subjective mood state, and on performance.

There is also considerable evidence to support the role of serotonergic neurons in the regulation of pain sensitivity. In animals, lesions of serotonergic neurons or consumption of a tryptophan-poor diet increases responsiveness to painful stimuli (Messing and Lytle, 1977). It has been reported that administration of tryptophan to patients with chronic pain is beneficial (Hosobuchi et al., 1980), and tryptophan in conjunction with a high carbohydrate diet decreases human pain sensitivity (Seltzer et al., 1982). Therefore, in a second experiment, tryptophan's effect on pain and thermal sensitivity was evaluated. Tyrosine was included as a second treatment in this experiment, because its administration may decrease the level of brain tryptophan (Wurtman et al., 1981).

Various behavioral functions have been associated with dopaminergic neurotransmission. These neurons participate in the regulation of motor activity, as demonstrated by the improvement in patients with Parkinson's disease following L-dopa administration (Cotzias et al., 1969). Tyrosine increases motor activity in animals, an effect similar to that seen after administration of stimulants such as amphetamine (Gibson et al., 1982). Amphetamine may in fact exert its effects on the brain by acting on catecholaminergic neurons (Goth, 1974). Another function associated with catecholaminergic neurons is regulation of moods (Schildkraut, 1965). Certain psychiatric disorders, particularly schizophrenia, are associated with catecholaminergic dysfunction (Carlsson, 1978). It was therefore of interest to determine whether tyrosine altered human sensorimotor performance and mood state.

**EXPERIMENT I: THE EFFECT OF TRYPTOPHAN AND TYROSINE ON PERFORMANCE AND MOOD**

The aim of this experiment was to determine whether the two neurotransmitter precursors, tryptophan and tyrosine, alter human performance and mood.

**Subjects**

The participants in the study were 16 healthy men, aged 18 to 45.* After the experimental protocol was described to them informed consent was obtained from all the subjects.

*Data from only 12 subjects is reported for the RT tasks due to a procedural error which resulted in the loss of data from the first four subjects.
**Experimental design**

Tryptophan (50 mg/kg) and tyrosine (100 mg/kg) were each administered in a single dose using a double-blind, placebo-controlled, crossover design. 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 order of substance ingestion for each subject was systematically varied by use of the Latin-square design. Before each session, the subject fasted for 12 h and then, at 0715, ingested the substance designated for that session. Testing began 2 h later.

**Test battery**

Four tests of sensorimotor performance and two self-report mood questionnaires were administered.

**Simple auditory reaction time.** Reaction time is a method often used to measure human sensorimotor performance. In this version of the test the subject responded as rapidly as possible to the onset of a 75 dB, 1900 Hz tone. After five warmup trials, 100 test trials were presented in rapid succession. A visual cue presented on a cathode-ray tube (CRT) indicated the start of a trial. Reaction time was recorded with better than ms accuracy.

**Two-choice visual reaction time.** In the two-choice visual reaction time task, 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, a masking stimulus appeared after each trial. The brief duration of the stimuli and their small size demanded a high degree of concentration by the subject. Reaction time was assessed with better than ms accuracy.

**Grooved pegboard.** The grooved pegboard task measures manipulative dexterity of the hand and fingers. 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.** The Thurstone tapping test required visually guided reaching to four targets in rapid succession (Thurstone, 1941; Corkin, 1968). First, the subject held a metal stylus in one hand and tapped, in a specific sequence, the sectors of a 13-cm circle divided into four quadrants. Next, the subject used both hands, simultaneously tapping different patterns with each hand. This task is difficult, especially in the bimanual portion. The dependent variable is number of taps per time allotted.

**Visual analogue mood scales (VAMS).** The VAMS is a self-report mood questionnaire that measures the extent to which a subject reported each of three factor-analytically derived mood states: Alert, Sad and Calm. Each of 32 adjectives was rated by the subject by moving a pointer along a 24-cm horizontal line presented on a 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. The results obtained with this method are as reliable and valid as those obtained with traditional mood questionnaires (Folstein and Luria, 1973).

**Profile of mood states (POMS).** The POMS is a self-report mood questionnaire that yields six factors: Tension-Anxiety, Depression-Dejection, Anger-Hostility, Vigor-Activity, Fatigue-Inertia and Confusion-Bewilderment (McNair et al., 1971). The test
consists of 65 adjectives each of which must be rated on a 5-point scale. All scales have internal consistency reliabilities in the range of 0.90. The POMS has been employed in many psychopharmacological studies and is sensitive to the effects of several classes of psychoactive drugs, including hypnotics (File et al., 1982) and stimulants (Cole et al., 1978).

Results

The data from each test were analyzed by the Latin-square analysis of variance (ANOVA). The within-subjects main factors in this analysis were substance and test session order. The between-subject variable was order of substance administration. Post-hoc comparisons, when appropriate, were made with a Neuman-Keuls statistic. Two-tailed confidence intervals were used for post-hoc significance testing.

Simple auditory reaction time. There was a trend for substance to alter simple auditory reaction time ($p < 0.10$). The difference was between tyrosine which decreased reaction time and tryptophan which increased it. This was the only sensorimotor performance test where an effect attributable to substance was observed (Table 1).

<table>
<thead>
<tr>
<th>Test</th>
<th>Tryptophan</th>
<th>Tryptophan placebo</th>
<th>Tyrosine</th>
<th>Tyrosine placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>POMS:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vigor</td>
<td>7.31 ± 0.88</td>
<td>12.12 ± 1.19</td>
<td>11.94 ± 1.49</td>
<td>13.38 ± 1.57</td>
</tr>
<tr>
<td>Fatigue</td>
<td>14.62 ± 1.16</td>
<td>9.69 ± 0.98</td>
<td>9.56 ± 1.31</td>
<td>9.88 ± 1.80</td>
</tr>
<tr>
<td>VAMS:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alert</td>
<td>31.17 ± 1.57</td>
<td>37.34 ± 1.61</td>
<td>39.08 ± 1.81</td>
<td>37.31 ± 2.10</td>
</tr>
<tr>
<td>Simple RT</td>
<td>150.09 ± 5.19</td>
<td>145.96 ± 4.99</td>
<td>143.45 ± 4.48</td>
<td>145.50 ± 4.69</td>
</tr>
</tbody>
</table>

Two-choice visual reaction time. Analyses of variance were performed for each of the two stimulus durations of the two-choice visual reaction time task. Neither amino acid had any effect on two-choice reaction time.

Grooved pegboard. Separate analyses of variance were performed on time to complete the grooved pegboard and number of pegs dropped. There were no significant effects of substance.

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

VAMS. The analysis of variance performed on the Alert scale of the VAMS detected a significant main effect for both substances ($p < 0.001$) and test session order ($p < 0.01$). The substance effect was attributable to tryptophan, which on post-hoc testing was found to significantly decrease Alertness as compared to either placebo or tyrosine ($p < 0.01$; Table 1). The other two VAMS scales, Calm and Sad, detected no effects due to substance or order.

POMS. Two of the POMS scales, Fatigue–Inertia, and Vigor–Activity, elicited significant differences due to substances (Table 1). On post-hoc testing, tryptophan was
found to significantly increase Fatigue–Inertia ($p < 0.02$), and decrease Vigor–Activity ($p < 0.01$) compared to either its placebo or tyrosine (Table 1). Significant effects of test session order were also detected by these two scales. The other POMS scales yielded no significant effects.

Discussion

This study has shown that ingestion of 50 mg/kg tryptophan significantly modified certain aspects of mood in healthy men. The drowsiness induced by tryptophan was detected consistently by three different scales of two different self-report mood questionnaires. The change in alertness produced by administering tryptophan is quite large when compared with a placebo. For example, on the POMS Vigor scale, subjects indicated that they felt 40% less vigorous after tryptophan ingestion. This effect is particularly large when one considers that tryptophan is a normal dietary constituent, and that no attempt was made to optimize its effects by selection of a particular population, or by manipulation of diet (Fernstrom and Wurtman, 1971).

The most likely mechanism to account for the effect of tryptophan on sleepiness is increased activity of the sleep-promoting serotonergic neurons in the midbrain raphé. The rate at which such neurons synthesize and release serotonin has been shown to increase with greater tryptophan availability (Wurtman et al., 1981). Ingestion of carbohydrate could have a similar although certainly smaller effect since its ingestion also increases the availability of tryptophan to the brain (Fernstrom and Wurtman, 1971).

The hypnotic properties of tryptophan may have some clinical use (Hartman and Elion, 1977). Tryptophan, while clearly inducing drowsiness, does not impair performance, at least on the specific sensorimotor tests we presented. Most of these tests have been shown to be sensitive to hypnotic-induced decrements in performance (Johnson and Chernik, 1982). Standard prescription hypnotics do impair performance, even when they are administered at bedtime and testing takes place the next day (Johnson and Chernik, 1982).

Tryptophan may possibly be distinguished from the leading class of prescription hypnotic drugs, the benzodiazepines, by its lack of effect on anxiety level. The benzodiazepines significantly reduce anxiety levels in normal as well as in anxious populations (Byck, 1975; File et al., 1982). Our data indicate that tryptophan does not alter anxiety levels in normal subjects. While the absence of an effect on anxiety may reduce the usefulness of tryptophan as a sleep aid for anxiety-induced insomnia, it may be an advantage in other populations where mood-altering properties are not needed. Tryptophan's specific effect on mood, altering only alertness but not inappropriately reducing anxiety in normal subjects, indicates its best application would be as a mild hypnotic. It may be useful for individuals who suffer from occasional, non-chronic types of insomnia.

There may be a subgroup of more severe insomniacs whose disorder is related to a central serotonergic deficit, who may also benefit from tryptophan. For example, it has been reported by Möller et al. (1980) that some depressed patients respond to tryptophan administration, particularly those subjects in whom the pretreatment ratio of plasma tryptophan to competing LNNA levels was low. Evaluation of the plasma ratio of tryptophan to other LNAAAs may provide a useful screening device for selecting a subcategory of insomniacs who would be responsive to tryptophan administration.
EXPERIMENT II: THE EFFECT OF TRYPTOPHAN AND TYROSINE ON THERMAL AND
PAIN PERCEPTION

In this experiment we examined the effects of tryptophan and tyrosine on pain and
thermal sensitivity.

Pain is one of the most difficult sensations to measure objectively since it is readily
influenced by motivational and cognitive factors (Clark, 1969). A method based on the
theory of signal detection (TSD) can separate sensitivity changes from nonsensory
cognitive components of perception (Green and Swets, 1966). TSD has been applied
successfully to a wide range of sensory dimensions. Sensitivity (discriminability of
stimuli) is measured in TSD by $d'$ or $P(A)$ (the nonparametric equivalent of $d'$), which
indicate the ability of a subject to discriminate correctly among stimuli that vary along
some stimulus dimension. Response bias or criterion, the non-sensory motivational
component of behavior, is computed independently as beta (or $B$ in nonparametric
TSD). $B$ and beta may be thought of as measures of the labels used to describe the stimuli
that are presented. They can be altered by changes in cognitive state brought about by
anxiety, instructions to the subject, or a placebo effect (Clark, 1969; Clark and
Goodman, 1974). $P(A)$ and $d'$, however, measure the sensory component of percep
tion and are not modified by non-sensory cognitive components. For example, two
subjects may each easily discriminate two stimuli [as measured by $d'$ and $P(A)$], but may
select, depending on their mood or based on prior experience, different labels to describe
the same stimuli (measured by $B$ or beta). A traditional sensory threshold is a complex
combination of both discriminability and response criterion.

Methods

Subjects

The participants in this study were 8 healthy men, ranging in age from 18 to 25. One
subject participated in both Experiments I and II. After the experimental protocol was
described informed consent was obtained from all the subjects.

Experimental design

Tryptophan (50 mg/kg), tyrosine (100 mg/kg) and a placebo were administered to all
subjects using a double-blind, crossover design. Before each test session, the subjects fasted
for 12h and then at 0715 ingested the substance designated for that session. Testing began
at 0900.

Measurement of pain and sensitivity

In order to measure pain and thermal discriminability and changes in criterion, we used
a TSD method specifically adapted for the study of pain (Clark, 1974). This procedure
used a modified Hardy-Wolff-Goodell dolorimeter, a gun-like projector containing a
100-W bulb, to present thermal and pain stimuli. A series of internally mounted lenses
collimated the light from the bulb onto a 2-cm diameter spot. The dolorimeter was
calibrated to produce six stimulus intensities: 0, 90, 180, 270, 320, 370 mcalds/cm^2. The
lower intensities produced only a thermal sensation, the higher ones pain. Before testing
began, 12 India ink spots, approximately 2-cm in diameter, were applied to the volar
surfaces of the subjects' forearms. A testing session consists of 144 trials: 24 presentations
of each stimulus intensity in a pseudorandom order. The heat stimuli were applied to the
ink spots by the subject, who was instructed to withdraw the stimulus if it became "too hot or too painful". The stimulus duration of each trial was 3 s unless the subject withdrew the dolorimeter. Withdrawal latency was measured electronically with an accuracy of \( \pm 0.001 \) s. Immediately after each stimulus presentation, the subject assigned a verbal rating to the stimulus on an 11-point scale. Each numerical value on the scale corresponded to a verbal category ranging from "absolutely nothing" to "withdrawal" (Table 2).

<table>
<thead>
<tr>
<th>Verbal category</th>
<th>Numerical value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nothing</td>
<td>1</td>
</tr>
<tr>
<td>Maybe something</td>
<td>2</td>
</tr>
<tr>
<td>Faint warmth</td>
<td>3</td>
</tr>
<tr>
<td>Warm</td>
<td>4</td>
</tr>
<tr>
<td>Hot</td>
<td>5</td>
</tr>
<tr>
<td>Very hot</td>
<td>6</td>
</tr>
<tr>
<td>Very faint pain</td>
<td>7</td>
</tr>
<tr>
<td>Faint pain</td>
<td>8</td>
</tr>
<tr>
<td>Pain</td>
<td>9</td>
</tr>
<tr>
<td>Very painful</td>
<td>10</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>11</td>
</tr>
</tbody>
</table>

**Results**

The data were analyzed using the nonparametric signal detection method of McNichol (1972). The subject's ratings for each stimulus and the withdrawal latencies were used to compute five pairs of \( P(A) \)s and \( B \)s. Each of these pairs represented comparisons across adjacent thermal and pain stimuli. For example, \( P(A)1 \) was a measure of the discriminability of the first from the second most intense stimulus intensity (370 and 320 mcal/s\(^{-1}\)/cm\(^2\)), while \( B(1) \) was a measure of the response bias associated with these two stimuli. \( P(A)2 \) and \( B(2) \) compared the second and third stimuli (320 mcal and 270 mcal/s\(^{-1}\)/cm\(^2\)). \( P(A)3 \) and \( B(3) \) compared the third and fourth most intense stimuli (270–180 mcal/s\(^{-1}\)/cm\(^2\)); and \( P(A)4 \) and \( B(4) \) and \( P(A)5 \) and \( B(5) \) compared across the fourth, fifth, and sixth stimulus intensities (0, 90, and 180 mcal/s\(^{-1}\)/cm\(^2\)); A high \( P(A) \) indicated that the subject correctly discriminated between adjacent stimuli. A high \( B \) reflected many reports of pain or withdrawal and few reports of nothing, warm, or hot; i.e. the subject was "biased" towards reporting the stimuli as more intense. These data were then analyzed by means of a repeated measures analysis of variance performed for each stimulus comparison. All \( P(A) \) values were transformed to 2 arcs in square root \( P(A) \) (McNichol, 1972). When appropriate, post-hoc testing was performed using the Neuman–Keuls statistic. Two-tailed confidence intervals were used for significance testing.

A significant main effect of substance on pain sensitivity \( [(F(2, 21) = 3.84; \ p < 0.05] \) was detected for \( P(A)2 \). The stimuli compared at this level are 320 vs 270 mcal/s\(^{-1}\)/cm\(^2\). Subjects labelled these intensities painful or very painful. Tryptophan significantly reduced pain discriminability at \( P(A)2 \) compared to placebo \( (p < 0.05, \ Fig. 1) \). Neither tryptophan nor tyrosine altered pain or thermal discriminability for \( P(A)1 \), \( P(A)3 \), \( P(A)4 \), and \( P(A)5 \) (Fig. 1). No significant effect of substance was noted on any of the five measures of criterion (B) (Fig. 2).
Fig. 1. The effects of substance administration on discriminability [P(A)] of the five stimulus comparisons.

Fig. 2. The effects of substance administration on response bias (B) on the five stimulus comparisons (see Fig. 1 for key).

**Discussion**

Tryptophan, as expected, reduced pain sensitivity in healthy men. This effect was specific to the discriminability of stimuli that were moderately painful P(A)2 (320–270 mcal/s\(^{-1}\)/cm\(^2\)) as opposed to non-painful or maximally painful stimuli. Yang *et al.* (1979) who used the same technique to evaluate the effect of morphine and diazepam on pain and
thermal sensitivity, have noted that manipulations that modify discriminability do not induce differences at every intensity pair, because of the lack of independence between consecutive pairs. In fact, Yang et al. (1979) reported that even morphine (0.14 mg/kg IV, on the high side of the recommended IV dose, Jaffe and Martin, 1975) does not produce a change in $P(A)$ at every stimulus intensity; out of 42 comparisons of placebo vs morphine, significant effects on $P(A)$ were noted only 13. Diazepam, at a dose of 0.14 mg/kg IV, also fails to consistently reduce $P(A)$ across all stimulus intensities; out of 42 comparisons Yang et al. (1979) made, diazepam compared to placebo reduced $P(A)$ values on 9. Neither morphine nor diazepam significantly reduced $P(A)$. In our experiment, this level was the most intense pain presented; it was not affected by tryptophan. The most consistent effect of morphine and diazepam on $P(A)$ was at the less intense stimulus intensities, which do not induce painful sensations, thus indicating that morphine and diazepam are nonspecific drugs that impair both thermal and pain perception.

Diazepam and morphine also significantly modify response criterion ($B$), a finding consistent with the powerful effect that these drugs have on mood, specifically anxiety and euphoria as reported by Jaffe and Martin (1975) and File et al. (1982). In contrast, tryptophan, as demonstrated in Experiment I, only alters alertness.

Tryptophan's analgesic properties are apparently quite specific, as are its hypnotic properties (Experiment I). Unlike morphine or diazepam, it may not generally impair sensory discrimination or alter mood as indicated by response criterion. Its most appropriate clinical applications may be: (a) as a mild analgesic, like aspirin or acetaminophen; (b) in combination with diazepam of a similar mood-altering compound, to avoid the use of narcotics; (c) for treatment of a subclass of chronic pain patients with a disorder of serotoninergic neurotransmission. It may be possible to identify such patients by measurement of plasma tryptophan/LNAA ratios.

GENERAL COMMENTS

Methods for detecting the effects of food constituents on behavior

The measurement of food-induced changes in behavior presents the investigator with some unique problems. Based on the data presented in Experiments I and II, food constituents are likely to have effects on behavior that are subtle and therefore difficult to demonstrate experimentally. Standard neuropsychological and psychopharmacological techniques, or methods taken from any other discipline, may therefore fail to detect important behavioral phenomena induced by the consumption of foods.

Even in cases where substantial behavioral effects of drugs have been documented, disagreement exists as to the most sensitive tests to employ (Johnson and Chernick, 1982). For example, there is no consensus as to which sensorimotor tests are most sensitive to impairments induced by hypnotics like the benzodiazepines. These drugs are more potent than any food constituent is likely to be. Similar disagreements exist as to which sensorimotor and mood tests are most sensitive to stimulants like amphetamine or caffeine (Cole et al., 1978). In order to detect subtle effects of foods, it may be necessary to develop completely new strategies for measuring subtle changes in behavior. Such techniques would be applicable for studying the effects of environmental agents other than food.
**Foods that alter brain levels of tryptophan and tyrosine**

Because tryptophan is present in protein but not carbohydrate, it is often assumed that consumption of a protein meal, as opposed to a carbohydrate meal, will elevate brain tryptophan. Actually, the opposite is true. Ingestion of a high-carbohydrate meal will substantially increase both brain tryptophan and serotonin (Fernstrom and Wurtman, 1971), whereas a high-protein meal actually decreases brain tryptophan and serotonin (Fernstrom and Wurtman, 1972). The paradoxical effect that a high-protein meal has on brain tryptophan is attributable in part to the small amount of tryptophan present in protein relative to other LNAAs. All the LNAAs compete for entry into the brain via a single species of carrier molecule that transports them across the blood–brain barrier. Because protein contains only a small amount of tryptophan, protein ingestion reduces the ratio in plasma of tryptophan to other LNAAs, and thus less tryptophan (and more tyrosine) is transported to the brain. A high carbohydrate meal, which induces the release of insulin, and the consequent transport of amino acids from the plasma into skeletal muscle, reduces the plasma level of all LNAAs except tryptophan. This effect is due to tryptophan’s unique property of binding to albumin in the plasma, unlike the other LNAAs that circulate as free molecules. Tryptophan is thereby largely prevented from moving into skeletal muscle from plasma. Thus, when carbohydrate is ingested, relatively more tryptophan is available for transport to the brain and therefore brain tryptophan and serotonin levels increase.

**CONCLUSION**

The data from Experiments I and II, as well as the findings of many other laboratories cited above, demonstrate that food constituents can affect human behavior. Although the effects of food constituents are subtle compared to many drugs, the fact that dietary substances affect human behavior at all is surprising. It may be possible to demonstrate different or even larger effects of foods and nutrients on behavior by testing more sensitive subpopulations, such as elderly subjects or individuals who are under stress. Elderly people are known to be more sensitive to certain drugs. They may also be more susceptible to the effects of food constituents on behavior. Environmental stress such as anxiety or lack of sleep may also increase the susceptibility of individuals to the behavioral effects of food constituents. Another way to amplify the behavioral effects of food constituents may be to use them in combinations, such as administering a high-carbohydrate meal in conjunction with tryptophan (Wurtman et al., 1981; Seltzer et al., 1982).

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