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The Effect of Protein or Carbohydrate Breakfasts on Subsequent Plasma Amino Acid Levels, Satiety and Nutrient Selection in Normal Males[1]

KAREN L. TEFF,*[2] SIMON N. YOUNG*†[3] AND JOHN E. BLUNDELL‡

**Department of Medicine, Division of Experimental Medicine, McGill University, Montreal, Canada*
†Department of Psychiatry, McGill University, 1033 Pine Avenue West, Montreal Canada H3A 1A1
‡Biopsychology Group, Psychology Department, University of Leeds, Leeds, England LS2 9JT

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TEFF, K. L., S. N. YOUNG AND J. E. BLUNDELL. *The effect of protein or carbohydrate breakfasts on subsequent plasma amino acid levels, satiety and nutrient selection in normal males.* PHARMACOL BIOCHEM BEHAV **34**(4) 829–837, 1989.—Normal subjects were fed protein or carbohydrate breakfasts. Both meals were in the form of a chocolate pudding and had similar sensory qualities. At lunchtime subjects were allowed to select from a buffet. The protein breakfast had a greater satiating power than the carbohydrate breakfast, but there was no difference in overall selection of protein or carbohydrate at lunchtime. However, the carbohydrate breakfast did decrease selection of apple, the only pure carbohydrate food available at lunchtime. In a second experiment changes in plasma amino acid levels were studied after subjects received carbohydrate breakfasts containing 0, 4, 8 or 12% protein, or a danish pastry. Only the 0% protein breakfast increased tryptophan availability to the brain. These experiments were performed to test the hypothesis that alterations in brain 5-hydroxytryptamine, brought about by dietary alterations in brain tryptophan, regulate selection of protein and carbohydrate. The results suggest that this mechanism was not operating in our experiments.

Protein Carbohydrate Satiety Amino acids Tryptophan 5-Hydroxytryptamine

THE neurotransmitter, 5-hydroxytryptamine (5HT), is a factor in the regulation of food intake. Generally, pharmacological and lesion studies in rodents have shown that depleting brain 5HT results in hyperphagia, while increases in brain 5HT have an anorectic effect (7). More recently, it has been demonstrated that animals, in addition to regulating their total kilocalorie intake, can maintain the proportion of protein and carbohydrate in their diet on a meal-to-meal basis (21). Some experiments have shown that 5HT manipulations can alter relative protein and carbohydrate intake, while there is also some evidence that dietary protein and carbohydrate can themselves alter brain tryptophan and 5HT. An hypothesis has developed based on the biochemical relationship between tryptophan, 5HT, and macronutrient intake (1,32).

To enter the brain, tryptophan must compete with other large neutral amino acids for transport by a common carrier system (22). Therefore, it is the plasma ratio of tryptophan to the sum of its competitors which becomes the determining factor of tryptophan availability to the brain. The dietary macronutrients protein and carbohydrate affect the ratio in opposite ways. Protein, which contains a high concentration of competitors relative to tryptophan can, in some circumstances, lower the plasma ratio, and subsequently brain tryptophan (15). In contrast, carbohydrate increases brain 5HT. Insulin, released after carbohydrate ingestion, causes uptake of the branched-chain amino acids into muscle. The concentration of the competitors is then lowered, allowing more tryptophan to enter the brain and increasing brain 5HT (13). It has been argued that the raising or lowering of brain 5HT will initiate compensatory mechanisms to alter macronutrient selection (1,30). For example, after a protein meal, the decline in brain tryptophan (15) may lead to a decline in brain 5HT. The decrease in brain 5HT is presumed to cause an increase in selection of carbohydrate relative to protein at the next meal, which, to complete the cycle, should alter brain 5HT. Conversely, carbohydrate raises brain 5HT, which will decrease subsequent selection of carbohydrate relative to protein. In this way the intake of macronutrients could be regulated within certain limits [see Wurtman and Wurtman (34)

[1]This work was supported by the Medical Research Council of Canada.
[2]Present address: Monell Chemical Senses Center, 3500 Market Street, Philadelphia, PA 19104-3308.
[3]Requests for reprints should be addressed to Dr. S. N. Young, Department of Psychiatry, McGill University, 1033 Pine Avenue West, Montreal, Quebec, Canada H3A 1A1.

for a review of this position].

In the rat, pharmacological manipulations of 5HT are consistent with this hypothesis (4,31), but dietary treatments have given both positive (2,29) and negative (23) results. The outcomes of experiments involving a choice between diets are heavily dependent upon the experimental parameters (6).

In humans, protein and carbohydrate meals result in changes in the plasma tryptophan ratio that are similar to those seen in rodents (12,20). However, few human experiments examining the role of 5HT on food selection have been undertaken. Hrboticky *et al.* (18) examined the effect of 3 different doses of tryptophan. Energy intake was reduced with 2 or 3 g of tryptophan, but no effect was observed on the proportion of carbohydrate or protein selected. Tryptophan (2 g) was also used in subjects with a propensity for carbohydrate snacks (32), though no significant effects were observed. Strain *et al.* (27) administered 1 g of tryptophan, with 10 g of carbohydrate, 3 times a day for 3 months to obese subjects. Again, no significant effects were observed. However, Blundell and Hill (9) studied the effect of giving 1 g of tryptophan along with a high protein or high carbohydrate lunch. They found that tryptophan decreased carbohydrate selection when given with the high protein meal. In addition, when 1.5 g tryptophan was administered as a preload disguised with chocolate, this treatment intensified the satiating action of food and maintained the suppression of postingestive motivational measures (17). These studies emphasize that the results in food selection experiments are sensitive to the procedural aspects of experimental design and to the planned objectives of the experimenter.

In an earlier study we examined the effect of lowering plasma tryptophan on food selection in normal males (36). A tryptophan deficient amino acid mixture was administered orally, reducing plasma tryptophan by 71%. Five hours later, when plasma tryptophan was at its lowest, the subjects were allowed to select from a buffet lunch. We found a small, but significant decline in protein intake associated with tryptophan depletion. This suggests that a decrease in brain 5HT can alter protein selection in humans. This is consistent with the presumed effect and mode of action of the prior ingestion of a high protein meal. However, the effect of tryptophan depletion on brain tryptophan will be much greater than that of protein ingestion, and there is no direct evidence that a similar effect would be obtained with consumption of a high protein meal. Therefore, we have performed two experiments designed to examine how the amount of protein consumed in a meal influences subsequent food selection and plasma tryptophan ratios. The outcome of these studies should disclose whether the effects of protein intake upon subsequent nutrient selection are mediated via changes in the plasma ratio of tryptophan to the sum of the other large neutral amino acids and therefore via changes in brain tryptophan and 5HT.

METHOD

Subjects

The subjects were normal males between the ages of 18 and 30 who were recruited through newspaper advertisements. All had at least a high school education, no history of psychiatric disorders or food allergies, and were within 10% of their ideal body weight for their height. They were not taking any prescription medication and found the foods in the study acceptable. Each subject signed an informed consent form concerning the nature of the experiment. The protocol was approved by the Ethics committee of the Department of Psychiatry, McGill University. In Experiment 1, 32 subjects took part and in Experiment 2 there were 50 subjects.

Diets

In Experiment 1, subjects received either a protein or carbohydrate meal in the form of a chocolate pudding. The protein pudding consisted of three 9 oz packets (mixed with 210 ml of water) of a protein supplement manufactured by Bariatrix International Inc. of Montreal. Each pudding contained 45 g of protein, 12 g of carbohydrate and approximately 3 g of fat. The total caloric content was 210 kcal. The carbohydrate pudding was made up in our laboratory. It consisted of 40 g of cornstarch, 28 g of Hershey's chocolate syrup and 53 g of polycose, a nonsweet caloric supplement from Ross laboratories, totaling 100 g of carbohydrate and approximately 400 kcal. It was prepared by adding 210 ml of water to the cornstarch and cooking over boiling water until thick. The polycose and the chocolate syrup were then added slowly to the mixture. The carbohydrate meal contained more calories than the protein meal because a normal diet contains more carbohydrate than protein. Also, protein has a greater satiating capacity than carbohydrate in humans (9, 16, 24). Thus, to be able to observe an effect on nutrient selection without altering total kilocalorie intake, it seemed appropriate to administer less protein. Before the actual experiment, puddings were rated with respect to taste, appearance and texture by 15 students. Subjects were required to taste both puddings, rate them on a five point scale for taste, texture and appearance and guess their nutrient composition. No significant differences were found between the two puddings on any of the variables tested and the guesses of the macronutrient composition were not significantly different for the two puddings. An important methodological feature of this study was to equate the physical state of the protein and carbohydrate meals so as to prevent the subjects from responding in accordance with the familiar distinction between the savory and sweet aspects of these nutrients. Thus, differences in response to the two meals could be attributed to the different metabolic effects of the nutrients and not to any taste sensation or cognitive attributions.

In Experiment 2, subjects received one of five different meals. Four of the treatments consisted of isocaloric (400 kcal) chocolate puddings with protein contents of 0, 4, 8, and 12%. The carbohydrate pudding (0% protein) was the same as in Experiment 1. Protein content was adjusted by mixing in appropriate amounts of the Bariatrix chocolate pudding mix, while equivalent amounts of carbohydrate pudding were removed. To simulate a common North American breakfast, the fifth treatment consisted of a cherry danish pastry (purchased from Steinberg's Inc.) and 1 cup of coffee. The pastry contained 46 g carbohydrate, 5 g protein, 16 g fat and 342 kcal.

Experimental Procedure

In Experiment 1 a double-blind counterbalanced crossover design was used. Each subject came into the laboratory on two days, one week apart. On one occasion they were given the protein pudding and on the other day the carbohydrate pudding. Seventeen of the subjects were given the protein pudding first, while fifteen received the carbohydrate pudding first. Subjects arrived in the laboratory at 8:00 a.m. after an overnight fast. They were told the purpose of the study was to investigate the behavioral effects of nutrients and were required to fill out various psychological tests during the course of the study. They were not told of the dietary composition of the pudding, though they were told it was composed of normal dietary constituents. At 9:00 a.m. they were required to eat the entire chocolate pudding after which they were permitted to read and watch a movie provided. They were not allowed to leave the laboratory. Three hours later, the subjects were individually brought into a room and allowed to select their lunch from a buffet. The foods offered were the same that we used previously (36) and their nutritional values are shown in Table 1.

TABLE 1

FOODS AVAILABLE FOR SELECTION AND THEIR MACRONUTRIENT CONTENT

Food	Amount Served	Approximate Weight Served (g)	kcal/g	Nutrients (g/g food) Protein	Carbohydrate	Fat
White bread	12 slices	350	2.71	0.09	0.50	0.03
Butter	2 tablespoons	50	7.10	0.01	0.01	0.81
Ham	10 slices	400	2.33	0.19	0	0.17
Salami	10 slices	300	3.14	0.18	0.01	0.26
Cheddar cheese	10 slices	200	3.98	0.25	0.02	0.32
Brick cheese	10 slices	200	3.71	0.22	0.02	0.30
Tomato	2 (sliced)	300	0.20	0.01	0.04	0
Apple	2 (quartered)	300	0.55	0	0.14	0.01
Coconut cookies	8	100	4.94	0.06	0.64	0.25
Chocolate chip cookies	8	125	4.71	0.06	0.70	0.21

The menu was identical on each visit. For each type of food, enough was given so that some always remained at the end and therefore was always available for selection. Subjects ate alone in the room for 30 minutes. All food and water were previously weighed. Food intake was determined by weighing what was left at the end of the meal and subtracting from the original weight. Subjects were unaware that their food intake was being monitored. At the end of the second trial, they were told of the real purpose of the study and paid for their participation.

In Experiment 2 each subject came into the laboratory at 8:30 a.m. after an overnight fast and was randomly assigned to one of the five treatment groups with 10 subjects in each group. After completion of the questionnaires, a 10 ml venous blood sample was taken. At 9:00 a.m. they were required to eat either the entire chocolate pudding or danish pastry, after which they were permitted to read and watch a movie provided. Two hr later, at 11:00 a.m., 10 ml of blood was drawn again. Two food questionnaires were given, before 9:00 a.m. and at 10:45 a.m. The first, a forced choice, contained a list of 16 food pairs, one high in protein and one high in carbohydrate. The subjects were required to select which of each pair they would prefer. The measure used was the total number of high protein or high carbohydrate foods selected. The second questionnaire consisted of a list of 32 foods together with portion sizes. The subjects were asked to indicate the foods they would prefer to eat in a meal at that time. The macronutrient composition of the meal was calculated. This method provides a more convenient way of looking at food selection than the real food selection performed in the first experiment. These procedures have previously been shown to be sensitive to nutrient manipulations (9).

Analytical Methods

Blood was collected into heparinized evacuated tubes and centrifuged immediately. The plasma was used for the determination of free and total plasma tryptophan as well as the plasma levels of the other large neutral amino acids. The free plasma tryptophan concentration was taken as the concentration in an ultrafiltrate of plasma prepared at 25°C in an Amicon MPS-1 centrifugal ultrafilter using YMT membranes. Tryptophan in the ultrafiltrate and in the plasma were measured by the fluorometric method of Denckla and Dewey (11). Plasma was prepared for amino acid analysis by adding 50 mg of 5-sulfosalicylic acid to 1 ml of plasma. Samples were vortexed, left for 1 hr at 4°C and centrifuged at 6000 rpm for 10 min. The supernatant was mixed with 0.3 N lithium hydroxide in a ratio of 2.5:1.0, then assayed on an LKB Alpha Plus amino acid analyzer.

Statistical Analysis

The effect of protein and carbohydrate meals on total kcal, macronutrient selection and individual foods selected was assessed using a two-tailed paired *t*-test. The effect of varying protein content on plasma amino acids was analyzed using a two-way ANOVA. Comparisons of selected means were made using Tukey's test. A probability of 5% was taken as the level of statistical significance.

RESULTS

Experiment 1

Figure 1 shows differences in total kilocalorie intake with respect to previous carbohydrate or protein intake, day of trial, and the effect of each macronutrient depending on the order of administration. There was no significant difference in the amounts of food consumed in the meals following the high protein or high carbohydrate breakfasts, although slightly fewer calories were consumed after the protein. However, since the carbohydrate breakfast (400 kcal) was almost double the energy value of the protein breakfast (210 kcal), it is clear that calorie for calorie the protein breakfast had a much greater satiating effect. In addition, a significant decrease in total kilocalorie intake was observed on the second day taking both breakfasts together. Due to this order effect, the group of subjects was broken down into those who had received the protein breakfast first and those who had received carbohydrate first. Although no differences were found in the energy intake in the group which had received protein first, there was a significant decrease in kilocalorie intake in the group that had received carbohydrate first. Thus, when protein was given as the second treatment, even though it contained about half the calories of the carbohydrate breakfast, there was a significant decrease in the absolute number of calories consumed in the test meal, indicating a very potent satiating action.

Figures 2 and 3 show protein and carbohydrate intake with respect to previous carbohydrate or protein intake, day of trial and the effect of each macronutrient depending on the order of

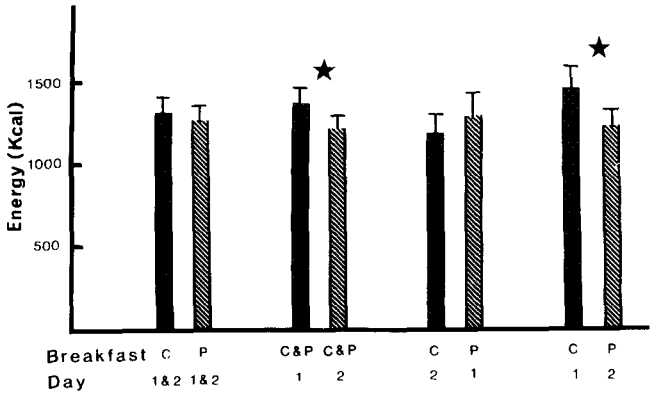

FIG. 1. The effect of carbohydrate or protein breakfasts on energy selection at lunchtime. The key refers to carbohydrate (C) or protein (P) breakfasts given on either day 1 or 2 or both. Thus, the C, 1&2 under the first bar refers to values for energy selection at lunchtime in subjects who received a carbohydrate breakfast on either day 1 or 2. Under the third bar C&P, 1 refers to values all subjects on day 1 whether they received a protein or carbohydrate breakfast. Under the fifth bar C, 2 refers to the subjects who received a carbohydrate breakfast on day 2. Values are mean ± SE. For the first 4 bars, i.e., the whole group, n = 32. Of these, 17 received protein first and 15 received carbohydrate first. A two-tailed paired *t*-test revealed that, taking the whole group together, subject ate significantly less on the second day ($t = 2.39$, $p<0.05$). In the subjects who had the carbohydrate breakfast on the first day, and the protein breakfast on the second day, energy intake at lunchtime was significantly smaller on the second day ($t = 2.19$, $p<0.05$).

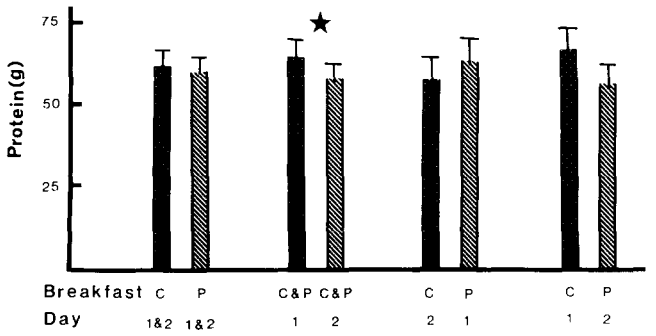

FIG. 2. The effect of carbohydrate or protein breakfasts on protein selection at lunchtime. The explanation of the figure is the same as in the caption to Fig. 1. Taking all the subjects together, significantly less protein was ingested on the second day ($t = 2.28$, $p<0.05$). In the subjects who had the carbohydrate breakfast on the first day, and the protein breakfast on the second day, the decline in protein intake on the second day was close to significance ($t = 2.0$, whereas a t of 2.4 is necessary to achieve significance).

administration. Overall, there was no effect of the different premeals on subsequent selection of protein or carbohydrate. Subjects selected significantly less protein on the second day compared with the first day. There was a similar trend for carbohydrate, but it was not statistically significant. The groups were broken down into those who had received the protein breakfast first and those who had received carbohydrate first. This revealed that the decline in subsequent total kilocalorie intake after the protein breakfast, which occurred only in the subjects who received protein second, was due to declines in both protein and carbohydrate intake. The declines in total kcal, protein and carbohydrate were 16%, 15.9% and 15.6% respectively, although the decline just failed to reach statistical significance for the protein intake. Once again, since the effects of the protein breakfast were achieved with approximately half the energy value of the carbohydrate breakfast, the protein is clearly exerting a more potent suppressive action on the subsequent intake of both macronutrients. In Table 2, the amount of each individual food selected after both treatments is shown. The trend for the protein breakfast to decrease subsequent food intake is seen for many of the individual foods. However, the only significant finding is in the opposite direction to this trend. Thus, significantly less apple was selected after the carbohydrate pudding then after the protein pudding. The apple was the only item available for selection which consisted almost entirely of a single macronutrient (Table 2) suggesting that this seemingly inconsequential result may have had biological significance. This is dealt with in greater detail in the discussion.

Experiment 2

Meals taken at breakfast which differ only by 20% in their protein content lead to differences in the plasma tryptophan ratio (5). Therefore, the protein and carbohydrate breakfasts in Experiment 1 would have led to differences in the plasma tryptophan ratio. These biochemical differences are accompanied by one main behavioral difference. The protein breakfast resulted in a greater satiating effect (taking into account the calories ingested at breakfast) than the carbohydrate breakfast. However, this effect was seen equally on protein and carbohydrate intake at lunch. The differences in breakfast macronutrient composition did not lead to alterations in relative macronutrient selection at lunch. Thus, our data are not consistent with one part of the hypothesis which relates food-induced alterations in brain 5HT to subsequent macronutrient selection. Experiment 2 was designed to look at another of the links in this hypothesis. Foods differing greatly in macronutrient will result in differences in the plasma tryptophan ratio. We wished to study how large differences in the ratio of protein to carbohydrate in a meal must be in order to result in significant differences in the plasma tryptophan ratio. We also studied the effect of different breakfasts on changes in subsequent intended food consumption. However, because this was not the primary purpose of the experiment, and because of the number of conditions in the study, nutrient preferences was not measured directly, as in Experiment 1, but indirectly by checklists and forced choice procedures.

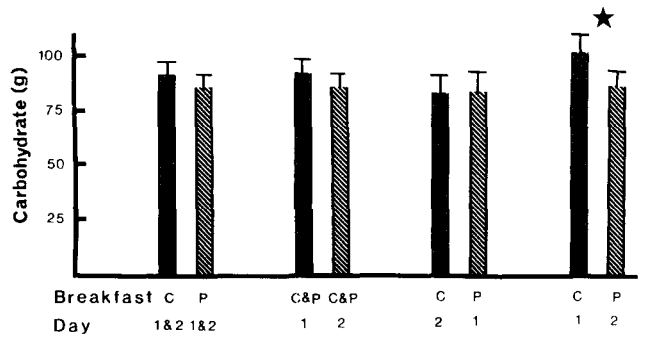

FIG. 3. The effect of carbohydrate or protein breakfasts on carbohydrate selection at lunchtime. The explanation of the figure is the same as in the caption to Fig. 1. In the subjects who had the carbohydrate breakfast on the first day, and the protein breakfast on the second day, carbohydrate intake at lunchtime was significantly smaller on the second day ($t = 2.29$, $p<0.05$).

TABLE 2

AMOUNT OF FOOD SELECTED AT LUNCHTIME AFTER CARBOHYDRATE OR PROTEIN BREAKFASTS AND RELATIVE MACRONUTRIENT COMPOSITION OF FOODS OFFERED

	Amount of Foods Selected at Lunchtime (g)		Relative Macronutrient Content of Foods Available for Selection at Lunch		
	Carbohydrate Breakfast	Protein Breakfast	Carbohydrate/ Protein	%Protein	%Protein Energy (kcal)
Bread	95.4 ± 41.0	91.8 ± 42.0	5.80	8.6	12.7
Butter	7.31 ± 6.71	7.78 ± 6.63	1.00	0.7	0.4
Ham	87.3 ± 55.8	85.3 ± 70.0	0.00	19	33
Salami	52.9 ± 38.2	52.8 ± 35.7	0.08	15	23
Cheddar Cheese	44.3 ± 32.9	42.7 ± 32.6	0.08	25	25
Brick Cheese	50.3 ± 34.1	59.1 ± 35.4	0.09	22	24
Tomato	97.9 ± 78.0	91.4 ± 73.0	4.00	1.1	20
Coconut cookies	8.16 ± 13.8	5.66 ± 11.4	10.0	6.2	5.0
Choc. chip cookies	33.1 ± 29.7	25.3 ± 31.3	12.0	5.5	4.7
Apple	70.1 ± 82.8	10.5 ± 87.5*	68.0	0.2	1.5

Values for the amount of foods selected are given as mean of 32 ± S.D.

*$p<0.05$ by two-tailed paired t-test comparing amount of food selected at lunchtime after carbohydrate or protein breakfasts.

In Experiment 2 we looked at plasma amino acids after isocaloric carbohydrate breakfasts containing 0, 4, 8 and 12% protein. Mean plasma levels of all the large neutral amino acids declined after the pure carbohydrate and 4% protein treatment, though the declines were smaller in the 4% group (Table 3). At 8 and 12% protein none of the changes were statistically significant. Tryptophan and histidine exhibited the smallest declines after carbohydrate. This particular effect, along with the larger decreases in the other neutral amino acids, resulted in a significant increase in the ratio of tryptophan to the sum of the competing amino acids after a carbohydrate breakfast (Table 4). There was an increase in the histidine ratio of the same magnitude, but it failed to achieve statistical significance. The addition of as little as 4% protein to the carbohydrate breakfast prevented the increase in the tryptophan ratio. The 4, 8 and 12% protein breakfasts and the danish pastry all failed to influence any of the amino acid ratios significantly. In Table 4A, the ratio was calculated using the traditional five amino acids; tryptophan, valine, leucine, isoleucine, phenylalanine and tyrosine. The ratios in Table 4B were calculated using the same five amino acids, but histidine and methionine were also included. These two amino acids are also competitors at the blood-brain barrier (22). When the ratios were calculated in this manner, the changes in the tryptophan ratio after the 0% protein meal did not quite reach significance. Results of the food selection and forced choice questionnaires are shown in Table 5. No statistically significant effects were observed, although there is a trend towards decreasing protein selection as the protein content of the breakfast increased.

DISCUSSION

The first experiment was designed to determine if physiological amounts of the macronutrients could alter selection at the following meal. We required treatments that would approximate proportions and quantities of macronutrients normally ingested. As most meals generally contain twice as much carbohydrate as protein, we decided on a nonisocaloric approach. The protein treatment contained slightly less than half the amount of kilocalories as the carbohydrate treatment. The amount of protein we used, 45 g, is a moderate quantity, and might be ingested in a single meal. Protein has been shown to possess a greater satiating capacity than carbohydrate in humans (9,16) and monkeys (19). Thus, to be able to observe an effect on nutrient selection without altering total kilocalorie intake, it seemed appropriate to administer less protein. This approach was justified by the absence of any difference between treatments on total kilocalorie intake as seen in Fig. 1. We did find that a protein meal decreased subsequent energy intake when it was given on the second occasion, but not when it was given on the first occasion. Psychological factors may have played a part in the order effect. On the second day not only were the foods familiar and thus possibly less appealing, but the subjects were anxious to be paid and to leave. These factors may have combined with the susceptibility of protein to suppress subsequent food intake and caused the order effect that we found. Rolls *et al.* (24) found that high protein and high starch foods produced greater satiety than high fat, high sucrose or mixed content foods. Our carbohydrate meal was less than half starch. The major ingredient was polycose, a glucose polymer derived from controlled hydrolysis of cornstarch, which presumably behaved more like glucose than like starch as far as satiety was concerned.

Our results indicate that high protein and high carbohydrate meals given in the morning displayed different satiating capacities. A high protein breakfast, with half the energy value of a high carbohydrate breakfast, exerted an approximately equipotent effect on a lunchtime test meal. Since the protein and carbohydrate breakfasts were similar in sensory qualities, and, therefore, presumably similar in their capacity to provoke cognitive attributions, it is a reasonable assumption that their different actions on satiety were mediated by different metabolic effects. The exact metabolic substrate of this effect is unknown, but our data indicate that it is not 5HT. If the carbohydrate breakfast raised, and the protein breakfast lowered brain 5HT, then a difference should have been seen at lunchtime in the absolute number of calories selected. In fact, the number of calories selected was approximately the same after the two breakfasts and the greater satiating power of the protein breakfast could only be inferred from the fact that intake was the same after protein breakfast even though fewer calories were ingested.

The lack of effect of the different breakfasts on energy intake is not surprising as human studies designed to investigate the acute

TABLE 3

EFFECT OF DIETARY TREATMENTS ON PLASMA AMINO ACID LEVELS

Breakfast	Pre- or Postmeal	Trp	Free Trp	Tyr	Phe	Val	Ile	Leu	His	Met
0% protein	pre	72.6 ± 18.7	10.9 ± 3.7	61.0 ± 10.5	54.4 ± 8.9	226 ± 60	70.2 ± 12.3	124 ± 49	85.5 ± 9.6	28.2 ± 4.6
	post	59.6 ± 17.2	7.7 ± 1.8*	38.5 ± 8.9*	40.6 ± 11.4	162 ± 42†	38.7 ± 8.6†	82 ± 17*	73.4 ± 14.8	17.9 ± 3.4†
4% protein	pre	67.0 ± 8.11	9.3 ± 1.6	51.7 ± 8.6	50.2 ± 7.7	232 ± 44	65.3 ± 14.3	133 ± 22	82.1 ± 15.8	23.7 ± 4.1
	post	56.8 ± 7.27	7.4 ± 1.1	41.1 ± 5.8	42.3 ± 4.3	189 ± 28*	46.6 ± 6.1*	92 ± 11*	71.6 ± 12.1	18.8 ± 2.6*
8% protein	pre	72.1 ± 12.7	10.3 ± 2.0	56.5 ± 13.1	50.2 ± 9.2	213 ± 42	64.5 ± 12.2	123 ± 23	74.7 ± 11.3	23.9 ± 5.7
	post	65.2 ± 13.3	8.5 ± 1.6	58.1 ± 8.6	51.3 ± 5.1	209 ± 24	58.9 ± 6.0	109 ± 13	77.3 ± 9.5	24.4 ± 3.2
12% protein	pre	65.7 ± 10.8	9.8 ± 1.5	54.1 ± 6.3	53.3 ± 7.0	230 ± 49	70.7 ± 14.4	141 ± 86	86.5 ± 12.9	25.4 ± 2.7
	post	63.4 ± 10.5	8.4 ± 1.2	57.1 ± 8.2	56.1 ± 7.2	246 ± 47	70.9 ± 13.1	136 ± 35	86.9 ± 13.8	25.7 ± 2.6
Danish pastry	pre	78.6 ± 14.7	11.8 ± 3.5	66.5 ± 25.2	62.7 ± 13.8	242 ± 73	86.6 ± 47.0	162 ± 66	91.8 ± 15.3	28.5 ± 8.7
	post	67.6 ± 14.8	9.9 ± 2.7	60.1 ± 25.4	63.1 ± 15.8	219 ± 58	68.8 ± 31.6*	130 ± 48	88.2 ± 9.7	24.1 ± 8.3*

Results are presented as mean of 10 ± S.D. in μmoles/l. A two-way analysis of variance was carried out on the values for each of the individual amino acids. There was a significant effect of time on total plasma tryptophan, $F(1,18) = 8.11$, $p<0.01$, and free plasma tryptophan, $F(1,18) = 17.7$, $p<0.01$. Tukey's test revealed a significant decline in free tryptophan with the 0% protein meal ($q = 3.95$, $p<0.05$). For tyrosine there was a significant effect of time, $F(1,18) = 7.22$, $p<0.05$, and a significant time by condition interaction, $F(4,72) = 2.71$, $p<0.05$. Tukey's test revealed a significant decline in plasma tyrosine after the 0% protein breakfast ($q = 5.06$, $p<0.05$). For phenylalamine there was no significant effect of time, but there was a significant time by condition interaction, $F(4,72) = 2.65$, $p<0.01$. There was a significant effect of time for valine, $F(1,18) = 9.99$, $p<0.01$, isoleucine, $F(1,18) = 17.7$, $p<0.01$, and leucine, $F(1,18) = 13.4$, $p<0.05$. Tukey's test revealed significant declines for the branched chain amino acids for the 0% breakfast (for Val, $q = 5.38$, $p<0.01$; for Ileu, $q = 5.64$, $p<0.01$; for Leu, $q = 4.0$, $p<0.05$) and the 4% breakfast (for Val, $q = 3.66$, $p<0.05$; for Ileu, $q = 3.33$, $p<0.05$; for Leu, $q = 3.88$, $p<0.05$) while the danish pastry caused a significant decline in Ileu ($q = 3.17$, $p<0.05$). For methionine there was a significant effect of time, $F(1,18) = 16.6$, $p<0.01$, and a significant time by condition interaction, $F(4,72) = 3.70$, $p<0.05$. Tukey's test revealed a significant decline in methionine after the 0% ($q = 7.06$, $p<0.01$) and 4% breakfast ($q = 3.36$, $p<0.05$) and after the danish pastry ($q = 3.01$, $p<0.05$). *$p<0.05$; †$p<0.01$ relative to premeal value.

role of 5HT in regulation of energy intake have shown mixed results. Although tryptophan administration led to a decrease in food intake in young men (18), the finding is confounded by the increased faintness and dizziness experienced by the treated subjects. Blundell and Hill (9) found that adding tryptophan to either a high carbohydrate or a high protein lunch failed to influence total calorie intake in a test meal three hours later. We also failed to detect any effect on total calorie selection in a test meal when tryptophan levels were altered. In our experiment plasma tryptophan was depleted markedly by a tryptophan-deficient amino acid mixture (36).

In the present study we did not find any changes in macronutrient selection after pretreatment with either protein or carbohydrate (Fig. 1). This is in contrast to the results of Blundell and Hill (9) who found a significant decrease in protein selection after a high protein meal. However, Blundell and Hill (9) used 66 g of protein, nearly 50% more than we used (45 g). It appears that the relatively small quantities of protein used in our study were not enough to alter macronutrient intake. Alternatively, the difference in energy intake at breakfast may have been a confounding factor. It may be that altered macronutrient selection would have been seen if the caloric intake of the protein and carbohydrate breakfasts had been equal. The lack of any effect should not be surprising as studies on the effect of altered tryptophan levels on macronutrient selection in humans, like those on total energy intake, have given mixed results. Changes in macronutrient selection after tryptophan administration have not been observed in some studies (18, 27, 32). However, when tryptophan was given with a high protein lunch, a significant reduction in carbohydrate selection was seen (9). Conversely, protein intake was diminished in subjects whose plasma tryptophan levels were lowered by a tryptophan deficient amino acid mixture (36). The results of these studies, together with those of the present study, suggest that 5HT can play a role in macronutrient selection in some circumstances, but that diet-induced changes in brain 5HT are unlikely to play an important role in regulating intake of protein and carbohydrate in humans.

Comparison of individual foods selected after macronutrient administration revealed a significant increase in apple consumption after protein pretreatment (Table 2). This seemingly inconsequential result led us to examine the relative amounts of protein and carbohydrate in the foods offered and to question why the effect was specific to this particular food. When the ratios of carbohydrate to protein were calculated we found the ratio for the apple was noticeably different from that of the other foods in that it was more than 5-fold higher than the next highest ratio (Table 2). It was the single food containing primarily carbohydrate, with only negligable amounts of protein. In contrast, the other "carbohydrate" foods contained more than 4% protein energy. A protein content of 4% is significant because, as discussed below, a protein content that small is capable of blocking the rise in the tryptophan ratio produced by carbohydrate. Therefore, as far as the plasma ratio is concerned, only the apple can be classified as a carbohydrate food. In terms of tryptophan availability, all the other foods would be perceived neurochemically as mixed carbohydrate and protein foods, even the tomato and cookies. The fact that a carbohydrate meal decreased selection of the only relatively pure carbohydrate food in the subsequent test meal suggests that this small finding did not occur only by chance. It may be that in humans the mechanisms altered by previous protein or carbohydrate meals are not involved so much in regulating overall protein or carbohydrate intake as in the control of intake of specific carbohydrate foods. This makes sense in evolutionary terms. Fruits such as mangoes are highly preferred by monkeys. A mechanism would be needed to stop monkeys eating nothing but mangoes during mango season, because this would result in negligible protein intake. Our results suggest that the intake of a

TABLE 4

EFFECT OF DIETARY TREATMENTS ON PLASMA AMINO ACID RATIOS

Breakfast	Pre- or Postmeal	Trp/LNAA	Free Trp/LNAA	Tyr/LNAA	Phe/LNAA	His/LNAA
A.						
0% protein	pre	0.133 ± 0.029	0.020 ± 0.006	0.110 ± 0.019	0.096 ± 0.008	0.144 ± 0.028
	post	0.168 ± 0.042*	0.022 ± 0.005	0.103 ± 0.022	0.105 ± 0.015	0.179 ± 0.051
4% protein	pre	0.129 ± 0.030	0.018 ± 0.004	0.095 ± 0.015	0.091 ± 0.006	0.137 ± 0.026
	post	0.140 ± 0.026	0.018 ± 0.004	0.097 ± 0.016	0.099 ± 0.008	0.153 ± 0.027
8% protein	pre	0.144 ± 0.025	0.020 ± 0.003	0.107 ± 0.015	0.095 ± 0.009	0.131 ± 0.021
	post	0.135 ± 0.029	0.018 ± 0.003	0.118 ± 0.015	0.103 ± 0.009	0.141 ± 0.022
12% protein	pre	0.122 ± 0.025	0.018 ± 0.004	0.099 ± 0.019	0.097 ± 0.049	0.142 ± 0.021
	post	0.112 ± 0.017	0.015 ± 0.003	0.101 ± 0.014	0.099 ± 0.015	0.140 ± 0.027
Danish pastry	pre	0.132 ± 0.026	0.019 ± 0.003	0.105 ± 0.013	0.102 ± 0.021	0.136 ± 0.025
	post	0.129 ± 0.025	0.019 ± 0.003	0.107 ± 0.016	0.118 ± 0.023	0.152 ± 0.024
B.						
0% protein	pre	0.110 ± 0.024	0.017 ± 0.006	0.091 ± 0.014	0.080 ± 0.006	0.134 ± 0.021
	post	0.134 ± 0.035	0.018 ± 0.004	0.082 ± 0.016	0.085 ± 0.012	0.172 ± 0.048
4% protein	pre	0.108 ± 0.024	0.015 ± 0.003	0.079 ± 0.013	0.076 ± 0.005	0.133 ± 0.025
	post	0.115 ± 0.021	0.015 ± 0.003	0.080 ± 0.014	0.082 ± 0.006	0.148 ± 0.026
8% protein	pre	0.120 ± 0.020	0.017 ± 0.003	0.090 ± 0.013	0.080 ± 0.007	0.126 ± 0.020
	post	0.111 ± 0.024	0.015 ± 0.003	0.098 ± 0.011	0.086 ± 0.007	0.135 ± 0.021
12% protein	pre	0.101 ± 0.020	0.015 ± 0.003	0.082 ± 0.014	0.081 ± 0.014	0.137 ± 0.020
	post	0.094 ± 0.013	0.013 ± 0.003	0.084 ± 0.011	0.082 ± 0.011	0.134 ± 0.026
Danish pastry	pre	0.109 ± 0.020	0.016 ± 0.002	0.088 ± 0.011	0.086 ± 0.017	0.131 ± 0.023
	post	0.106 ± 0.019	0.015 ± 0.002	0.089 ± 0.014	0.097 ± 0.019	0.146 ± 0.029

In section A the ratios are calculated using Trp, Tyr, Phe, Leu, Ileu and Val as the competing amino acids. In section B, Met and His are also included. Values are given as mean of 10 ± S.D. For each ratio a two-way analysis of variance ws carried out separately for the values in sections A and B. None of the time by condition interactions achieved significance, but the values for tryptophan in section A were close to significance [$F(4,72)=2.42$: for $p=0.05$ a value of 2.48 is needed]. Tukey's test revealed that only the 0% protein meal caused a significant change in the tryptophan ratio ($q=4.73$, $p<0.05$).

meal of mangoes might inhibit only the intake of further items containing high carbohydrate with little or no protein.

Because of the considerations above, we decided to look at the amount of protein in a carbohydrate meal necessary to block the rise in the tryptophan ratio. In addition, we looked at a commonly ingested breakfast, coffee and a danish pastry, that is generally regarded as a carbohydrate breakfast. In fact, in such a breakfast the amount of protein is about 10% the amount of carbohydrate. Previously published reports had only looked at the effect of larger amounts (20% or over) of protein or pure carboyhydrate (3,14). The effect of smaller quantities of protein on human plasma amino acids had not been examined. The results from our second study supported the idea that only relatively pure carbohydrate significantly elevated the tryptophan ratio. We found that the addition of only 4% protein was sufficient to inhibit the increase (Table 4). Beginning at the 8% protein level, a trend towards a decrease in the tryptophan ratio was seen, increasing with the increased protein content of the meal. The breakfast of a coffee and a danish pastry caused no significant change in the tryptophan ratio, indicating that it was not a carbohydrate meal as far as the tryptophan ratio is concerned.

Interestingly, the ratio of histidine to the sum of the neutral amino acids showed the same response as tryptophan, with an increase of about 25% after the carbohydrate treatment. This amino acid precursor has been virtually ignored in behavioral studies, even though it is able to compete at the blood-brain barrier with the other neutral amino acids and histidine availability can influence brain levels of histamine (25).

A trend towards an inverse relationship between protein content and protein selection was seen in the food selection and forced choice questionnaires (Table 5), though these differences did not reach statistical significance.

Our human data concerning the effects of small amounts of protein, added to a carbohydrate meal, on the plasma tryptophan ratio is supported by the animal work of Yokogoshi and Wurtman (35) who found that 5% casein added to a 70% carbohydrate meal blocked the expected increase in the tryptophan ratio. Therefore, in both rats and man, significant changes in the ratios will occur only at extreme levels of macronutrient ingestion, i.e., when either pure carbohydrate or high concentrations of protein are consumed. This supports our contention that the tryptophan ratio may be involved in a mechanism used to distinguish between foods containing pure macronutrients. A free ranging animal would perhaps be in a situation where foods of extreme macronutrient content exist and would be forced to select among them. Upon examination, very few foods actually contain less than 4% protein. The foods falling into this category would be primarily fruit, which are usually associated with a sweet taste. For animals in the

TABLE 5

	Food Selection			
	Protein (g)		Carbohydrate (g)	
Premeal	Pre	Post	Pre	Post
0% protein	133 ± 63	191 ± 102	236 ± 114	253 ± 114
4% protein	141 ± 59	180 ± 51	201 ± 115	206 ± 112
8% protein	125 ± 93	146 ± 78	222 ± 140	180 ± 116
12% protein	130 ± 70	129 ± 84	266 ± 124	259 ± 161
breakfast	136 ± 107	160 ± 108	255 ± 165	254 ± 178
	Forced Choice			
	Number of High Protein Foods		Number of High Carbohydrate Foods	
Premeal	Pre	Post	Pre	Post
0% protein	9.0 ± 4.8	11.6 ± 3.6	6.9 ± 4.7	4.4 ± 3.6
4% protein	10.2 ± 2.5	11.7 ± 2.0	5.8 ± 2.5	4.3 ± 2.0
8% protein	7.0 ± 5.4	8.0 ± 3.7	9.0 ± 5.4	7.9 ± 3.7
12% protein	8.8 ± 5.0	6.9 ± 5.2	8.2 ± 4.9	9.1 ± 5.2
breakfast	7.5 ± 5.0	8.0 ± 4.8	8.5 ± 5.0	8.0 ± 4.8

Values for food selection show the amount of protein and carbohydrate in a meal selected by the subject from a menu before and after ingestion of a protein or carbohydrate breakfast. Values are the mean of 10 ± SD. Results of the forced choice questionnaire are given as mean of 10 ± SD for number of high protein or high crbohydrate foods selected. Two-way analysis of variance indicated no significant time by condition interactions, indicating that pre-post changes were not different for the different treatments.

wild, the purpose of the mechanism may be to inhibit an animal from feeding solely on a food which is preferable for its sensory rather than its nutritional quality.

In humans, the physiological relevance of this mechanism is questionable, as most meals contain a mixture of protein, carbohydrate and fat in quantities unlikely to increase the tryptophan ratio significantly. A second factor which must be considered is the magnitude of change found after the carbohydrate breakfast. Ashley et al. (5) have suggested that a 50–100% increase or a 30–50% decrease in the tryptophan ratio would be required to alter brain 5HT metabolism in humans. Recently, we have given protein and carbohydrate meals to patients before they had a lumbar puncture. Measurements of tryptophan and the 5HT metabolite, 5-hydroxyindoleacetic acid, in cerebrospinal fluid were consistent with the idea that changes of the plasma tryptophan ratio of the size mentioned or smaller will not lead to alterations in CNS 5HT synthesis (28). In our present study, the carbohydrate meal only resulted in an increase in the 20% range. It is unlikely that this degree of change would effect brain 5HT. We found no effect of protein or carbohydrate meals on subsequent overall selection of protein or carbohydrate. Under other experimental circumstances such an effect might have occurred. Increasing dietary levels of protein causes increasingly large changes in the plasma tryptophan ratio (12,20). Thus, larger meals at breakfast may have altered macronutrient selection at lunch. The three-hour interval between meals in our study was chosen because three hours is slightly after the peak alteration in the plasma tryptophan ratio (5,20) and alterations in brain 5HT might be expected to follow those in the plasma with a small lag. However, it is possible that if we had used a smaller interval between the meals an effect on macronutrient selection would have been apparent. Finally, there is a diurnal variation in the capacity of food to induce satiety (10). If the same were true for macronutrient selection we might have obtained positive results if we had carried out the experiment at a different time of day. However, although it is not possible to generalize too far from our data, the results of the two experiments, taken together, indicate that the feedback loop, in which food intake influences brain 5HT, which alters subsequent macronutrient selection, is not a general phenomenon in humans. It remains to be seen whether the feedback loop operates with extremes of food intake or in clinical populations with abnormal eating patterns or biochemistry.

The lack of evidence for a role of the tryptophan ratio in regulation of food intake does not imply that 5HT itself is not involved in the behavior. Abundant animal data points towards 5HT as an important neurotransmitter in the regulation of food intake, but as experimental design becomes more sophisticated we are finding that these effects are very subtle. One example is the role of 5HT in the termination of eating (8,26). Regulation of food intake is a highly complex behavior, especially in humans. In addition to physiological mechanisms, cultural, psychological and sensory factors combine to influence human dietary intake. It is these combined factors which make interpretation of dietary experiments so difficult and which accounts for differences observed in various dietary paradigms. It will be necessary to develop experimental paradigms for humans that are as finely structured as those existing for animals in order to determine the precise role of 5HT and its relationship to dietary intake.

In conclusion, the results of the experiments presented here indicate that high protein or high carbohydrate breakfasts may exert metabolic effects which result in changes in satiety and subtle alterations in subsequent dietary selection. However, our results do not support the idea that changes in the plasma tryptophan ratio and in brain 5HT, resulting from carbohydrate or protein ingestion, are directing subsequent macronutrient selection.

REFERENCES

1. Anderson, G. H. Control of protein and energy intake: role of plasma amino acids and brain neurotransmitters. Can. J. Physiol. Pharmacol. 57:1043–1057; 1979.
2. Ashley, D. V. M.; Anderson, G. H. Correlation between the plasma tryptophan to neutral amino acid ratio and protein intake in the self-selecting weanling rat. J. Nutr. 105:1412–1421; 1975.
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 differing nutritional composition. Am. J. Clin. Nutr. 36:143–153; 1982.
4. Ashley, D. V. M.; Coscina, D. V.; Anderson, G. H. Selective decrease in protein intake following brain serotonin depletion. Life Sci. 24:973–984; 1979.
5. Ashley, D. V. M.; Liardon, R.; Leathwood, P. D. Breakfast meal composition influences plasma tryptophan to large neutral amino acid ratios of healthy lean young men. J. Neural Transm. 63:271–283; 1985.
6. Blundell, J. E. Processes and problems underlying the control of food selection and nutrient intake. In: Wurtman, R. J.; Wurtman, J. J., eds. Nutrition and the brain. vol. 6. New York: Raven Press; 1983: 164–221.
7. Blundell, J. E. Serotonin and appetite. Neuropharmacology 23: 1537–1551; 1984.
8. Blundell, J. E. Serotonin manipulations and the structure of feeding behavior. Appetite 7(Suppl.):39–56; 1986.
9. Blundell, J. E.; Hill, A. J. Influence of tryptophan on appetite and food selection in man, In: Amino acids in health and disease: New perspectives. New York: Alan R. Liss; 1987:403–419.
10. de Castro, J. M. Circadian rhythms of the spontaneous meal pattern, macronutrient intake, and mood in humans. Physiol. Behav. 40: 437–446; 1987.
11. Denkla, W. D.; Dewey, H. K. The determination of tryptophan in plasma, liver and urine. J. Lab. Clin. Med. 69:160–169; 1967.
12. Fernstrom, J. D. Dietary effects on brain serotonin synthesis: relationship to appetite regulation. Am. J. Clin. Nutr. 42:1072–1082; 1985.
13. Fernstrom, J. D.; Wurtman, R. J. Brain serotonin content: Increase following ingestion of carbohydrate diet. Science 174:1023–1025; 1971.
14. Fernstrom, J. D.; Wurtman, R. J.; Hammarstrom-Wiklund, B.; Rand, W. M.; Munro, H. N.; Davidson, C. S. Diurnal variations in plasma concentrations of tryptophan, tyrosine, and other neutral amino acids; effect of dietary protein intake. Am. J. Clin. Nutr. 32:1912–1922; 1979.
15. Glaeser, B. S.; Maher, T. J.; Wurtman, R. J. Changes in brain levels of acidic, basic and neutral amino acids after consumption of single meals containing various proportions of proteins. J. Neurochem. 41:1016–1021; 1983.
16. Hill, A. J.; Blundell, J. E. Macronutrients and satiety: the effects of a high protein or a high carbohydrate meal on subjective motivation to eat and food preferences. Nutr. Behav. 3:133–144; 1986.
17. Hill, A. J.; Blundell, J. E. Role of amino acids in appetite control in man. In: Heuther, G., ed. Amino acid availability and brain function in health and diseases, NATO ASI Series H Cell biology. vol. 20. Berlin: Springer-Verlag; 1988:239–248.
18. Hrboticky, N.; Leiter, L. A.; Anderson, G. H. Effects of L-tryptophan on short term food intake in lean men. Nutr. Res. 5:595–607; 1985.
19. Jen, K. L. C.; Bodkin, N. L.; Metzger, B. L.; Hansen, B. C. Nutrient composition: Effects on appetite in monkeys with oral factors held constant. Physiol. Behav. 34:655–659; 1985.
20. Moller, S. E. Effect of various oral protein doses on plasma neutral amino acid levels. J. Neural Transm. 61:183–191; 1985.
21. Musten, B.; Peace, D.; Anderson, G. H. Food intake regulation in the weanling rat: self-selection of protein and energy. J. Nutr. 104: 563–572; 1974.
22. Oldendorf, W. H.; Szabo, J. Amino acid assignment to one of three blood-brain barrier amino acid carriers. Am. J. Physiol. 230:94–98; 1976.
23. Peters, J. C.; Harper, A. E. Influence of dietary protein level on protein self-selection and plasma and brain amino acid concentrations. Physiol. Behav. 33:783–790; 1984.
24. Rolls, B. J.; Hetherington, M.; Burley, V. J. The specificity of satiety: the influence of food of different macronutrient content on the development of satiety. Physiol. Behav. 43:145–153; 1988.
25. Schwartz, J. C.; Lampart, C.; Rose, C. Properties and regional distribution of histidine decarboxylase in rat brain. J. Neurochem. 17:1527–1534; 1970.
26. Shor-Posner, G.; Grinker, J. A.; Marinescu, C.; Brown, O.; Leibowitz, S. F. Hypothalamic serotonin in the control of patterns and macronutrient selection. Brain Res. Bull. 17:663–671; 1986.
27. Strain, G. W.; Strain, J. J.; Zumoff, B. L-Tryptophan does not increase weight loss in carbohydrate-craving obese subjects. Int. J. Obes. 9:375–380; 1985.
28. 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.
29. Wurtman, J. J.; Moses, P. L.; Wurtman, R. J. Prior carbohydrate consumption affects the amount of carbohydrate that rats choose to eat. J. Nutr. 113:70–78; 1983.
30. Wurtman, J. J.; Wurtman, R. J. Fenfluramine and fluoxetine spare protein consumption while suppressing calorie intake by rats. Science 198:1178–1180; 1977.
31. Wurtman, J. J.; Wurtman, R. J. Drugs that enhance central serotoninergic transmission diminish elective carbohydrate consumption by rats. Life Sci. 24:895–904; 1979.
32. Wurtman, J. J.; Wurtman, R. J. Suppression of carbohydrate consumption as snacks and at mealtime by DL-fenfluramine or tryptophan. In: Garattini, S.; Samanin, R., eds. Anorectic agents: Mechanisms of action and tolerance. New York: Raven Press; 1981:169–182.
33. Wurtman, R. J.; Wurtman, J. J. Nutrients, neurotransmitter synthesis and the control of food intake. In: Stunkard, A. J.; Stellar, E., eds. Eating and its disorders. New York: Raven Press; 1984:77–86.
34. Wurtman, R. J.; Wurtman, J. J. Carbohydrate craving, obesity and brain serotonin. Appetite 7(Suppl.):99–103; 1986.
35. Yokogoshi, H.; Wurtman, R. J. Meal composition and plasma amino acid ratios: effect of various proteins or carbohydrates, and of various protein concentrations. Metabolism 35:837–842; 1986.
36. Young, S. N.; Tourjman, S. V.; Teff, K. L.; Pihl, R. O.; Anderson, G. H. The effect of lowering plasma tryptophan on food selection in normal males. Pharmacol. Biochem. Behav. 31:149–152; 1988.