

CORRESPONDENCE



SUGAR AND CHILDREN'S BEHAVIOR

To the Editor: Wolraich et al. (Feb. 3 issue)¹ concluded that neither dietary sucrose nor aspartame affects children's behavior or cognitive function, even when intake exceeds typical dietary levels. This conclusion is not justified.

The dependent variables were cognition and conduct problems, but only 5 of 48 subjects had attention-deficit disorder, and 4 had oppositional defiant disorder. The proportion of potential responders is so small that significant improvement in mean conduct scores for the group is not possible, even if sucrose caused the misconduct. At best, one might (and does) find slightly larger standard deviations and higher mean scores on the conduct measures during the sucrose "challenge."

Likewise, children with diets consisting of about 20 percent sucrose, whose average IQ is in the top 2 percent, could hardly be expected to have sucrose-impaired cognition, since they are already near the top intellectually. At most, the study shows that extremely bright children who already eat moderate amounts of sucrose do not become even brighter when placed on low-sucrose diets for three weeks.

The authors accept the null hypothesis in the abstract rather than failing to reject it; the latter is not the same as proving the null hypothesis. On the contrary, the study showed that atypically bright children who normally received about 20 percent of their diet from sucrose, showed little evidence of hyperkinesis or conduct disorders, and had parents who thought they might be sensitive to sugar did not have substantial changes in behavior when their sucrose consumption was reduced from 20 percent of their diet to 4 percent for three weeks.

The study ignored the fact that high-sucrose diets, with sucrose ranging from 25 to 60 percent of caloric intake, may be displacing essential minerals, vitamins, and amino acids

necessary for brain function.² This would explain why most controlled, low-dose, short-duration, double-blind trials fail to find a relation between sucrose and behavior, despite widespread public belief to the contrary.

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1. Wolraich ML, Lindgren SD, Stumbo PJ, Stegink LD, Appelbaum MI, Kiritsy MC. Effects of diets high in sucrose or aspartame on the behavior and cognitive performance of children. *N Engl J Med* 1994;330:301-7.
2. Improvements of IQ and behavior as a function of dietary supplementation: a symposium. Eysenck HJ, Eysenck SBG, eds. *Per Individ Differ* 1991;4:329-65.

To the Editor: Wolraich et al. claim to have analyzed the effects of diets high in sucrose or aspartame on the behavior and cognitive performance of children. The mean amounts of aspartame ingested in the total daily diet during the aspartame trials were 693 mg and 834 mg for preschool and school-age children, respectively; hence, there was less than 0.35 g of aspartic acid (the neurotoxic component of aspartame, which contains approximately 40 percent aspartic acid). Similarly, the mean amounts of sucrose ingested during an entire day were 1030 mg for preschool children and 1200 mg for school-age children, or roughly 3.6 oz (the amount found in one 5-oz candy bar and ½ cup of jello) and 4.2 oz (the amount found in one 5-oz candy bar and one 12-oz can of soft drink),* respectively. The use of low, not high, levels of sugar and aspartic acid and numerous other factors related to methods and statistics invalidate the conclusions drawn by the authors.

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*Dental Public Health Committee of the Academy of Dentistry, Toronto, Canada. Source of sugar content of common foods. In: Fleck, H. *Introduction to nutrition*. 2nd ed. New York: Macmillan, 1971.

To the Editor: The article by Wolraich et al. may appear to lay to rest the claims of parents who say that sugar affects their child's behavior and cognitive function. I write to express a different point of view.

Between January 1, 1973, and December 31, 1977, I saw 182 new pediatric patients with hyperactivity, attention defi-

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cits, and other behavioral and learning problems. In studying those patients, I used elimination-challenge diets. The ingredients eliminated from the diet were food coloring and additives, sugar, milk, wheat, eggs, corn, chocolate, and citrus. If a child showed convincing improvement in behavior after following the diet for five to seven days, the child was challenged with the eliminated foods, one food per day, and the reactions were noted.

The parents of 128 of these children reported that they were certain that their child's hyperactivity and other nervous symptoms were related to one or more of the dietary ingredients. They identified an average of three foods (or other dietary ingredients) as responsible. The offending foods included sugar (associated with symptoms in 77 children); additives, flavors, and coloring (especially red food coloring) (48 children); milk (38 children); chocolate (28 children); eggs (20 children); and wheat (15 children). Many other foods were also mentioned.¹

Several other observers have published studies showing that some children are sensitive to sugar.²⁻⁴ What is the explanation for these sharply differing results? Although I do not claim to have all the answers, here is one of them: sensitivity to a dietary ingredient can best be determined by an elimination-challenge diet. More than 40 years ago, Rinkel and associates⁵ discussed the mechanisms that may be operative in people with delayed-onset sensitivities. I also reported my favorable experience with elimination-challenge diets more than 30 years ago in a study of 50 children with systemic and nervous symptoms.⁶

I was happy to see that Wolraich and associates stated, "Despite the generally negative findings of this study, it is possible that there are some children who respond adversely to sugar."

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1. Crook WG. Can what a child eats make him dull, stupid, or hyperactive? *J Learn Disabilities* 1980;13:53-8.
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To the Editor: In minimizing the effect of the Feingold diet,¹ Dr. Kinsbourne refers in his editorial (Feb. 3 issue)² to a number of double-blind studies in which less than 27 mg of additive was given to hyperkinetic children as a challenge and only a small number of reactive children were found. Along with Swanson, Kinsbourne pointed out that the average eight-year-old consumed 76 mg of additive daily.³ After a negative low-dose challenge study, they demonstrated unequivocal deterioration when 100 to 150 mg of additive was given.³ Apparently, Dr. Kinsbourne does not believe his own results, failing to stress that three other double-blind studies using over 100 mg of additive have also demonstrated adverse behavioral changes in children.⁴⁻⁶ A fourth double-blind study using low-dose tartrazine additive with only a three-day washout period similarly demonstrated hyperkinesia.⁷

The logical conclusion should be that the highly publi-

cized negative low-dose challenge studies were fatally flawed and do not represent actual clinical conditions. Only the high-dose challenge studies simulate actual clinical experience and lead to the behavioral improvement found in open trials.

As for Dr. Wolraich's study, readers should wonder whether here, too, there is a fatal flaw in a well-controlled, statistically proved study in which compliance was ensured. Since sugars and artificial colors, flavors, and preservatives coexist, were the parents' observations blaming sugar really attributable to additives? Does this study reflect the realities of populations in which children are fed protein-poor meals and sugar has been shown to cause hyperkinesia? Or is the fatal flaw the inappropriate selection of patients for the study, in which essentially normal children were studied instead of children with attention deficit-hyperactivity disorder or behavioral problems with mood swings in which plasma catecholamines are elevated?⁸

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2. Kinsbourne M. Sugar and the hyperactive child. *N Engl J Med* 1994;330:355-6.
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To the Editor: The conclusions of Wolraich et al. are the same as those in our study of 16 children known by their parents to react adversely to sugar.* Unlike Wolraich et al., we also conducted an open challenge with 3 g of sucrose candy per kilogram of body weight. Only 7 of the 16 children showed any increase in activity or behavioral measures in this phase of the study. The lack of response to an open challenge in front of the parents may thus save the considerable time and expense that would be required for further blinded evaluations. Our study also included double-blind challenge tests with sucrose, aspartame, honey, or tapioca starch given after a standardized meal. These confirmed a lack of relation between sugar or aspartame and adverse behavior.

Of most interest, however, was what we learned from the parents by telephone several months after the study was concluded. Despite evidence showing a lack of relation between their child's sugar consumption and behavior, most parents continued to believe that sugar caused aggressive, overly active, loud, or noncompliant behavior in their child. They modified their beliefs somewhat by stating that this occurred only sometimes when sugar was ingested, rather than every time, and they continued to restrict sugar in their

*Mahan LK, Chase M, Furukawa CT, et al. Sugar "allergy" and children's behavior. *Ann Allergy* 1988;61:463-8.

child's diet. It would be interesting to know what the parents believe now, after learning the evidence. We suspect that their belief system will be modified, not cast out, by such scientific evidence. If so, these parents and children will need continued support, education, and evaluation by experts on child behavior. Just showing parents the scientific evidence may not change their beliefs.

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The authors reply:

To the Editor: With regard to Samuels's criticism of the amount of aspartame and sucrose in the diet, consideration must be given to other studies in which large single-bolus doses of sucrose or aspartame have been tested, also without effect.^{1,2} Our study used real foods, sweetened to reflect current formulations and fed to children at home. The levels of sweetener ingested were set by the usual eating pattern of the child and in each case were clearly at or above the upper end of usual intake. This is shown in Table 1 for children four to six years old.

The mean sugar intake of our preschool subjects was 3.6 oz ($\frac{1}{2}$ cup); for our school-age children it was 4.2 oz (close to $\frac{2}{3}$ cup). Both amounts are substantial for these children, especially those presumed to be sensitive to sugar. Samuels's statement that aspartate is the neurotoxic component of aspartame is not correct. All three components of aspartame (aspartate, phenylalanine, and methanol) are potentially neurotoxic, but not at the levels ingested by the general population or in our study.

Schoenthaler's description of the dependent measures we used failed to note that the measures were not limited to cognition and conduct but included a wide range of behavioral, motor, and learning tasks. Because the measures were not at their ceiling levels, positive change should have been measurable if it occurred; there was also ample range for detecting adverse effects.

In the controlled studies cited by Crook, sucrose was one of many variable dietary components, making it impossible to tease out its effects alone. Our findings suggest that sucrose is probably not a contributory agent. Crook's clinical experience cannot be considered objective evidence of a relation between sucrose and behavior. A recent study³ demonstrates the powerful effect of suggestion. In that study, all children received drinks sweetened artificially. When mothers were informed that their children were receiving sugar, their ratings of the children's behavior were significantly worse. Parents were also more controlling and critical of

their children than were mothers who were told that their children had received an artificial sweetener. The effect of suggestion was greater than the dietary effects reported in almost all the controlled studies of sugar. In contrast to Crook's report, our study was double-blind, and every attempt was made to minimize bias.

In our study, subjects were chosen who were likely to respond to sucrose regardless of their IQ or clinical diagnosis. Schoenthaler provides no evidence that intelligence affects children's response to sucrose. With each subject serving as his or her own control, we should have been able to detect effects even in children with above-average intelligence. Brenner also provides no evidence for his claim that sugar causes hyperkinesis or affects children with a diagnosis of attention deficit-hyperactivity disorder. To the contrary, none of the challenge studies in children with attention deficit-hyperactivity disorder^{1,4,5} found any effect of sugar on behavior.

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1. Gross MD. Effect of sucrose on hyperkinetic children. *Pediatrics* 1984;74:876-8.
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To the Editor: Dr. Brenner argues that Wolraich and colleagues were barking up the wrong tree. The children identified as sensitive to sugar were really sensitive to additives. But the literature on additives has the same ambiguities as the literature on sugar. Whereas claims based on observations¹ and open studies (such as Brenner's own) are vehement, controlled studies of diet and dietary challenge yield minimal findings. To elicit a response of inattention, we had to challenge all at once with 50 to 100 percent more food dye than an average child ingests all day.² Individual children with attention deficit-hyperactivity disorder who reacted adversely to food dyes subsequently benefited to varying degrees from the Feingold diet but benefited uniformly from stimulant therapy (unpublished data).

People tend to remember when two events they expect to occur together do so, but not when they occur independently.³ Moreover, a putative cause and effect may fail to occur at the same time either when the putative effect does not occur (i.e., the "agent" is inert) or when a different cause precedes the effect (i.e., there are multiple causes). Hence, when a strategy of eliminating particular classes of nutrients fails, it is either because they are behaviorally inert or because there are additional substances in the diet that exert similar effects.

If reactive children respond adversely to a wide (but idiosyncratic) mix of nutrients,⁴ then the successfulness of

Table 1. Aspartame and Sucrose Intake in the Preschool Children Studied.

INTAKE	ASPARTAME mg/kg	SUCROSE g
Usual eating pattern	4	76
Upper end of usual intake*	34	98
Intake during study	38	104

*Denotes the 99th percentile of aspartame intake and the 90th percentile of sucrose intake.

studying a single class depends on how these substances interact to impair behavior. If their adverse effects are additive, then eliminating even a single class should improve behavior measurably (but not normalize it). The effects of the substances might be redundant, however: any one class impairs behavior maximally whether or not others are also ingested, and only if all are removed does behavior improve. If so, we can explain the positive anecdotes: suspect substances sometimes do impair behavior, specifically when the other detrimental substances happen not to have been consumed recently. We can also explain the negative controlled studies of diet and challenge: eliminating a single class from the diet and reintroducing it has limited effect.

Whether nutrients can substantially influence behavior remains uncertain. But before discounting this possibility, one could investigate the redundancy model for multiple dietary sensitivities. One would begin with an elimination diet^{4,5} and then reintroduce the suspect substances serially, using placebo as control. The findings to date from elimination diets^{4,5} are sufficiently suggestive to justify such further research.

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1. DiBattista D, Shepherd M-L. Primary school teachers' beliefs and advice to parents concerning sugar consumption and activity in children. *Psychol Rep* 1993;72:47-55.
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MORE ON LORENZO'S OIL

To the Editor: The use of Lorenzo's oil in patients with adrenomyeloneuropathy, the form of adrenoleukodystrophy that occurs in adults, has recently been reported by Aubourg et al. (Sept. 9 issue),¹ with an editorial by Rizzo.² In contrast to rapidly progressive adrenoleukodystrophy in children, which affects the brain, adrenomyeloneuropathy develops at a slower rate and involves primarily the spinal cord and the peripheral nervous system. Although they present data on the inability of the oil to stop the progression of adrenomyeloneuropathy, Aubourg et al. make no reference to its potential for preventing the onset of adrenoleukodystrophy and, by implication, that of adrenomyeloneuropathy, nor does Rizzo mention this possibility. Indeed, the article and editorial portray Lorenzo's oil as a concoction totally useless in combating the adrenoleukodystrophy-adrenomyeloneuropathy complex. This portrayal is inaccurate.

There is a consensus among researchers studying adrenoleukodystrophy and adrenomyeloneuropathy that Lorenzo's oil almost invariably eliminates the abnormal accumulation of very-long-chain saturated fatty acids, the biochemical hallmark of adrenoleukodystrophy. As for its clinical effects, a world authority on adrenoleukodystrophy, Dr. Hugo Moser, believes that it either prevents the onset of the disease or greatly reduces its severity in boys who have the biochemical defect of adrenoleukodystrophy but are still neurologically intact.³ If these boys are untreated, adrenoleukodystrophy will develop in 48 percent and adrenomyeloneuropathy in 25 percent; the remaining 27 percent will

either have hybrid forms of the disease or, in some rare cases, escape it altogether.

A trial conducted by Moser et al. and sponsored by the National Institutes of Health and the Food and Drug Administration is now in its fourth year; it has studied 86 children with presymptomatic adrenoleukodystrophy, including 50 boys who have been treated for more than 12 months. During the period of the study, the rate of occurrence of adrenoleukodystrophy in this group of children has been strikingly lower than that suggested by trends among historical controls. Of the 50 boys, only 4 (8 percent) have had full-blown symptoms of cerebral childhood adrenoleukodystrophy.³

The indiscriminately negative account of the effects of Lorenzo's oil in a prestigious medical journal may induce parents not to start treatment with the oil in their children with presymptomatic adrenoleukodystrophy, or to stop the treatment if it has already begun. If this happens, symptoms will develop in children "destined" to have childhood adrenoleukodystrophy, and they will die. The "lucky" ones, who escape adrenoleukodystrophy, will have adrenomyeloneuropathy (or some hybrid form of the disease) and will be incapacitated for most of their adult lives. In sum, the misinformation engendered by the article and editorial has the potential to cause innumerable tragedies that could be averted by a simple change in dietary habit.

As for the negative conclusions of Aubourg et al. about the effects of Lorenzo's oil in patients who already have symptomatic adrenomyeloneuropathy, these are a bit perplexing. The authors' study was too short (two years) and involved too few patients (14 men) to provide reliable data. If, however, future, better-designed studies also conclude that Lorenzo's oil does not work after the symptoms have started, this would not be surprising. Most researchers believe that adrenoleukodystrophy has an autoimmune component, probably triggered by the abnormal accumulation of very-long-chain fatty acids. It is possible that the autoimmune response and accompanying inflammation persist even after Lorenzo's oil has eliminated this fatty-acid abnormality.

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3. Moser HW, Kok F, Neumann S, et al. Adrenoleukodystrophy update: genetics and effect of Lorenzo's oil therapy in asymptomatic patients. *Int J Pediatr* (in press).

The authors reply:

To the Editor: We agree with Michaela and Augusto Odone, Lorenzo's parents, that no therapeutic efforts should be interrupted in patients with adrenoleukodystrophy as long as the treatment could still prove to have efficacy. Our report was not intended to discourage participation in well-designed clinical trials. We support additional studies of the potential preventive effects of the oil; we enrolled 21 patients with presymptomatic adrenoleukodystrophy in a trial of the oil four years ago. The long-term results, as well as those of the study by Moser et al., are eagerly awaited.

It is clear, however, that the dietary intervention has no