

Psychobiological Effects of Carbohydrates

Bonnie Spring, Ph.D., June Chiodo, Ph.D., Margarette Harden, Ph.D., Michael J. Bourgeois, M.D., James D. Mason, M.Ed., and Lorenz Lutherer, M.D., Ph.D.

The authors studied whether the fatiguing effects of eating lunch are greater for carbohydrate-rich meals than for other meals, and related the time course of behavioral change to plasma glucose, insulin, and amino acids. On different occasions, in counterbalanced order, normal women (N=7) fasted overnight, ate a standard breakfast, and at lunch either continued to fast or ate a high-carbohydrate, low-protein meal; a hedonically similar meal containing both carbohydrate and protein; or a high-protein, low-carbohydrate meal. Meals were isocaloric and equated for fat content. Only the carbohydrate meal significantly increased fatigue, which could not be attributed to hypoglycemia because plasma glucose remained elevated. Fatigue began approximately when the carbohydrate meal elevated the plasma tryptophan ratio but ended even though the ratio remained elevated. Fatigue after a high-carbohydrate lunch could not be explained by reactive hypoglycemia or sweet taste, and could partially be explained by the hypothesis that fatigue parallels an elevation of the tryptophan ratio.

(J Clin Psychiatry 50(5, Suppl):27-33, 1989)

Behavioral change after intake of carbohydrate-rich foods has been documented in normal humans.¹ Fatigue^{2,3} and impaired performance on tests of concentration and speed⁴ occur approximately 2 hours after carbohydrate consumption. Alertness has been lowered to a greater extent by both simple and complex⁵ carbohydrates than by protein⁶ or fasting,⁷ but a full comparison of a high-carbohydrate meal to fasting, high protein, and balanced meals has not previously been reported. We performed this comparison to determine the extent to which the fatiguing effects of eating lunch are greater for carbohydrate-rich meals than for other meals. To examine the mechanism underlying postlunch drowsiness, we studied the time course of fatigue in relation to plasma glucose, insulin, and the ratio of plasma tryptophan to other large neutral amino acids (LNAA).

Because carbohydrate test meals are typically sweet, dessert-type foods, either the hedonic taste properties of these meals or their nutrient composition could underly behavioral effects. To vary both hedonic and nutrient properties, we compared three different meals against a fasting condition. Two meals were hedonically similar (sweet, dessert-type foods) but nutritionally different. One (CHO meal) was rich in carbohydrate and protein-

poor; the other (balanced meal) contained a mixture of protein and carbohydrate. A third (protein meal) was rich in protein, carbohydrate-poor, and bland in taste.

METHOD

Subjects

Seven normal women between 18 to 29 years of age participated in the study. None had a history of diabetes, hypoglycemia, eating disorder, obesity, substance abuse, or psychiatric hospitalization. Screening procedures also excluded any subject who had, in the past 6 months, met Research Diagnostic Criteria⁸ for mania, hypomania, or major depression. Also excluded were subjects taking any medication, including birth control pills. Before entering the protocol, subjects were examined by a physician to ensure that they were in good physical health and not at risk from study procedures. After a full explanation of the study, subjects gave written informed consent; they were subsequently paid for their participation.

Procedure

Before 4 test days separated by 1-week intervals, subjects fasted from 8:00 p.m. At 7:30 a.m. the following morning, they arrived at the laboratory and ate a standard breakfast. The breakfast was two pieces of whole wheat toast with 1/2 tsp butter and 1 tbsp jam, 4 oz orange juice, and 1 cup skim milk. With breakfast, subjects also drank their usual amount of coffee or tea, as determined prior to study entry, to avoid caffeine withdrawal. Then they remained in the laboratory, refrained from eating or drinking anything except water, and engaged in sedentary activities of their own choosing for the remainder of the morning.

At 11:00 a.m., an indwelling intravenous catheter was inserted into each subject's antecubital fossa region, distal forearm, or hand to permit blood samplings. Blood was drawn 30 minutes before lunch and 45, 90, 135, and 165 minutes after the meal. Mood and performance were as-

From the Department of Psychology, UHS/The Chicago Medical School, North Chicago, Illinois (Dr. Spring); the Department of Internal Medicine, Temple University Medical School, Philadelphia (Dr. Chiodo); the Departments of Food and Nutrition (Dr. Harden), Pediatrics (Dr. Bourgeois) and Mr. Mason, and Physiology, (Dr. Lutherer), Texas Tech University Health Science Center, Lubbock.

Supported in part by a grant from the Institute for Nutritional Sciences and the Graduate School, Texas Tech University.

The authors thank Debra Harner, Sherry Crowell, Geoffrey Suope, and Ray Valencia for assistance in data collection and Rita Tsay, Chizi Research Dietician, MITCRC, for developing the recipes.

Reprint requests to: Bonnie Spring, Ph.D., Department of Psychology, UHS/The Chicago Medical School, 3333 Green Bay Road, North Chicago, IL 60064.

essed 45 minutes before lunch and 30, 75, 120, and 150 minutes after eating. Subjects consumed the test meals or fasted between 12:15 and 12:45 p.m. The meals, given in counterbalanced order, were carbohydrate lunch, balanced lunch, protein lunch, or no lunch. Subjects were tested as a group, including at least one individual who received each test meal, to minimize any potential influence of experimenter expectancies on the dependent measures.

Test Meals

The protein lunch was turkey breast salad. It consisted of 318.8 g turkey breast with mayonnaise and supplied 105 g protein, 33.3 g fat, and 780 calories. The carbohydrate and balanced lunches were both six sweet-tasting, cookie-like lunch bars. The carbohydrate meal supplied 105 g CHO, 0.7 g protein, 42.7 g fat, and 799 calories. The balanced meal, providing carbohydrate and protein in approximately a 3:1 ratio, supplied 76 g CHO, 27.7 g protein, 40 g fat, and 774 calories. Both the carbohydrate and balanced meals supplied a mixture of complex and simple carbohydrate in a 2.9:1 ratio for the carbohydrate lunch and a 2.6:1 ratio for the balanced lunch. The carbohydrate lunch was identical to the test meal used in two prior studies on the behavioral effects of carbohydrate.²² The same protein meal has also been studied previously.²³

Mood Tests

Mood was assessed by the Profile of Mood States (POMS).¹⁰ The POMS presents 65 self-descriptive adjectives that are rated on 5-point scales to describe the subject's mood. The "right now" version of the test was used. The POMS yields scores on six-factor, analytically derived scales that describe the full range of normal mood fluctuations: tension-anxiety, depression-dejection, anger-hostility, vigor-activity, fatigue-inertia and confusion-bewilderment. All scales possess internal consistency reliability values in the range of .90 and evidence of construct and predictive validity.¹⁰

The Visual Analogue Mood Scale (VAMS) supplied an additional measure of mood.¹¹ Subjects received 32 sheets of paper, each showing a 128-mm line labeled with a different potentially self-descriptive adjective. The instructions were to mark the line at the point corresponding to the subject's mood at the moment. Marking the left end of the line signified that the mood was completely absent; marking the right end of the line signified that the mood was maximally present. Scales were scored by measuring the distance in millimeters from the left end of the line to the subject's mark. Prior factor analysis of the VAMS¹¹ indicate that the responses can be summarized by three factors: alertness, dysphoria, and calmness. Factor scores, computed for each subject by means of weights from the factor score coefficient matrix,¹¹ were used as the dependent variables for analysis.

The Stanford Sleepiness Scale (SSS), a 7-point self-rating scale, was used to quantify progressive increments in sleepiness.¹² The SSS has been successfully validated against subjective state and performance under sleep deprivation.¹²

Performance Tests

The Digit Symbol Substitution Test (DSST), a subtest of the Wechsler Adult Intelligence Scale-Revised,¹³ was used as a speeded test of psychomotor performance. Subjects were given a key that associated a set of symbols with digits. The task was to draw the correct symbols into empty boxes that were positioned beneath a string of digits. The subject had 90 seconds to complete as many items as possible. Scores on the DSST assessed visual-motor coordination and speed.

A letter cancellation test measured concentration. Subjects received a form showing six long strings of upper case letters; each string was preceded by three target letters presented in lower case. The task was to detect and delete as many target letters as possible in 60 seconds. Equivalent forms of the test were administered in counterbalanced order.

An addition task served as another speeded test of concentration. Subjects were given a form that showed 15 horizontal arrays of 8 digits. The task was to mentally group the numbers into two double-digit numbers at the left and two at the right, and to add the pairs of numbers. Subjects completed equivalent forms of the test in counterbalanced order.

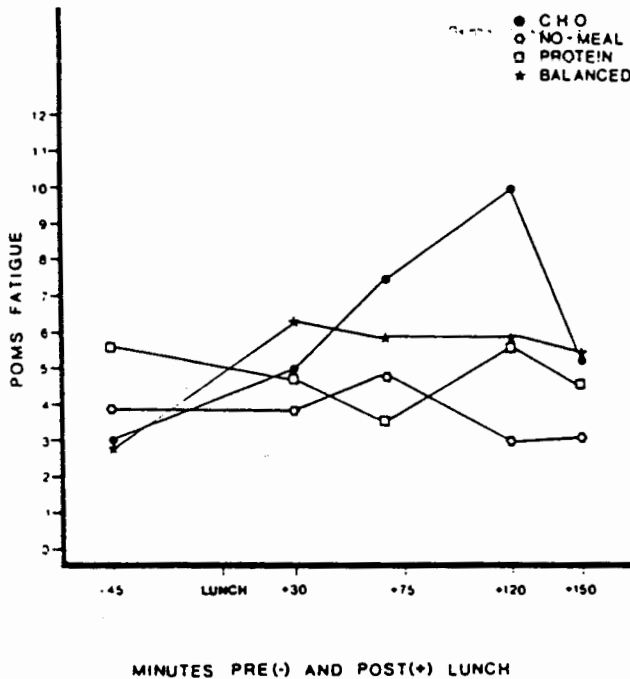
Plasma Constituents

Blood samples were divided into two aliquots: one with EDTA anticoagulant and one without anticoagulant. The anticoagulated aliquot was centrifuged and the plasma collected for glucose and amino acid determination. The glucose measurement was performed within 10 minutes of the separation. The remainder of the plasma was frozen at -20°C until the amino acid analyses. The aliquot without anticoagulant was allowed to clot at room temperature and was centrifuged, and the serum was removed and frozen at -20°C until the insulin assay was performed.

Plasma glucose was determined by the glucose oxidase method with a Beckman Glucose Analyzer 2 (Beckman Instruments, Dallas, Tex.). Intra-assay and interassay variability were 0.92% and 3.4%, respectively. Serum insulin levels were determined by solid-phase ¹²⁵I radioimmunoassay using a commercially available kit (Coat-A-Count by Diagnostic Products Corporation, Los Angeles, Calif.). Intra-assay and interassay variability were 11.3% and 4.1% respectively.

Trichloroacetic acid (TCA) was used to deproteinize the samples for amino acid analysis:¹⁴ 0.75 mL plasma was mixed with 0.25 mL of a solution containing 8% TCA and 0.4 M citrate buffer. After 30 minutes' refrigeration, centrifugation at 12,000 G for 45 minutes resulted in 0.65 mL of clear supernatant at a pH of 2.4-2.8, which was loaded onto a Beckman 121 automated amino acid analyzer. Aliquots of 0.25 mL were automatically injected into each column, with a maximum of no more than 16 hours' waiting time for overnight runs. Tryptophan was analyzed by using a 70 × 9 mm column of PA-35 resin. Elution was accomplished by using a 0.2 M citrate buffer at pH 5.20. All other LNAA were analyzed on a 520 × 9 mm column of AA-15 resin. The first buffer was 0.20 M

Figure 1. Profile of Mood States Fatigue Reported Before and After Eating a High-carbohydrate, Low-protein Lunch (CHO), a High-protein, Low-carbohydrate Lunch (Protein), or a Balanced Lunch Containing Both Carbohydrate and Protein (Balanced) or Fasting (No Meal)



citrate at pH 3.25, followed by a buffer change at 140 minutes to 0.20 M citrate, pH 4.25. Pumping speed was 70 mL/hour, with column temperature maintained at 54°C, allowing tryptophan and the other LNAA to be analyzed alternately.

Data Analysis

Data were analyzed by repeated measures analysis of variance with meal and time as within-subjects factors. Significant interactions between meal and time were interpreted by supplementary comparisons using the Newman-Keuls test. On the basis of prior findings,⁴ we hypothesized that the carbohydrate meal would cause drowsiness

and performance impairments 2 hours after lunch, and would, concurrently, elevate the ratio of tryptophan to other LNAA. Therefore, in the absence of significant meal \times time interactions, we undertook planned orthogonal contrasts¹⁵ to test the prediction that 120 minutes after eating the carbohydrate lunch, as compared with fasting, would increase fatigue, decrease vigor, decrease performance, and elevate the tryptophan ratio.

RESULTS

Mood

Figure 1 shows self-reported fatigue after each of the test meals. Subjects reported significantly greater fatigue 2 hours after eating the carbohydrate lunch than after skipping lunch ($t=2.17$, $df=24$, $p<.05$, two-tailed test, planned orthogonal contrast). Although hedonically similar to the carbohydrate meal, the balanced lunch did not cause greater fatigue than fasting, nor did the protein meal.

Table 1 shows scores for the other activational mood scales: POMS vigor, VAMS alertness, and SSS. Subjects reported the greatest proportional decrease in vigor (46.7%) 2 hours after eating the carbohydrate lunch, but differences from the other meal conditions were not significant. Neither the VAMS alertness scale nor the SSS detected changes in mood as a result of eating.

Performance

Data for the three performance tests are shown in Table 2. Eating did not significantly influence performance. The general tendency was for scores to improve over time, except that throughout the afternoon after the carbohydrate lunch, letter cancellation was somewhat worse than at baseline.

Plasma Constituents

The test lunches had differential effects on plasma glucose ($F=2.95$, $df=12,120$; $p<.01$), as shown in Figure 2. From 45 through 165 minutes after eating, the carbohy-

Table 1. Mood Scores Before and at Intervals After Eating Lunches of Different Nutrient Compositions*

Scale and Meal Condition	Baseline		Minutes After Lunch							
	Mean	SD	30		75		120		150	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD
POMS Vigor										
Fast	17.14	8.32	13.14	7.56	13.29	4.82	13.86	7.47	14.43	8.58
Protein	10.71	6.45	9.57	7.02	9.14	6.09	8.14	6.87	10.29	5.19
Balanced	16.43	6.50	12.71	6.30	12.86	8.61	14.86	7.93	17.14	8.19
CHO	17.43	8.79	13.43	5.71	11.29	2.98	9.29	3.25	15.00	4.55
VAMS Alert										
Fast	8.98	0.89	8.89	0.66	9.41	0.81	9.02	0.74	9.31	0.73
Protein	9.14	0.92	8.69	0.67	8.49	0.43	8.76	0.82	8.71	0.62
Balanced	9.22	0.77	8.45	0.79	8.44	0.43	8.83	0.66	8.56	0.78
CHO	9.30	0.58	8.89	0.46	8.83	0.41	8.84	0.87	8.67	0.85
SSS										
Fast	2.57	1.72	2.29	0.76	2.00	0.82	1.71	0.76	1.57	0.79
Protein	3.14	1.07	2.57	0.79	2.57	1.13	3.00	1.15	2.71	1.25
Balanced	2.14	1.07	2.57	1.27	2.43	0.79	2.57	0.79	2.14	0.90
CHO	2.43	0.98	2.29	0.49	2.57	0.79	2.57	0.98	2.14	0.69

*Abbreviations: CHO=carbohydrate-rich, protein-poor meal; POMS=Profile of Mood States scale; SSS=Stanford Sleepiness Scale; VAMS=Visual Analogue Mood Scale.

Table 2. Performance Scores Before and at Intervals After Eating Lunches of Different Nutrient Compositions*

Test and Meal Condition	Minutes After Lunch									
	Baseline		30		75		120		150	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Letter Cancellation										
Fast	11.29	4.23	11.71	3.95	12.57	4.61	13.14	3.39	12.14	4.38
Protein	9.86	3.72	12.00	2.00	11.86	3.94	13.00	2.58	10.71	2.81
Balanced	10.43	4.08	11.86	4.56	11.29	3.82	11.86	6.20	11.71	3.55
CHO	11.86	4.60	11.71	5.59	10.71	4.07	10.43	2.51	10.43	2.88
Addition										
Fast	13.29	5.82	13.14	7.27	14.14	5.37	15.29	6.68	15.71	7.43
Protein	14.71	6.92	14.43	8.64	14.00	6.27	15.00	7.07	14.14	6.67
Balanced	12.00	7.46	15.14	8.49	14.29	6.80	14.86	6.74	15.14	7.20
CHO	12.57	6.37	12.57	6.05	12.57	5.32	13.29	5.47	13.29	7.27
DSST										
Fast	78.29	11.74	78.57	11.54	82.71	11.09	83.71	8.69	84.00	8.47
Protein	81.29	18.45	82.00	14.21	82.29	12.84	83.00	12.56	82.71	14.45
Balanced	81.43	13.51	81.71	11.83	83.57	10.71	83.71	9.81	83.86	10.96
CHO	76.86	13.12	79.42	11.86	81.57	8.90	84.71	8.22	82.71	11.27

*Abbreviations: CHO=carbohydrate-rich, protein-poor meal. DSST=Digit Symbol Substitution Test.

drate-rich, protein-poor lunch elevated plasma glucose more than the protein meal, the balanced meal, or fasting.

The meals also differentially affected serum insulin ($F=4.52$, $df=12,120$; $p<.001$). Glucose elevations following both the carbohydrate and balanced lunches were sufficient to trigger insulin release, as shown in Figure 3. By 45 minutes after the balanced meal and 90 minutes after the carbohydrate meal, insulin exceeded the level produced by eating protein or fasting.

Each meal produced a specific pattern of change in the combined plasma levels of the LNAA: leucine, isoleucine, valine, tyrosine, and phenylalanine ($F=13.95$, $df=12,120$; $p<.001$). From 45 minutes after lunch onward, the protein lunch increased these LNAA signifi-

cantly more than any other meal, and the balanced meal increased them more than the carbohydrate lunch or fasting. Moreover, by 135 minutes after lunch and onward, the carbohydrate lunch significantly decreased these LNAA to a greater extent than any other meal or fasting. Both protein and balanced meals but not carbohydrate or fasting also increased plasma tryptophan significantly ($F=2.49$, $df=12,120$; $p<.01$). Consequently, the meals had different effects on the ratio of plasma tryptophan to the other LNAA ($F=2.12$, $df=12,120$; $p<.05$). The protein meal increased tryptophan less than it increased the other LNAA; it, therefore, lowered the ratio of plasma tryptophan to the other LNAA. The decrease in the tryptophan ratio was relative to both other meals and fasting from 45 to 135 minutes after eating, and relative only to

Figure 2. Plasma Glucose (mg/dL) Before and After Eating a High-carbohydrate, Low-protein Lunch (CHO), a Low-carbohydrate Lunch (Protein), or a Balanced Lunch Containing Both Carbohydrate and Protein or Fasting

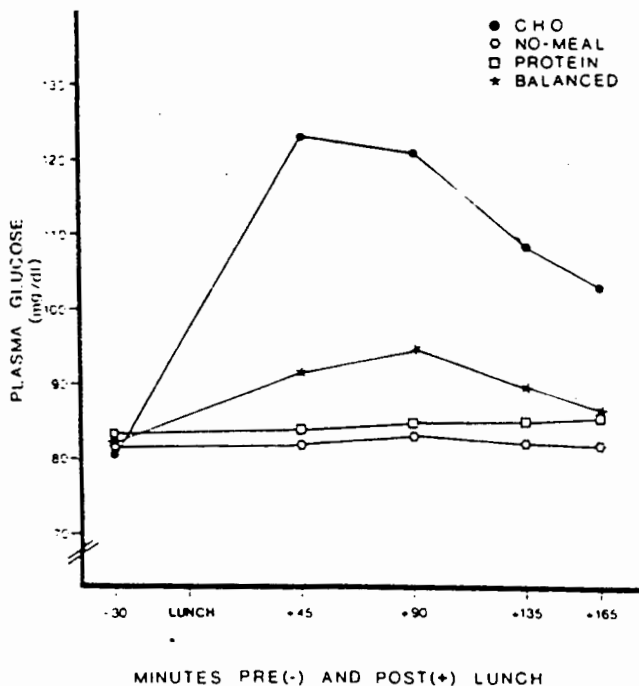


Figure 3. Serum Insulin ($\mu\text{IU}/\text{mL}$) Before and After Eating a High-carbohydrate, Low-protein Lunch (CHO), a Low-carbohydrate Lunch (Protein), or a Balanced Lunch Containing Both Carbohydrate and Protein or Fasting

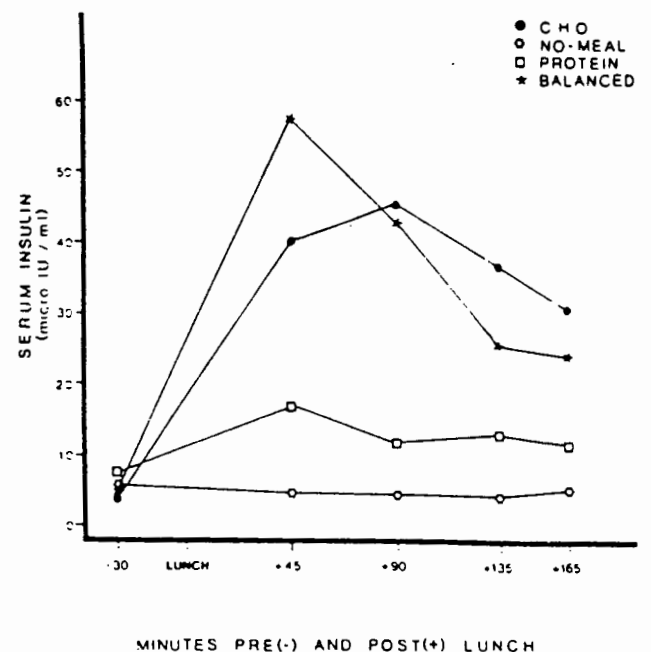
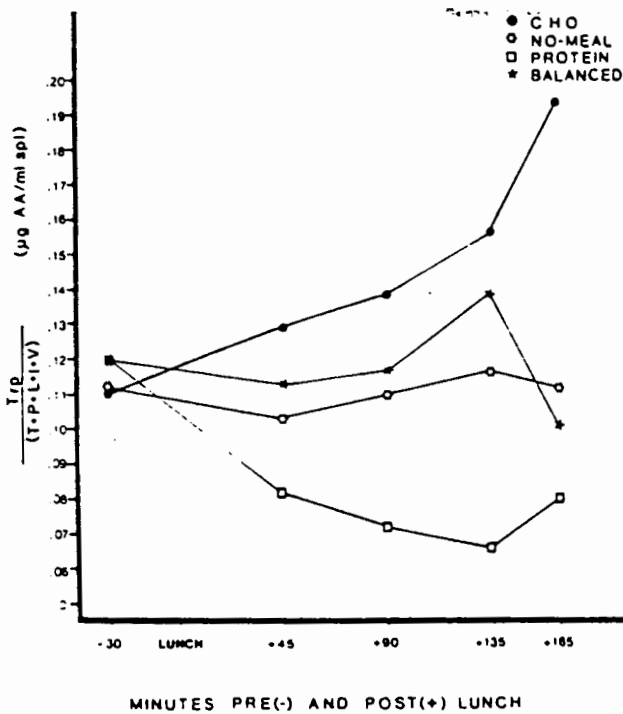


Figure 4. The Ratio of Plasma Tryptophan (Trp) to the Sum of Plasma Tyrosine (T), Phenylalanine (P), Leucine (L), Isoleucine (I), and Valine (V) Before and After Eating a High-carbohydrate, Low-protein Lunch (CHO), a Low-carbohydrate Lunch (Protein), or a Balanced Lunch Containing Both Carbohydrate and Protein or Fasting



the carbohydrate meal by 165 minutes after lunch. The balanced meal elevated plasma tryptophan approximately proportionally to the other LNAA, leaving the ratio relatively constant. By failing to alter tryptophan but by lowering the other LNAA, the carbohydrate lunch significantly elevated the tryptophan ratio compared with fasting from 135 to 165 minutes after eating.

DISCUSSION

These results indicate that a high-carbohydrate, low-protein meal eaten as lunch caused fatigue in healthy women 2 hours after eating. Neither a high-protein, low-carbohydrate meal nor a balanced lunch containing a mixture of carbohydrate and protein significantly increased fatigue in this population. There was no evidence to suggest that eating carbohydrates caused a mood of high energy (the "sugar buzz") or depression (the "sugar blues") in these healthy young women.

Three mechanisms have been proposed to explain the behavioral effects of high-carbohydrate, low-protein foods: hedonic properties, hypoglycemia, and enhanced synthesis of the brain neurotransmitter serotonin.¹ Many carbohydrate-rich foods combine sugar(s) with fat, making a highly palatable sweet taste.¹⁰ It seemed possible that the hedonically appealing sweet taste of a carbohydrate-rich food or its pleasant associations with dessert might have behavioral consequences. If so, we would expect comparable effects from both the balanced and the carbohydrate-rich lunches because both were sweet, high-fat, dessert-type foods. That the balanced lunch failed to

increase fatigue is inconsistent with a hedonic explanation.

A second mechanism by which carbohydrates might induce behavioral change is by triggering reactive hypoglycemia.¹⁷ When given in excess exogenously, insulin can profoundly lower plasma glucose sufficiently to affect brain glucose. Epinephrine secretion, triggered by hypoglycemia, causes both a compensatory breakdown of glycogen into glucose and clinical symptoms, including trembling and weakness. It has been proposed that eating sugary foods can also trigger hypoglycemia and its associated symptoms. The putative mechanism is that such foods cause a sharp rise in plasma glucose that, in turn, triggers oversecretion of endogenous insulin. A reactive plasma glucose fall to a hypoglycemic level allegedly causes the behavioral effects of carbohydrate foods.^{18,19}

If fatigue were a symptom signifying hypoglycemia, we would expect to find lowered plasma glucose at the time when the symptom occurred. Fatigue emerged 120 minutes after the carbohydrate lunch; the temporally closest blood sample was 135 minutes after eating. By conservative criteria (plasma glucose less than 80 mg/dL), no subject exhibited hypoglycemia at approximately the time when fatigue occurred. In fact, in comparison with fasting, plasma glucose remained significantly elevated at this time. Clearly, then, fatigue following a high-carbohydrate, low-protein meal cannot normally be attributed to absolute hypoglycemia.

A third hypothetical mechanism is that carbohydrates might initiate behavioral change by enhancing the synthesis and release of the brain neurotransmitter serotonin.^{20,21} A monoamine neurotransmitter, serotonin is synthesized from its amino acid precursor, tryptophan. Although the body's nutritional supply of tryptophan is obtained from protein, a high-protein meal does not elevate brain tryptophan or serotonin. Instead the opposite occurs: brain tryptophan declines, as does serotonin synthesis. This paradox occurs because tryptophan is scarce in protein (1-1.6%) in comparison with the other LNAA: leucine, isoleucine, valine, tyrosine, and phenylalanine (25%). In addition, tryptophan is significantly metabolized in its passage through the liver, whereas the branched chain amino acids (leucine, isoleucine, and valine) are not. Consequently, the branched chain amino acids can represent as much as 90% of all amino acids to enter systemic circulation from the liver and portal systems after a high-protein meal. All LNAA compete for access to the same carrier molecules for transport across the blood-brain barrier. Because a high-protein meal increases the competing LNAA in plasma, relative to plasma tryptophan, such a meal lowers the brain influx of tryptophan and also reduces brain serotonin synthesis.^{19,20}

A carbohydrate-rich, protein-poor meal, in contrast, increases brain tryptophan and serotonin synthesis, even though such a meal lacks tryptophan. In animals that have fasted over night, the insulin secretion triggered by a carbohydrate meal causes a 40% to 60% fall in plasma leucine, isoleucine, and valine and a 15% to 30% fall in plasma tyrosine. Plasma tryptophan levels do not decline because tryptophan binds to albumin molecules in plasma

as insulin strips away the free fatty acids that are usually albumin-bound. Because tryptophan remains in plasma, while most competing LNAA are taken up into muscle, tryptophan's access to blood-brain carrier molecules is enhanced. Brain tryptophan influx and serotonin synthesis and release are also increased, insofar as the latter can be assessed by CSF levels of serotonin's metabolite, 5-HIAA.²² To increase brain serotonin synthesis, a test meal must be not only carbohydrate-rich but also protein-poor. A balanced meal containing protein directly contributes sufficient LNAA to the bloodstream to compensate for the insulin-mediated fall in LNAA that is triggered by carbohydrate.²³ Cell bodies of many brain serotonergic neurons are localized in the midbrain raphe nuclei that play a role in sleep onset. Drowsiness or sleep reliably follow ingestion of the amino acid L-tryptophan,^{24,26} suggesting that fatigue following carbohydrate consumption might be triggered by the same mechanism.

If fatigue after a carbohydrate meal were caused by enhanced brain tryptophan influx and serotonin synthesis, we would expect to see an elevation of the tryptophan:LNAA ratio at the time when fatigue occurred. Indeed the ratio became significantly elevated 135 minutes after the carbohydrate lunch, at approximately the time when fatigue occurred. The onset of fatigue, then, did parallel an elevation in the tryptophan:LNAA ratio. On the other hand, no biological correlate was identified for the offset of fatigue. Paradoxically, the tryptophan ratio continued to rise even after fatigue had subsided. This finding is consistent with other results^{4,27,28} and indicates an important temporal discrepancy between behavior and the plasma tryptophan ratio. Although the onset of fatigue after carbohydrate consumption might be associated with enhanced brain influx of tryptophan, the offset of fatigue remains unexplained. Our findings are consistent with the possibility of feedback inhibition, saturation of precursor enhancement of serotonergic neurotransmission, or counterregulatory influences on behavior. They are also consistent with the possibility that some other mechanism explains fatigue after eating carbohydrates.

The behavioral findings reported here are subtle. Scales other than POMS fatigue failed to detect significant differences with this small sample size. Fatigue was only evident 2 hours after eating carbohydrate, not earlier or later. Similarly, Thayer⁴ found that sugary snacks caused tiredness 2 hours after consumption, but not earlier. This may explain why Brody and Wolitzky,²⁹ who measured mood 20 minutes and 4 hours after sucrose loading, failed to detect mood changes. The results cannot be assumed to generalize to meals of similar nutrient composition that are eaten at a different time of day. The extent to which the biological and behavioral effects of foods show diurnal variation remains uncertain.^{5,29,30} Also, these results will not hold true for all subgroups of the population. For example, obese individuals who snack on mixed nutrients report fatigue after eating carbohydrates, but obese individuals who snack preferentially on carbohydrates report activation.⁶ Patients with seasonal affective disorder and carbohydrate preference also report activation after eating carbohydrates.

Some findings, including, occasionally, our own, suggest that the behavioral effects of carbohydrate and protein may differ in degree rather than kind. Protein as well as carbohydrate meals are sometimes^{4,9} found to induce fatigue,³¹ the latter more strongly.^{4,9} Very large meals, supplying 1000 or more calories, reliably lower vigilance and alertness even when they supply mixed nutrients.³² The mechanisms that could underly such generalized caloric effects are unknown.

In summary, the current study replicates and extends prior findings indicating that moderate-sized lunchtime meals that are high in carbohydrate and low in protein selectively induce drowsiness in normal individuals 2 hours after eating. We found no evidence to support the popular belief that fatigue in normal individuals results from reactive hypoglycemia, nor did we find that fatigue could be directly related to the hedonic properties of the meal or to fluctuations in serum insulin. Fatigue occurred at approximately the same time as an elevation in the ratio of plasma tryptophan:competing LNAA, which predicts enhanced synthesis of the brain neurotransmitter serotonin. The onset of fatigue following carbohydrate consumption might accompany an initial enhancement of brain tryptophan influx and serotonin synthesis. It remains unclear why fatigue subsequently ceases, even though brain tryptophan influx apparently remains elevated.

REFERENCES

1. Spring B, Chiodo J, Bowen DJ: Carbohydrates, tryptophan, and behavior: A methodological review. *Psychol Bull* 102:234-256, 1987
2. Hartmann E, Spinweber CL, Ware C: L-tryptophan, L-leucine, and placebo: Effects on subjective alertness. *Sleep Research* 5:57, 1976
3. Spring B, Maller O, Wurtman J, et al: Effects of protein and carbohydrate meals on mood and performance: Interactions with sex and age. *J Psychiatr Res* 17:155-167, 1983
4. Lieberman HR, Spring BJ, Garfield GS: The behavioral effects of food constituents: Strategies used in studies of amino acids, protein, carbohydrate and caffeine. *Nutr Rev (Suppl)* 44:61-69, 1986
5. Thayer RE: Energy, tiredness, and tension effects of a sugar snack versus moderate exercise. *J Pers Soc Psychol* 52:119-125, 1987
6. Lieberman HR, Wurtman JJ, Chew B: Changes in mood after carbohydrate consumption among obese individuals. *J Clin Nutr* 44:772-778, 1986
7. Simonson E, Brozek J, Keys J: Effects of meals on visual performance and fatigue. *J Appl Psychol* 1:270-278, 1948
8. Spitzer RL, Endicott J, Robins E: Research Diagnostic Criteria: Rationale and reliability. *Arch Gen Psychiatry* 35:773-782, 1978
9. Rosenthal NE, Genhart MJ, Cabellero B, et al: Psychobiological effects of carbohydrate- and protein-rich meals in patients with seasonal affective disorder and normal controls. *Biol Psychiatry* (in press)
10. McNair DM, Lorr M, Droppleman LF: Manual: Profile of Mood States. San Diego, Educational and Industrial Testing Service, 1971
11. Bond A, Lader M: The use of analogue scales in rating subjective feelings. *Br J Med Psychol* 47:211-218, 1974
12. Hoddes E, Zarcone V, Smythe H, et al: Quantification of sleepiness: A new approach. *Psychophysiology* 10:431-436, 1973
13. Wechsler D: Wechsler Adult Intelligence Scale—Revised. Manual. San Antonio. The Psychological Corporation, 1981
14. Berridge BJ, Chao WR, Peters JH: Column chromatographic analysis of tryptophan with some basic amino acids. *Anal Biochem* 41:256-264, 1971
15. Kirk RE: Experimental Design: Procedures for the Behavioral Sciences, 2nd ed. Monterey, Calif. Brooks/Cole, 1982

16. Drewnowski A, Greenwood MRC: Cream and sugar: Human preferences for high-fat foods. *Physiol Behav* 30:629-633, 1983
17. Harris S: Hyperinsulinism and dysinsulin. *JAMA* 83:729-733, 1924
18. Langseth L, Dowd J: Glucose tolerance and hyperkinesis. *Food and Cosmetics Toxicology* 16:129-133, 1978
19. Virkkunen M: Reactive hypoglycemic tendency among habitually violent offenders. *Nutr Rev (Suppl)* 44:94-103, 1986
20. Fernstrom JD, Wurtman RJ: Brain serotonin content: Increase following ingestion of carbohydrate diet. *Science* 174:1023-1025, 1971
21. Fernstrom JD, Wurtman RJ: Brain serotonin content: Physiological regulation by plasma neutral amino acids. *Science* 178:414-416, 1972
22. Wurtman RJ, Hefti F, Melamed E: Precursor control of neurotransmitter synthesis. *Pharmacol Rev* 32:315-335, 1981
23. Yokogoshi H, Wurtman R: Meal composition and plasma amino acid ratios: Effects of various proteins or carbohydrates, and of various protein concentrations. *Metabolism* 35:837-842, 1986
24. Spinweber CL: L-tryptophan administered to chronic sleep-onset insomniacs: Late-appearing reduction of sleep latency. *Psychopharmacology* 90:151-155, 1986
25. Hartmann E, Greenwald D: Tryptophan and sleep: An analysis of 43 studies. In Schlossberger HG, Kochen W, Linzen B, et al (eds): *Progress in Tryptophan and Serotonin Research*. New York, Walter de Gruyter and Company, 1984, pp 297-304
26. Lieberman HR, Corkin S, Spring B, et al: Mood, performance and sensitivity: Changes induced by food constituents. *Psychiatr Res* 17:135-145, 1983
27. Greenwood MH, Lader MH, Kantamneni BD, et al: The acute effects of oral (-) tryptophan in normal subjects. *Br J Clin Pharmacol* 2:165-172, 1975
28. Yuwiler A, Brammer GL, Morley JE, et al: Short-term and repetitive administration of oral tryptophan in normal men. *Arch Gen Psychiatry* 38:619-626, 1981
29. Spring B, Lieberman H, Swope G, et al: Effects of carbohydrates on mood and behavior. *Nutr Rev (Suppl)* 44:51-60, 1986
30. Ashley DVM: Dietary control of brain 5-hydroxytryptamine synthesis: Implications in the etiology of obesity. In Mauron J (ed): *Nutrition: Neurotransmitter Function and Behavior*. Bern, Switzerland, Hans Huber Publishers, 1986, pp 27-40
31. Brody S, Wolitzky DL: Lack of mood changes following sucrose loading. *Psychosomatics* 24:155-162
32. Smith A, Leekam S, Ralph A, et al: The influence of meal composition on post-lunch changes in performance efficiency and mood. *Appetite* 10:195-203, 1988
33. Craig A: Acute effects of meals on perceptual and cognitive functioning. *Nutr Rev (Suppl)* 44:163-171, 1986