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EFFECTS OF DIETS HIGH IN SUCROSE OR ASPARTAME ON THE BEHAVIOR AND COGNITIVE PERFORMANCE OF CHILDREN

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Abstract Background. Both dietary sucrose and the sweetener aspartame have been reported to produce hyperactivity and other behavioral problems in children.

Methods. We conducted a double-blind controlled trial with two groups of children: 25 normal preschool children (3 to 5 years of age), and 23 school-age children (6 to 10 years) described by their parents as sensitive to sugar. The children and their families followed a different diet for each of three consecutive three-week periods. One diet was high in sucrose with no artificial sweeteners, another was low in sucrose and contained aspartame as a sweetener, and the third was low in sucrose and contained saccharin (placebo) as a sweetener. All the diets were essentially free of additives, artificial food coloring, and preservatives. The children's behavior and cognitive performance were evaluated weekly.

Results. The preschool children ingested a mean (\pm SD) of 5600 ± 2100 mg of sucrose per kilogram of body

weight per day while on the sucrose diet, 38 ± 13 mg of aspartame per kilogram per day while on the aspartame diet, and 12 ± 4.5 mg of saccharin per kilogram per day while on the saccharin diet. The school-age children considered to be sensitive to sugar ingested 4500 ± 1200 mg of sucrose per kilogram, 32 ± 8.9 mg of aspartame per kilogram, and 9.9 ± 3.9 mg of saccharin per kilogram, respectively. For the children described as sugar-sensitive, there were no significant differences among the three diets in any of 39 behavioral and cognitive variables. For the preschool children, only 4 of the 31 measures differed significantly among the three diets, and there was no consistent pattern in the differences that were observed.

Conclusions. Even when intake exceeds typical dietary levels, neither dietary sucrose nor aspartame affects children's behavior or cognitive function. (N Engl J Med 1994;330:301-7.)

REFINED sugar (especially sucrose) and aspartame (α -aspartyl-L-phenylalanine-o-methyl ester) have each been considered a possible cause of hyperactivity and other behavior problems in children.^{1,2} The presumed reaction to sucrose has been attributed to several possible causes, including a rise in blood sugar shortly after ingestion, reactive hypoglycemia several hours after ingestion, and an allergic response.³ The presumed reaction to aspartame has been attributed to the possibility that its metabolism results in elevated plasma phenylalanine concentrations, which in turn may alter the transport of essential amino acids to the brain.^{1,4,5}

Despite subjective reports about the behavioral effects of sugar and aspartame, most controlled studies have not found consistent adverse effects.^{6,7} Previous studies with controlled designs have examined the behavior of children immediately after a dietary challenge, but these studies have been criticized for their

brief duration and laboratory settings.⁶ Some argue that preschool children may be especially sensitive to sugar⁸ and that its effects may vary depending on the ratio of sugar to protein and carbohydrate in food recently consumed.⁶ Such arguments have not resolved the issue of whether dietary sweeteners have long-term behavioral effects.

Despite the lack of consistent objective data demonstrating the behavioral or cognitive effects of sugar or aspartame, subjective reports of such adverse effects continue to be widespread. Because sucrose and aspartame are common components of children's diets, any possible relation between these sweeteners and behavior is a major health concern. To test the hypothesis that sucrose or aspartame affects behavior and cognitive performance in children, we evaluated children placed on diets high in sucrose, aspartame, or saccharin (placebo) in a double-blind study with a Latin square design and a broad range of dependent measures.

METHODS

Subjects

The subjects were recruited through advertisements in the popular media and presentations at preschool programs. Sugar-sensitive children were identified on the basis of reports by their parents.

Two cohorts of children were studied concurrently. One group

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consisted of 23 children of primary-school age (6 to 10 years) reported by their parents to respond adversely to sugar, and the other group consisted of 25 normal preschool-age children (3 to 5 years of age).

Design

The study protocol was approved by the University of Iowa Committee on Research Involving Human Subjects. The subjects and their families were placed on a different diet for each of three consecutive three-week periods. One of the three diets was high in sucrose with no artificial sweeteners, another was low in sucrose and contained aspartame, and the third was low in sucrose and contained saccharin (the placebo). All diets were essentially free of additives, artificial food coloring, and preservatives. Two of the diet sequences are shown in Table 1.

The children, their families, and the research staff were kept unaware of the sequence of the diets. This blinding was reinforced by visible changes made weekly in the diets (sham diets), but the sweetener was changed only every third week. Families were informed that the diets would change weekly and were given a list of the dietary components that were either varied or controlled. The parents were asked to identify the experimental variables each week, if they could.

Provision of Diets

Immediately before the beginning of the study, a dietitian supervised the removal of food from the children's home. During the nine-week study period, all foods were provided for the subject and his or her immediate family. Family members were allowed items not included in the diet when they were out of the home and away from the subject, and coffee and alcohol were allowed to remain in the home as long as they were not consumed by the children. The food was delivered in a van equipped to serve as a mobile testing laboratory. All food was removed from the home at the end of each week, and a new supply delivered. In addition, parents kept records of all food consumed by the subjects and were encouraged to report any deviations from the specified diet.

During each three-week diet period, foods were sweetened with sucrose, aspartame, or saccharin, depending on which diet was assigned for that period. Care was taken to keep the appearance of the sweetened products identical, regardless of the sweetener used. Sweetened foods included pure fruit juice, fruit, cereals, pudding, flavored yogurt, cookies, fruit toppings, and bottled carbonated soft drinks. The soft drinks were supplied by three national bottlers in unmarked but coded bottles; unsweetened fruit juice and unsweetened cereal were provided by two national distributors. Small amounts of saccharin were used to sweeten items, such as condiments, that were consumed in small amounts by the subjects during all nine weeks. The use of various food components popularly believed to influence behavior was kept to a minimum. These included artificial colors, artificial flavors, additives, monosodium L-glutamate, chocolate, and caffeine. Shortenings and oils used in the diets did not contain butylated hydroxyanisole or butylated hydroxytoluene, and the use of frozen meats and baked products treated with these antioxidants was kept to a minimum. The three sham diets consisted of abundant quantities of red and orange foods (diet A); beef and pork, with only raw fruits and vegetables (diet B); and chicken and fish, with only cooked fruits and vegetables (diet C) (Table 1).

Dietary Intake

Dietary intake was documented in diaries by the parents and reviewed weekly with the dietitian. Parents were taught how to estimate the amounts of food consumed, and each week they received seven diary sheets listing the daily menus. The study design imposed no restrictions on the quantity of each food consumed, and parents were asked not to restrict access to any food.

Compliance

To determine dietary compliance, 1 mg of ascorbic acid per milligram of aspartame was added to foods sweetened with aspartame, and 1 mg of riboflavin per 5 g of sucrose was added to foods sweet-

Table 1. Diet Sequences for Two Subjects in a Latin-Square Design for Experimental Diets with a Random Distribution of Sham Diets.*

PERIOD	SUBJECT 1		SUBJECT 2	
	EXPERIMENTAL DIET	SHAM DIET	EXPERIMENTAL DIET	SHAM DIET
1				
Week 1	Sucrose	C	Aspartame	B
Week 2		B		A
Week 3		A		C
2				
Week 4	Saccharin	C	Sucrose	B
Week 5		A		C
Week 6		B		A
3				
Week 7	Aspartame	A	Saccharin	A
Week 8		B		B
Week 9		C		C

*Experimental diets were provided during three three-week periods in a Latin-square design. Subject 1 had the sucrose-saccharin-aspartame sequence, and Subject 2 had the aspartame-sucrose-saccharin sequence. The other four sequences were sucrose-aspartame-saccharin, aspartame-saccharin-sucrose, saccharin-sucrose-aspartame, and saccharin-aspartame-sucrose. The sham diets were assigned randomly; each three-week period included all three sham diets.

ened with sucrose. These concentrations provide at least 10 times the recommended dietary allowances,⁹ with the amount excreted roughly proportional to the amount of sweetener ingested. Urine samples were obtained weekly and tested for ascorbate, riboflavin, and creatinine.¹⁰⁻¹²

Behavioral and Cognitive Measures

The children were initially evaluated by means of a structured psychiatric interview with the parent (Diagnostic Interview Schedule for Children — Parent Version),¹³ the Wechsler Intelligence Scale for Children — Revised¹⁴ or the Wechsler Preschool and Primary Scale of Intelligence,¹⁵ and the Wide Range Achievement Test — Revised¹⁶ (for school-age children only). At base line and during each of the nine weeks of the study, the subjects were evaluated with behavioral and cognitive measures hypothesized to be sensitive to the effects of sweetener (Table 2). During base-line testing, children were oriented to the tests, and appropriate levels of difficulty were determined for the learning and academic tasks. This served to minimize the effects of practice during the study period. Motor activity was assessed with a solid-state device for measuring motion.²⁸ Five-second time sampling was used to assess behavior and activity levels during the performance of a writing or drawing task.²⁹ Several tasks (e.g., card sorting and academic tests) were too difficult to be administered to the preschool children. Children rated their mood and physical state on a visual-analogue scale²⁰ adapted from a self-report measure used to assess the effects of stimulants in previous studies.³⁰ Measures were administered in the mobile laboratory each week on the same day of the week and at the same time of day. In addition, structured ratings of specific types of behavior were completed by the children's parents, the children's teachers, and research assistants (Table 2). For the preschool-age children, the teacher's rating was completed by a preschool teacher or a caregiver other than the mother.

Biochemical Tests

Base-line biochemical tests included a fasting sucrose-tolerance test and fasting plasma amino acid analyses. Sucrose tolerance was calculated by determining blood glucose concentrations in samples drawn at 0, 0.5, 1, 2, 3, and 4.5 hours after a sucrose drink (1.75 g per kilogram of body weight). On the third, sixth, and ninth weeks of the study, postprandial blood samples for plasma glucose and amino acid analyses were drawn 2 to 3 hours after a meal and 30 to 60 minutes after the subject had drunk 250 ml (8 oz) of an uncarbonated beverage (providing 170 mg of aspartame, 30 g of sucrose, or 40 mg of saccharin). Plasma glucose concentrations were assessed by the glucose-6-phosphate dehydrogenase method. Plasma amino acid levels were determined with automated amino acid ana-

Table 2. Cognitive and Behavioral Measures Administered Weekly.*

MEASURE	RATER	COGNITIVE FUNCTION OR BEHAVIOR ASSESSED
Pediatric Behavior Scale ¹⁷	Parent	Attention, impulsivity, hyperactivity, aggression, oppositional behavior, mood, cognition, and somatic symptoms.
ADDH Comprehensive Teacher's Rating Scale ¹⁸	Teacher	Attention, hyperactivity or impulsivity, social skills, and oppositional or aggressive behavior
Behavior Symptom Checklist ¹⁹	Examiner	Attention, impulsivity, hyperactivity, and mood
Pediatric Assessment of Mood ²⁰	Child	Mood and physical symptoms
Paired Associate Learning ²¹	Examiner	Memory and learning
Wisconsin Card Sorting Test ²²	Examiner	Conceptual grouping and mental flexibility (task adapted for repeated presentation)
Continuous performance tests ^{23,24}	Examiner	Attention and impulsivity
Grooved Pegboard Test ²⁵	Examiner	Fine-motor speed and coordination
Static steadiness test ²⁶	Examiner	Hand tremor and motor control
Timed reading and mathematics tests ²⁷	Examiner	Academic performance
Motor-activity test ²⁸	Examiner	Motor activity
Structured behavioral observations ²⁹	Examiner	Attention to task and activity level

*ADDH denotes attention-deficit disorder with hyperactivity.

lyzers (Beckman 121 MB; Beckman Instruments, Palo Alto, Calif.),³¹ and these calculations included the molar ratio of the plasma phenylalanine concentration to the sum of the concentrations of the other large neutral amino acids³² sharing its transport to the brain.

Statistical Analysis

The analysis was designed to evaluate a large number of possible effects. At the same time, it was important that significance levels not be set so conservatively that we would incorrectly accept the null hypothesis despite clinically important differences; for this reason, Bonferroni corrections were not applied. Similarly, multivariate analyses were not used because of concern about a reduction in the degrees of freedom and difficulty in handling selective missing data in such analyses. Separate repeated-measures analyses of variance were carried out for each dependent variable, and individual comparisons among the three treatments were made with Tukey's test, each at the 0.05 level of significance. Although this approach increased the chance of a type I error, it maximized our ability to detect any differences attributable to the sweeteners. The use of a counterbalanced Latin square design³³ eliminated the possibility that practice or the sequence of the diets would account for differences in the cognitive or behavioral variables.

To increase the reliability of the cognitive and behavioral assessments, the three scores obtained for each dietary period were averaged, and these mean scores were compared by a repeated-measures analysis of variance. To detect possible cumulative effects, the results from the final week of each period were also compared. In addition, analyses of variance were performed to determine whether the sham diets had any influence on the cognitive and behavioral variables. Dietary intake was calculated for each treatment period and for each sham diet during that period. The intake of macronutrients, sweet-

eners, and vitamin markers was tabulated, and differences were evaluated with an analysis of variance.

To identify individual subjects who may have responded adversely to sugar or aspartame, the weekly scores for each of nine core neurobehavioral measures were ranked and examined to determine whether the poorest scores were clustered during a particular dietary period. This approach was considered preferable to setting a fixed cutoff point for differences (e.g., a 25 percent change) because of the wide variation in raw scores among the variables studied and in score levels at different ages.

RESULTS

Subjects

Fifty-eight subjects were recruited for the study. Pilot studies of the first three subjects were used to refine the protocol; these children were therefore eliminated from the final analysis. Three subjects were eliminated because of poor compliance, as confirmed by the weekly urine tests for ascorbate and riboflavin; three withdrew before completing the study; and one (the youngest) was unable to complete the cognitive and behavioral assessments.

The 48 remaining subjects (25 normal preschool children and 23 school-age children thought to be sensitive to sugar) tended to have average academic skills and above-average intellectual ability, with a mean IQ (\pm SD) of 125 ± 11 and 117 ± 10 , respectively (range, 95 to 144). The mean number of years of maternal education was 15.5 and 14.7, respectively (range, 12 to 20). The mean age was 4.7 years (range, 3 to 5) in the preschool group and 8.1 years (range, 6 to 10) in the school-age group; 48 percent of the younger children and 78 percent of the older children were boys. No psychiatric disorders were identified in the preschool group. Five of the presumably sugar-sensitive children met the criteria for attention-deficit disorder with hyperactivity, and two of the five also met the criteria for oppositional

Table 3. Mean Daily Intake of Energy and Nutrients during the Three-Week Diet Periods.

DIET	ENERGY (kcal)	PROTEIN (g)	FAT (g)	CARBOHY-DRATE (g)	SUCROSE (g)	ASPARTAME (mg)	SACCHARIN (mg)	ASCORBATE (mg)	RIBOFLAVIN (mg)
Preschool children (n = 25)									
Experimental diet									
Aspartame	1604	60.8	62.7	208	21.3	693*	1.2	732*	2.22
Saccharin	1587	61.3	62.3	202	19.6	0.4	214*	71	2.30
Sucrose	1847*	58.2	62.2	271*	103*	0.0	1.1	74	14.7*
Sham diet									
A	1654	56.9*	62.5	225	48.9	234	75.3	305†	5.87
B	1681	63.0	61.9	225	46.0	202‡	60.6*	272	5.96
C	1704	60.3	62.8	232	49.2	257	80.3	300	7.38*
School-age children (n = 23)									
Experimental diet									
Aspartame	1936	74.5	74.3	253	25.6	834*	1.60	868*	2.78
Saccharin	1980	79.0§	77.0	251	25.1	0.2	256*	134	2.98
Sucrose	2221*	73.8	73.1	326*	120*	0.0	0.9	112	16.2*
Sham diet									
A	2050	73.2	76.5	279	60.2‡	269	88.9	382	7.03
B	2087	80.2*	76.0	279	54.9	257	75.1*	354	7.05
C	2001	73.9	72.0	272	55.7	307*	93.5	375	7.96*

*Value differs significantly from the values for the other two diets ($P < 0.05$).

†Value differs significantly from that for sham diet B ($P < 0.05$).

‡Value differs significantly from that for sham diet C ($P < 0.05$).

§Value differs significantly from that for the sucrose diet ($P < 0.05$).

defiant disorder; two other children met the criteria for oppositional defiant disorder alone.

Dietary Consumption

The preschool children ingested a mean of 5600 ± 2100 mg of sucrose per kilogram per day while on the sucrose diet, 38 ± 13 mg of aspartame per kilogram per day while on the aspartame diet, and 12 ± 4.5 mg of saccharin per kilogram per day while on the saccharin diet. The respective values for the school-age children thought to be sensitive to sugar were 4500 ± 1200 mg of sucrose per kilogram, 32 ± 8.9 mg of aspartame per kilogram, and 9.9 ± 3.9 mg of saccharin per kilogram. The mean daily intake of energy and macronutrients (protein, fat, total carbohydrate, and sucrose), as well as saccharin, aspartame, riboflavin, and ascorbate, is shown in Table 3. The intake values were calculated from the dietary records, summarized separately for each experimental period and for each sham diet. The mean daily intake of total carbohydrate and sucrose was approximately 65 g and 82 g higher, respectively, during the sucrose diet than during the other two diets. The daily intake of sucrose, carbohydrate, and energy differed significantly between the sucrose diet and the other two diets. Some small but significant differences among the sham diets were also found for certain variables. The parents of children completing the study reported only a small number of dietary infractions, which were included in the dietary analysis. Only one parent correctly identified the sequence of diets.

Behavioral and Cognitive Measures

The mean behavioral and cognitive variables are summarized in Table 4. Two analyses were performed: one compared the mean values for the three-week dietary periods, and the other compared the mean values for the third week alone. The differences were identical in the two analyses, except for differences in pegboard performance, which were evident only in the analysis of the three-week means. Because the analyses were so similar, only the three-week means are presented.

In the group of school-age children thought to be sensitive to sugar, none of the 39 behavioral and cognitive variables differed among the three dietary periods. In the normal preschool group, there were no significant differences in the 31 variables, with two exceptions. Parents' ratings on the cognition subscale of the Pediatric Behavior Scale were significantly better during the sucrose diet than during the aspartame and saccharin diets ($P < 0.008$). Pegboard performance was significantly slower during the sucrose diet (Table 4), although it was still faster than average. No child in either group had an adverse response to sucrose or aspartame.

Biochemical Tests

The results of the base-line fasting sucrose-tolerance test were reviewed by a pediatric endocrinologist who was not one of the investigators. All the profiles

Table 4. Cognitive and Behavioral Variables during the Three Diet Periods.

VARIABLE	SUCROSE DIET	ASPARTAME DIET	SACCHARIN DIET
	<i>mean ± SD</i>		
Preschool children*			
Parent's rating of cognition (n = 25) (higher score worse)†	0.5 ± 1.3	0.9 ± 1.7	1.0 ± 1.9
Grooved pegboard (n = 25) (sec/row)			
Dominant hand‡	21.1 ± 4.5	19.1 ± 2.9	19.7 ± 3.6
Nondominant hand‡	25.2 ± 5.3	23.2 ± 4.3	24.4 ± 7.9
Total‡	46.3 ± 9.2	42.3 ± 6.6	44.0 ± 10.4
School-age children			
Parent's rating of behavior (n = 22) (higher score worse)			
Conduct	8.1 ± 6.7	8.6 ± 5.8	6.9 ± 6.1
Attention deficit	10.2 ± 7.0	8.6 ± 6.2	9.0 ± 6.7
Depression or anxiety	7.4 ± 7.2	7.3 ± 7.5	7.1 ± 6.5
Deviation	6.4 ± 5.6	5.5 ± 5.0	5.3 ± 5.4
Health	6.2 ± 6.8	5.6 ± 4.8	5.5 ± 5.2
Cognition	2.3 ± 3.0	2.4 ± 3.0	2.8 ± 4.6
Teacher's rating of behavior (n = 19)			
Attention (lower score worse)	23.3 ± 5.6	22.8 ± 6.7	23.2 ± 7.4
Hyperactivity (higher score worse)	11.9 ± 5.0	11.6 ± 5.6	12.3 ± 5.5
Social skills (lower score worse)	26.1 ± 5.7	26.7 ± 5.7	26.4 ± 6.1
Oppositional behavior (higher score worse)	11.1 ± 5.8	10.3 ± 4.8	10.8 ± 4.5
Behavior symptom checklist (n = 23)			
Total score (higher score worse)	10.1 ± 10.0	10.8 ± 12.3	10.8 ± 11.8
Child's assessment of mood (n = 23) (higher score better)			
Happy	8.6 ± 1.3	8.2 ± 2.0	8.6 ± 1.4
Calm	7.6 ± 1.8	7.7 ± 1.9	7.5 ± 2.0
Alert	7.9 ± 1.9	7.4 ± 1.9	8.2 ± 1.5
Healthy	8.3 ± 1.8	8.5 ± 2.0	8.7 ± 1.3
Hungry	7.5 ± 2.0	7.3 ± 2.4	8.3 ± 1.4
Paired associate learning (n = 23)			
No. of errors	14.1 ± 8.4	14.3 ± 11.4	15.9 ± 7.3
Wisconsin Card Sorting (n = 23)			
No. correct	50.0 ± 4.4	49.4 ± 6.1	50.0 ± 4.4
Time to complete (sec)	333.8 ± 107.8	329.1 ± 91.9	316.0 ± 66.7

*For the preschool children, only those measurements are shown that were significantly different between diets.

† $P < 0.05$ for the comparisons between sucrose and other sweeteners.

‡ $P < 0.05$ for the comparison between sucrose and aspartame.

were within normal limits, except that four subjects had slightly elevated glucose levels (173 to 187 mg per deciliter [9.61 to 10.4 mmol per liter]) one half-hour after the sucrose drink, and four subjects had low levels: three at two hours (55 to 59 mg per deciliter [3.06 to 3.28 mmol per liter]) and one at one hour (50 mg per deciliter [2.78 mmol per liter]). Postprandial glucose concentrations in the two groups of subjects did not differ significantly among the three diets.

Base-line plasma phenylalanine concentrations were similar in the two groups (Table 5) and within the normal fasting range (mean of upper and lower limits, 0.81 ± 0.13 mg per deciliter [49.0 ± 8.0 μmol per liter]).³⁴ Postprandial plasma phenylalanine concen-

Table 4. Continued.

VARIABLE	SUCROSE DIET	ASPARTAME DIET	SACCHARIN DIET
	<i>mean ±SD</i>		
School-age children			
Continuous performance (n = 23)			
Response task			
Omission (no. of errors)	19.7±18.2	16.1±12.5	18.2±17.4
Commission (no. of errors)	14.0±12.5	14.5±15.5	16.3±15.2
Total	33.8±26.8	30.6±26.0	34.5±29.0
Inhibition task			
Omission (no. of errors)	14.1±16.8	17.5±20.2	15.5±19.8
Commission (no. of errors)	14.2±6.9	13.9±5.1	15.4±12.9
Total	28.3±21.2	31.4±23.1	30.8±26.9
Grooved pegboard (n = 23) (sec/row)			
Dominant hand	14.0±2.3	13.7±3.4	14.0±2.6
Nondominant hand	16.3±3.0	16.1±3.3	16.2±3.9
Total	30.3±5.0	29.8±6.4	30.2±6.1
Static steadiness (n = 23)			
No. of contacts	169.4±54.5	164.7±61.5	176.2±68.2
Duration (sec)	16.6±5.8	17.6±7.8	18.4±7.8
Academic performance			
Mathematics (n = 19) (% correct)	1.0±0.0	1.0±0.1	1.0±0.0
Reading (n = 16) (% correct)	0.9±0.1	0.9±0.1	0.9±0.1
Motor activity (n = 19)			
Median movements (no./min)	209.5±57.8	238.3±26.7	213.7±66.0
Behavioral observations (n = 23)			
Attending to work (%)	91.1±15.7	94.6±9.3	93.3±5.5
Playing with toy (%)	0.4±1.2	0.6±2.0	0.0±0.0
Out of seat (%)	2.0±4.4	2.4±7.1	1.6±2.7
Quiet noise (%)	13.9±20.0	11.7±14.0	12.3±19.3
Loud noise (%)	13.6±24.8	13.8±23.6	15.7±28.4
Attention (no. of shifts)	2.7±3.3	2.7±2.9	3.4±3.0

trations and the ratio of phenylalanine concentrations to the sum of the values for the other large neutral amino acids were significantly higher than base-line values in both groups during all three diets and were also significantly higher in both groups during the aspartame diet than during the sucrose and saccharine diet. Postprandial plasma phenylalanine values were within the normal range (mean of upper and lower limits, 1.29 ± 0.19 mg per deciliter [78.1 ± 11.8 μ mol per liter]) in both groups during all three diets.³⁴

To evaluate the suggestion that people who are allergic to sucrose may need to be free of the nutrient before they respond to a challenge, we examined the data for all the children who were on the sucrose diet during the third dietary period. For each variable, the mean value for this period was subtracted from the mean value for the placebo (saccharin) period and the difference was compared with zero

to determine whether there were any significant differences. None were found.

DISCUSSION

The results of this study do not support the hypothesis that a diet high in either sucrose or aspartame adversely affects the behavior or cognitive functioning of children. There were few sweetener-related effects in either the preschool-age or the school-age children, and none of the children in either group had a consistently adverse response to either sucrose or aspartame. The findings were negative even though the older children were selected because their parents believed them to be sensitive to sugar and even though the children in both groups ingested substantial amounts of the sweeteners. Cognitive or behavioral differences were as likely to be found between sham diets as they were between experimental diets, and the few differences associated with the ingestion of sucrose were more consistent with a slight calming effect than with hyperactivity.

The absence of effects in our study could have resulted from the use of insensitive measures or an inadequate statistical power to detect small differences, but neither explanation seems likely. The measures we used have proved to be sensitive to hyperactivity, attention deficits, and the effects of medications and foods in earlier research.^{21,35} In addition, the study design provided sufficient statistical power to detect potential differences if they were present. On the basis of a calculation of power that used three core measures from the three primary sources of data (parents, teachers, and children), the study would have been able to detect an effect with an average size of 0.4 SD with a probability of approximately 0.55 or an effect with a size of 0.6 SD with a probability of 0.9. Given the large number of analyses, the number of differences found is no higher than the number that would be anticipated by chance alone.

Despite the generally negative findings of this study, it is possible that there are some children who

Table 5. Postprandial Plasma Phenylalanine and Glucose Concentrations and the Ratio of Phenylalanine to Large Neutral Amino Acids, According to Diet.*

VALUE	BASE LINE (FASTING)	DIETARY PERIOD		
		SUCROSE	ASPARTAME	SACCHARIN
		<i>mean ±SD</i>		
Phenylalanine (μ mol/liter)				
Preschool group	49.0±11.9	64.0±15.9	72.3±13.1†	61.8±14.5
School-age group	52.2±11.6	62.2±12.1	71.2±13.0‡	68.1±13.7
Phe/LNAA				
Preschool group	0.103±0.021	0.125±0.020	0.140±0.029†	0.120±0.019
School-age group	0.108±0.013	0.126±0.018	0.142±0.033†	0.126±0.018
Glucose (mmol/liter)				
Preschool group	4.49±0.34	5.63±1.19	5.87±1.34	5.72±1.05
School-age group	4.77±0.35	4.93±1.40	4.83±1.21	5.58±2.02

*Phe/LNAA denotes the ratio of the phenylalanine concentration to the sum of the concentrations of the other large neutral amino acids. To convert values for glucose to milligrams per deciliter, divide by 0.05551.

†P<0.05 for the comparison between the diet containing aspartame and the other two diets.

‡P<0.05 for the comparison between the diet containing aspartame and the diet containing sucrose.

respond adversely to sugar or aspartame. Our subjects had average or above-average intelligence, and children with less intellectual ability may respond differently. However, the groups of children we studied should have maximized the likelihood of finding dietary effects. One group was composed of children whose parents considered them sensitive to sugar, and the other consisted of preschoolers, a population reported to be sensitive to dietary effects.⁸

It could be argued that all three sweeteners had adverse effects. This possibility seems unlikely because behavior ratings and test scores generally improved during the dietary periods, as compared with the base-line values. Also, it is improbable that all three sweeteners could have had equally adverse effects on each of the diverse variables studied. It is particularly unlikely that our failure to observe any effects of aspartame or sucrose ingestion on behavior reflects an insufficient consumption of aspartame or sucrose. Calculations by the Market Research Corporation of America^{36,37} indicate that the highest daily aspartame intake under normal conditions ranges from 22 to 34 mg per kilogram, with a calculated 99th percentile of 34 mg per kilogram³⁷ — a value close to that observed in our study (32 mg per kilogram in the school-age subjects and 38 mg per kilogram in the preschool subjects). Data on sucrose intake in children are scarce, and comparisons require calculations. If the energy requirements of a 20-kg 4-to-6-year-old child range from 1300 to 2300 kcal per day, with 17 percent of the energy provided by sugar,⁹ the sucrose intake ranges from 2800 to 4900 mg per kilogram; similar calculations for a 28-kg 7-to-10-year-old child indicate an intake of 2500 to 5300 mg of sucrose per kilogram. In our study, the sucrose intake was 5600 ± 2100 and 4500 ± 1200 mg per kilogram in the preschool and school-age children, respectively — values clearly at the upper end of the normal range.

Large increases in the plasma phenylalanine concentrations (24.78 ± 3.80 mg per deciliter [1500 ± 230 μmol per liter]) and in the ratio of phenylalanine to the sum of the other large neutral amino acids (4.17 ± 1.42 ; normal value, 0.11 ± 0.01) are associated with adverse effects in children with phenylketonuria.³⁸ By comparison, these values were much lower in our subjects (Table 5). The slight increases noted in the children in our study while they were on the aspartame diet would be unlikely to produce adverse effects, particularly when these values are evaluated in the light of the data of Waisbren and Levy and colleagues. Their data indicate that untreated mild hyperphenylalaninemia (6.8 mg per deciliter [410 μmol per liter]) in women was associated with a normal outcome in their offspring, including a normal IQ.^{39,40}

We conclude from this carefully controlled nine-week study that neither sucrose nor aspartame produces discernible cognitive or behavioral effects in normal preschool children or in school-age children believed to be sensitive to sugar.

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