Dietary Replacement in Preschool-Aged Hyperactive Boys

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This was a Stage 2 Feingold-type diet, since salicylates were not eliminated

ABSTRACT. A 10-week study was conducted in which all food was provided for the families of 24 hyperactive preschool-aged boys whose parents reported the existence of sleep problems or physical signs and symptoms. A within-subject crossover design was used, and the study was divided into three periods: a baseline period of 3 weeks, a placebo-control period of 3 weeks, and an experimental diet period of 4 weeks. The experimental diet was broader than those studied previously in that it eliminated not only artificial colors and flavors but also chocolate, monosodium glutamate, preservatives, caffeine, and any substance that families reported might affect their specific child. The diet was also low in simple sugars, and it was dairy free if the family reported a history of possible problems with cow's milk. According to the parental report, more than half of the subjects exhibited a reliable improvement in behavior and negligible placebo effects. In addition, several nonbehavioral variables tended to improve while the children received the experimental diet, particularly halitosis, night awakenings, and latency to sleep onset. *Pediatrics* 1989;83:7–17; *attention deficit disorder, hyperactivity, diet, preschool age.*

In the brief but controversial period of laboratory investigations of the relationship between nutrition and behavior in hyperactive children, only two studies have used a design in which the entire nutrient intake of the subjects was manipulated.[1,2] This method, perhaps most accurately called a dietary replacement design,[3] is expensive; also, it is difficult to provide a placebo control period under double-blind conditions. On the other hand, the dietary replacement method permits the evaluation and control of many variables not possible with the more popular challenge designs.[4]

The two previous dietary replacement studies were primarily investigations of the Feingold diet in which artificial dyes and flavors were eliminated, as well as naturally occurring salicylates. Both studies have been criticized because of treatment order effects (experimental diet always had a more powerful effect when it followed the control diet) and because behavioral effects have been observed primarily in parent and teacher reports rather than in laboratory testing, which suggested that the parents were not actually blind to the interventions.[4]

The present dietary replacement study focused on several issues that previous research had suggested may be relevant to further understanding of this field. (1) As suggested by others,[5] and particularly as revealed in the results of a study by Harley et al,[1] it may be that younger children are more vulnerable to nutrition-behavior interactions, so we included only preschool-aged boys. (2) Although the mechanism by which diet might affect behavior is still unknown, our own research[6,7] showed that sleep problems and complaints of somatic allergy-type symptoms might be associated with a nutrition-behavior effect. For this reason, only children whose parents reported the occurrence of such problems were included in the research. (3) It seemed to us that susceptibility to nutrition-behavior effects might be more likely in poorly nourished children; therefore, several measures of nutritional status were included.

The design of our experimental diet was guided by one further consideration. The previous replacement studies[1,2] and challenge studies[4] targeted one substance or class of substances (eg, dyes, sugar, or flavors), and each found a relatively small number of children who were responsive to dietary intervention. The diet used in the present study focused

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on a broader range of substances to determine whether a larger proportion of children would be affected.

METHODS

Subjects

Letters were distributed to all parents of preschool-aged boys attending more than 100 day cares in a city of 600,000 persons. The letters explained that a research project was looking for "overly active or inattentive" boys. Parents who telephoned the laboratory as a result of this letter were interviewed to determine whether their child met the *Diagnostic and Statistical Manual of Mental Disorders*, ed 3,[8] criteria for attention deficit disorder with hyperactivity. They were also asked to fill out the 48-item parents' version of the Conners Behavior Rating Scale,[9] a checklist regarding estimated frequency of sleep problems (eg, difficulty falling asleep) and physical signs and symptoms (eg, stuffy nose, stomachache), and our adaptation of a Canada Health and Welfare questionnaire which we called the Food Attitude Questionnaire. An example of an item was "I believe that chemical food substances affect my child's behavior."

Parents of 196 children called to inquire about the study. There were a number of sources of attrition (Fig 1). The largest decrease in subjects occurred after the initial telephone inquiry: many families were not interested in making the time commitment, were anticipating moving out of the area, or were already involved in some other form of therapy. The second largest decrease occurred as a result of the day-care evaluation of the children's behavior: in 50 cases, children who were judged by parents to be a problem were not considered to be particularly difficult in the day cares, which tend to be relatively unstructured environments. A few families were eliminated because the extensive interview with a dietitian (J.M.) revealed an obstacle: for example, a few families were already eating a diet comparable to our experimental diet.

Each of the 24 boys in the final sample met the *Diagnostic and Statistical Manual of Mental Disorders*, ed 3, criteria for attention deficit disorder with hyperactivity, was more than 1 SD above the age-related mean on the parents' Conners Rating Scale (mean 3.37 SD above the mean, SD 1.26), and was reported by parents to have at least one sleep or physical problem that was "more than average" (ie, more than they believed to be typical). Their ages ranged from 3.5 to 6 years (mean 53.7 months, SD 12.5 months). No child received stimulant medication during the study.

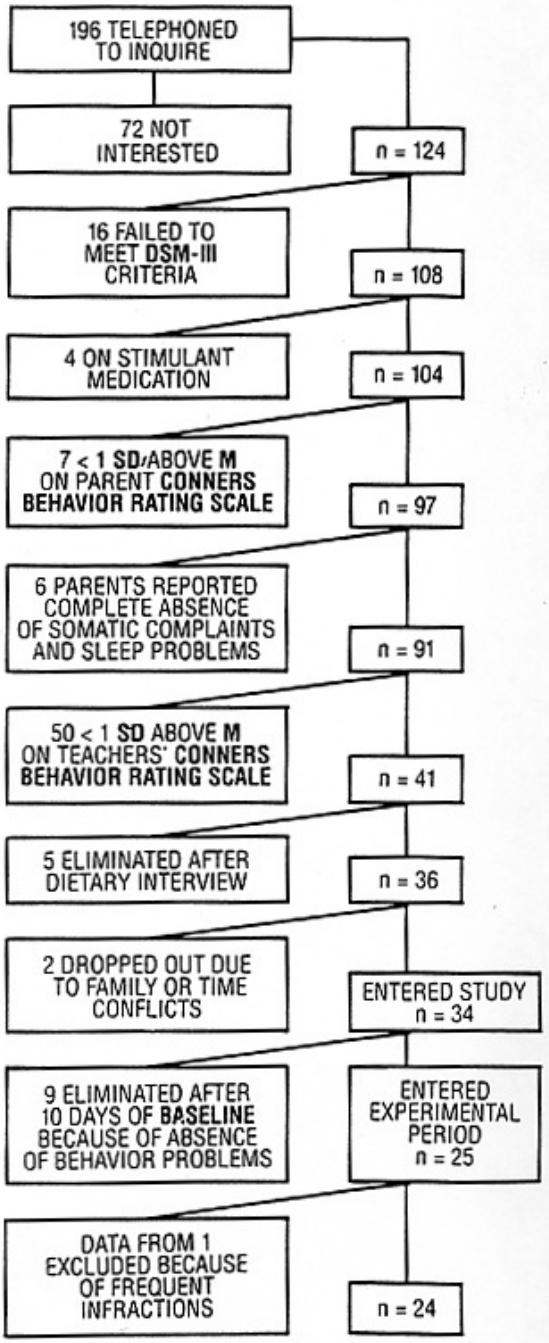

Fig 1. Sequence of screening phases used to arrive at final sample. Most eliminations were parent initiated (eg, due to lack of interest or concerns about time commitment); however, 50 children were excluded because they were not identified by the day-care facilities as having behavior problems.

Design and Procedures

It was expected that placebo effects would be powerful, so a placebo control period (equivalent phase) was included. The 10 weeks of the study consisted of 3 weeks of baseline diet, followed by 3 weeks of equivalent diet and 4 weeks of a diet that we called the Alberta Children's Hospital (ACH) diet, the latter two of which occurred in counterbalanced order across subjects. Of the final sample, 12 children received the baseline-equivalent-ACH order and 12 received the baseline-ACH-equivalent order. The design used in this study included one between-subject factor (treatment order) and one within-subject factor (baseline, equivalent, ACH). Only the last 2 weeks from each diet phase were included in the data analyses.

Intake Interview

Prior to beginning the baseline period, parents were invited for an interview in which they were told that many nutrients were going to be tested and that the test items might change as often as every two to three days. Parents were taught to weigh and measure food, and each dependent measure was explained to them. The consent form was signed, and the daily report forms were provided for two to three practice days prior to beginning the study.

Baseline

For 21 days, all daily dependent measures were collected, and the children came into the laboratory for testing once between days 18 and 20. Families bought and prepared their own food, as usual. They were urged to eat normally, because we would be determining the child's food preferences from their daily records to specify his diet during the experimental period. The baseline period was essential for several reasons: to determine normal eating patterns to be matched in the placebo control (equivalent) period and to determine the persistence of problem behaviors.

Experimental Period

For each child, the experimental period consisted of both the experimental (ACH) diet and the placebo control (equivalent) diet. All of the food for the equivalent and ACH diets was prepared at the hospital, packaged in unmarked wrappers, and sent home once a week with labels specifying the meal at which it was to be eaten. The children were fed six times per day (breakfast, midmorning snack, lunch, afternoon snack, supper, evening snack). Food orders took into account the freezer capacity of an individual home, the food preferences as indicated during initial assessments and daily food diaries from the baseline period, the number and age of the family members, and the amount of time available for food preparation. Food for a meal was often precooked and frozen, so that parents only had to heat it. Because parents were devoting some time each day to filling out the various forms, we thought that it was important to reduce food preparation time.

Food was provided for every member of the household. In addition, all previously purchased food (except staples like coffee, tea, sugar, salt, flour, vinegar) was packaged and stored at the beginning of the experimental period, as reported also by Harley et al.[1] Parents were told that they could eat out during their workdays or at other times, but they should not discuss it with the child and never bring restaurant food home. It was emphasized that the child should believe that the entire family was participating in this study. Honesty regarding infractions (eating food that was not provided by us) was encouraged by informing parents that some infractions were inevitable and that the important issue was that they be described as accurately as possible. Food was also provided to the child's day care, often including special items to fit their daily menus or special occasions such as holiday parties.

Equivalent Diet. The food intake for the child during this phase was matched for foods and nutrients on a day-by-day basis with his own baseline period. In other words, day 1 of equivalent was matched with his intake on day 1 of baseline, day 2 of equivalent was matched with day 2 of baseline, and so on. Even brands were usually matched and family recipes were prepared by the hospital kitchen. At the end of the study during the debriefing session, we found that no parent detected this matching procedure, perhaps because at least 3 weeks separated the paired days. If multivitamins were used during baseline, the same ones were given during the equivalent phase. If the child did not have them during baseline, then placebos were used during the equivalent phase so that the multivitamins given during the ACH phase did not indicate the treatment condition.

ACH Diet. For all children, food dyes, food flavors, preservatives, monosodium glutamate, chocolate, and caffeine were eliminated from the ACH diet. In all cases, the amount of simple sugars was decreased, and the children received a multivitamin supplement that contained no sugar or artificial colors/flavors. The ACH diet was designed to match each child's protein intake but to decrease the sugar content. In addition, several substances were avoided in selected children, when parents indicated that the foods might be a problem. Thus,

for 15 children, all milk and dairy products were eliminated during this period and they received 350 to 500 mg of elemental calcium (in the form of calcium carbonate) supplement each day, generally incorporated in the food, and for four children naturally occurring salicylates were avoided. Finally, if a parent mentioned during the screening assessment interview that he or she thought their child reacted to a particular food substance (eg, apples or carrots) and because it tended to be included in the diet rarely during baseline, that item would not be provided during the equivalent phase; it was also avoided during the ACH period, because the purpose of the study was not to test individual reactions to specific substances.

Thus, the ACH diet for all children was free of so-called "additives" and stimulants and was low in simple sugar (mono- and disaccharides). In addition, an attempt was made to reduce exposure to common environmental inhalants in the home. Perfumed toiletries and paper products were replaced with unscented ones. Markers and scented toys and stickers were replaced whenever possible. Obviously, there was much less control over these environmental variables than the food that was consumed, and in fact no attempt was made to quantify "infractions" (eg, exposure to wet paint) which would have been virtually impossible. Inhalants were not the focus of the research, but we thought it prudent to remove the major daily sources in the home.

Concealing Treatment Conditions

No study personnel (eg, the coordinator) in contact with the participants knew the design or even that there were two phases of the experimental period. The difference between the ACH and equivalent diets would have been readily apparent to study personnel and participants if the food had been placed side by side. Several steps were taken to ensure that these differences were not obvious.

Food Distractors. Menus often had salient but irrelevant variables so that parents believed we were testing a particular substance, such as a food color. Thus, a child might have two "red days" followed by three "corn days." The red days might contain several glasses of red juice, red fruits (apples, strawberries), red cake, red meat, and a red cabbage salad. The red was provided with a dye during the equivalent phase and cranberry juice during the ACH period. On a corn day, a child might be given corn muffins for breakfast, creamed corn for lunch, corn on the cob for supper, and a cornbread snack. This might happen during either the equivalent or ACH phase.

Nonfood Distractors. A menu sometimes contained specific instructions regarding timing or quantity of food, all of which were irrelevant. For instance, a child might be required to eat supper on several days at a fairly precise hour or he might be limited to only 250 mL of juice per meal for three days with residual thirst to be sated with water.

Parental Expectations. As indicated, during the intake interview parents were informed (accurately) that our dietary intervention would be more complex than in previous studies and we would be examining many dietary substances and, therefore, components of the diet might change as often as every few days. This was done by giving additional food only from the extras sent as supplements for that two- or three-day period and no other period if a child was particularly hungry one day and wanted a larger snack or meal than we had provided. This technique worked well and we knew of no child whose hunger was not satisfied by the food provided on the menu or the supplement, and parents believed there were many testing periods.

At the debriefing session, prior to describing the results, a structured interview was conducted in which three questions were asked of each family: Do you think your child has changed as a result of being in this study? What do you think we were doing with the different foods? Could you guess the sequence or order in which we were testing foods? Only one mother ventured a hypothesis that was relevant to the design: she said she thought that for about a week her son was given a health food type of diet. Interestingly, the ACH diet actually lasted for 4 weeks, and the child was not one of those whose behavior changed during the experimental period. All of the other parents claimed to be entirely mystified and could only guess that the study "had something to do with food."

Evaluation of Parental Bias. In addition to the measures taken to conceal the treatment conditions and to evaluate parental expectations to determine whether the expectations might affect the study results, the Food Attitude Questionnaire had been administered to all parents when initially screened. For comparison purposes, the questionnaire was administered to the parents of children without attention deficit disorder and hyperactivity who participated in other research.[6,7]

Dependent Measures

Daily Measures. Every day one parent (designated at the time of entrance to the study as the rater) filled out a ten-item version of the Conners Rating Scale, known as the Abbreviated Symptom Questionnaire (ASQ),[9] which asks about restlessness, impulsivity, disturbing other children, short attention span, fidgeting, distractibility, frustration, crying, mood changes, and temper outbursts. In some cases, parents told us that the ten items

failed to cover certain behaviors that they found particularly troublesome, such as whininess. Consequently, we added a section to the ASQ, which we called part 2, and permitted them to create up to four individualized items for their child. Of the 24 families, 19 designed a part 2, which contained an average of three items, and was completed once each day by the same parent rater. Sleep variables monitored by the parents each day included the usual time at which the child went to bed, number of times he got out of bed before falling asleep, time at which he fell asleep (to the nearest 15 minutes), number of times he awakened and got up during the night, time of waking in the morning, and the amount of time he napped each day at home. To determine sleep onset latency, parents were required to check every 15 minutes and to record the time at which he was found to be asleep. Several of these variables are subject to the parents' awareness of noise during the night, but all parents claimed that they always heard their children if they arose during the night. Although it was impossible to confirm the accuracy of such statements, their sensitivity to nighttime noises would not be expected to change across the different study phases and, therefore, would not contribute a systematic bias to the results. Other nighttime variables reported by parents were bed-wetting and nightsweats.

Three times a day the parent who was designated as the rater indicated the presence or absence of nine physical signs and symptoms (worded for lay people): skin rashes, red cheeks, dry skin, stomach bloat or cramps, leg cramps, stuffy/runny nose, headache, earaches, and bad breath.

The final daily form completed in the home was the food diary. Samples of adequate food diaries were distributed initially to serve as models. In addition to weighing and measuring the child's food, parents were required to provide recipes for all home-cooked items and brand names for prepared items used during the baseline phase.

The day care for each child also provided three types of daily information. A day-care worker filled out the ten-item ASQ but was not given an individualized part 2 section. The cook in the day-care facility weighed and measured the food eaten by the child, and recorded it on a food diary. Also, the naptime during day-care hours was recorded.

One other daily measure was attempted but terminated approximately halfway through the study because of unreliability. Observer ratings of positive and negative behaviors of various types were evaluated each day by trained volunteer observers who visited each day-care facility for 30 minutes of observation each day. It was thought that such observer data would be particularly desirable in evaluating the effects of dietary intervention in the free play setting of day cares, but a number of unanticipated difficulties arose. The frequent turnover of day-care staff led to great variability in the day-care environment regarding issues of directiveness and discipline. Turnover was also a problem with the observers themselves, because they were volunteers, and therefore, their reliability did not always exceed 80% (the initial criterion used during training).

To reduce the possibility of bias across days, the individuals completing home and day-care questionnaires did not have access to the previous day's data while working on the current day. Thus, both home and day-care questionnaires were inserted into dated envelopes and sealed, and the study coordinator picked up the envelopes every few days at unannounced times. In addition, the parents were required to score the ASQ, telephone the laboratory each evening, and report the ASQ scores to an answering mechine. If the parents failed to do so (which was infrequent), they were reminded by telephone the following morning. This requirement also reinforced the parents' belief that we were changing food items often, because it seemed to them that we required immediate feedback.

Periodic Measures. In addition to the daily measures, each child came to the laboratory for a half-day of testing within the last three days of each of the three phases. To prevent parents from using this scheduling information to figure out the three-phase experimental design, initially they were told that we would monitor the health of their child and do some learning and memory tests approximately once per month, at times convenient for them. On each laboratory test day, venous blood was drawn from the child to determine serum calcium, phosphorus, magnesium, copper, or zinc, whole blood lead levels, vitamin B_{12}, folate (RBC and serum), WBC count, RBC count, hemoglobin, and hematocrit. The child's weight and height were measured, and a study nurse checked for skin rashes. Finally, about 90 minutes of psychometric tests were performed: the Motor Accuracy test of the Southern California Sensory Integration test, Matching Familiar Figures test, Memory for Colors test, Visual Attention Span test, the Detroit Test of Learning Aptitude, Animal House test from the Wechsler Preschool and Primary Scale of Intelligence, and a paired associate learning test.

Data Analysis. Analyses were performed on the final 14 days of each of the three phases, to exclude data collected early during the baseline or experimental period when the family had not yet habituated to the record keeping. Days when the child was ill were also excluded: this occurred an average 1.3 days per child during each phase. Finally, days on which dietary infractions occurred were ex-

cluded: this occurred an average of 0.9 days per child. An infraction was defined as anything not permitted according to the guidelines of the ACH diet for that child.

We predicted significant effects of treatment on all variables, but particularly on ASQ scores, and on the sleep and somatic variables which had discriminated children with and without attention deficit disorder with hyperactivity in earlier research.[6,7] Significant effects of ACH over baseline and equivalent phases would indicate a treatment effect; a significant difference between equivalent and baseline phases would indicate a placebo effect.

In the following descriptions of the analyses of variance, order effects were always examined. No order effects were found for any dependent measures or any treatment-by-order interactions, and therefore, the children in both orders (baseline-ACH-equivalent and baseline-equivalent-ACH) were pooled. In all repeated-measures multivariate and univariate analyses of variance, there was one within-subject factor (treatment phase) with three levels (baseline, equivalent, ACH). For each univariate test, the guidelines of Hertzog and Rovine[10] were followed to decide when to use the T^2 F ratio, the within-contrast pooled F, or the within-contrast pooled with the Greenhouse-Geiser adjustment of degrees of freedom. Significant treatment effects were followed-up by the Tukey method of multiple comparisons at the .05 level.

RESULTS

Nutrient Intake

As an experimental check of our dietary manipulations, at the end of the study, nutrient intakes (including supplements) as coded from the daily food diaries were compared. A computer program that analyzes food into 49 nutrients was used to determine daily intake (NUTS version 2.02, Quilchena Consulting Ltd). The multivariate analysis of variance for calories, protein, carbohydrates, and sugar indicated a significant treatment effect ($F(8, 15) = 28.56$, $P < .0001$), and the univariate effects were significant for calories, carbohydrates, and sugar but not protein (Table). Tukey's multiple comparisons indicated that, as planned, the ACH diet was lower in simple sugar than either baseline or equivalent diets. As a consequence of reducing simple sugar, the overall consumption of calories and carbohydrates also decreased. The three phases were matched well for protein, which was also as planned. The only unexpected difference was the increase in sugar consumption during the equivalent compared with the baseline phase. Nutritional analyses were based on the foods and supplements actually eaten, not the foods that were sent home, which means that this difference may, in part, reflect selected eating preferences.

The repeated measures multivariate analysis of variance of the 11 vitamins analyzed with the NUTS program (Table) also indicated a significant treatment effect ($F(22, 1) = 652.36$, $P < .05$), and the univariate effects were significant for vitamin A, vitamin D, vitamin C, thiamine, niacin, vitamin B_6, vitamin B_{12}, folate, and biotin. All but the remaining two, riboflavin and pantothenic acid, increased consistently during ACH relative to baseline and equivalent phases.

Thus, this experimental check on our dietary intervention demonstrated that we succeeded in nutritionally enhancing the ACH diet and in keep-

TABLE. Nutrient Intake Across Treatments*

Nutrient	Dietary Phase		
	Baseline	Equivalent	Alberta Children's Hospital Diet
Calories (kcal)†	1,528 (279.0)	1,585 (191.9)	1,396 (240.7)
Protein (g)	49.53 (13.16)	49.36 (11.93)	50.89 (9.55)
Total carbohydrates (g)†	212.7 (35.7)	222.8 (28.8)	164.3 (32.7)
Simple sugars (g)†	73.85 (32.5)	89.12 (30.2)	38.88 (11.0)
Vitamins			
A (IU)†	5,562 (2,861)	5,939 (2,650)	8,120 (3,117)
D (IU)†	312.8 (183.2)	285.3 (178.4)	402.2 (98.7)
C (mg)†	145.0 (64.2)	135.7 (59.6)	104.2 (27.7)
Thiamine (mg)†	1.816 (1.1)	1.687 (1.1)	1.897 (0.7)
Riboflavin (mg)	1.994 (1.1)	1.870 (1.1)	1.897 (0.7)
Niacin (mg)†	15.77 (7.5)	15.21 (7.7)	20.24 (4.2)
B_6 (mg)†	1.530 (1.1)	1.391 (0.9)	2.817 (1.4)
B_{12} (mg)†	4.679 (3.8)	4.736 (3.9)	7.549 (3.5)
Pantothenic acid (mg)	5.322 (4.8)	5.221 (4.6)	6.456 (4.5)
Folate (μg)†	151.5 (50.3)	144.1 (49.2)	282.9 (35.1)
Biotin (μg)†	42.88 (25.8)	39.97 (23.1)	51.43 (25.9)

* Results are mean values with standard deviations in parentheses.
† Univariate F significant.

ing protein constant. The match between baseline and equivalent phases was excellent, except for one substance: sugar increased during the equivalent relative to the baseline phase ($P < .05$).

Definition of a Responder

As noted by others,[5] examination of only group data for this type of research often masks some important results. For instance, a few strong placebo responders can have a large impact on small-sample research. Prior to commencing the research, we defined the conventional 25% improvement in behavior as being a clinically significant change, and thus the parent ASQ scores were examined for children whose ACH phase scores were 25% better than baseline or equivalent scores but whose equivalent and baseline scores were similar (ie, who showed little placebo effect). When defined in terms of ACH phase relative to baseline phase, ten of the 24 children were designated responders (Fig 1). Further examination of the remaining 14, however, revealed that there was another group of four children who exhibited a responder pattern (improved during ACH and not during equivalent) but who did not change with the same magnitude; we refer to these as mild responders in Fig 2. When ACH scores were analyzed in relation to equivalent rather than baseline phase, only one child shifted categories: there were nine responders and five mild responders. The individual subject data for parent ASQ scores are given in Fig 3; the patterns of the responders (panel A) and nonresponders (panel B) are noticeably different.

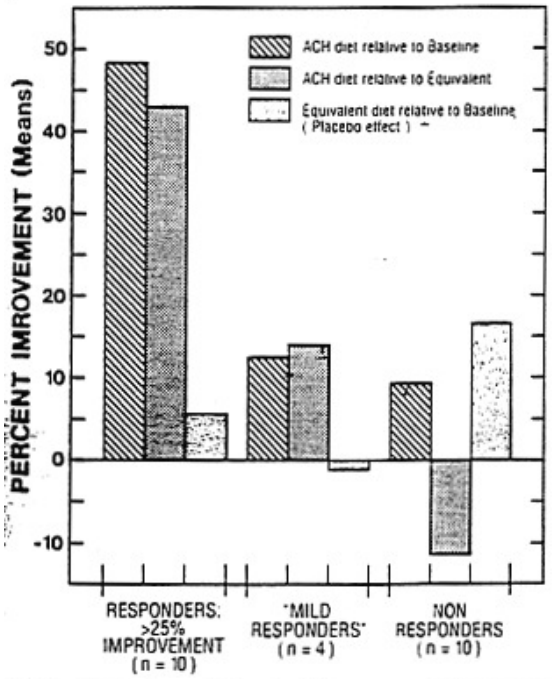

Fig 2. Percentage of behavioral improvement on parent Abbreviated Symptom Questionnaire, part 1, for responders (those showing 25% improvement while receiving hospital diet [ACH] and no placebo effect), mild responders (those showing reliable but moderate improvement while receiving ACH and no placebo effect), and nonresponders (those showing neither of those patterns).

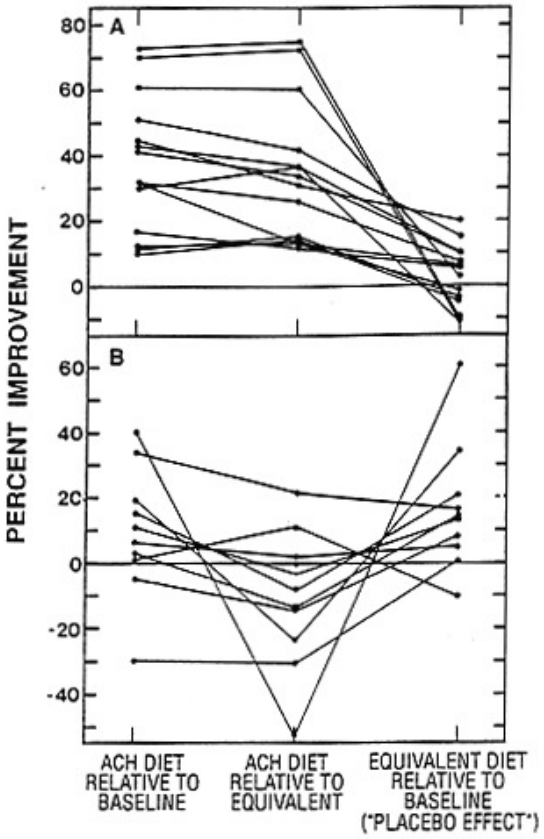

Fig 3. Percentage of behavioral improvement on parent Abbreviated Symptom Questionnaire, part 1, for each child. A, Data for ten responders and four mild responders, for whom hospital (ACH) diet improved behavior and there was little placebo effect. B, Nonresponders, for whom no pattern of change was discernible.

Behavior

Mean home ASQ scores for the last 14 days of each phase were 14.5 (SD 4.1) during baseline, 13.1 (SD 4.1) during equivalent, and 10.8 (SD 4.2) during ACH. A repeated-measures analysis of variance indicated a significant effect of treatment ($F(2, 46) = 17.24$, $P < .0001$). As predicted, ASQ scores were significantly lower during the ACH phase as compared with baseline phase ($P < .001$) and equivalent phase ($P < .01$). The difference between equivalent and baseline phases was not significant, indicating the absence of a placebo effect.

As mentioned, 19 families chose to design an extra set of ASQ items specific to their children, which we refer to as ASQ part 2. An analysis of variance indicated a significant effect of treatment ($F(2, 36) = 11.78$, $P = .0001$). ASQ scores were again significantly lower during the ACH phase than either baseline phase ($P < .001$) or equivalent phase ($P < .01$), with no evidence of a placebo effect of equivalent *v* baseline.

The overall analysis of behavioral change on the day-care ASQ scores indicated no significant treatment effect when data from all children were included. Because of the high turnover rate or absentee rate of day-care workers, the day-care ASQs for 14 children were not completed consistently by a single rater. Paired *t* tests were used to analyze the day-care ASQ scores for the small group remaining (n = 10). Although all means were in the expected direction (baseline mean 11.04, SD 7.96; equivalent mean 13.07, SD 6.97; ACH mean 10.73, SD 6.51), only the comparison of equivalent with baseline approached significance ($t\ (9df) = -2.22$, $P = .054$) but not the comparison of equivalent and ACH ($t\ (10df) = -1.62$) or baseline and ACH ($t\ (9df) = -.21$). In summary, the parent-reported data showed marked behavioral improvement while the children received the ACH diet, but the support from the day-care data was marginal.

Sleep

Based on other research,[6] we expected that treatment effects would be most noticeable on the number of night awakenings. As predicted, a repeated measures multivariate analysis of variance of the seven sleep variables revealed an overall treatment effect (multivariate $F(10, 14) = 5.19$, $P < .01$). In addition, univariate treatment effects were significant for night awakenings ($F(2, 46) = 5.05$, $P < .01$) and for latency ($F(2, 46) = 6.74$, $P < .01$) and were marginal for getting out of bed prior to falling asleep ($F(2, 46) = 4.63$, $P < .05$). Tukey's multiple comparisons indicated that ACH phase compared with equivalent and baseline phases was characterized by significantly shorter sleep latency. Getting out of bed prior to going to sleep and night awakenings were less frequent during the ACH phase in comparison to the baseline phase but not in comparison with the equivalent phase.

Physical Signs and Symptoms

Based on other research,[7] we expected that treatment effects would be most noticeable on the variables halitosis and chronic rhinitis. In the present study, a repeated measures multivariate analysis of variance indicated no overall treatment effect for the nine variables together ($F(16, 8) = 1.48$). A priori hypotheses for specific changes led us to examine the univariate results, which indicated a significant treatment effect for halitosis ($F(2, 44) = 6.26$, $P < .01$) and headache ($F(2, 46) = 4.19$, $P < .05$). The effect for rhinitis was marginal ($F(2, 46) = 2.79$, $P = .07$). Tukey's multiple comparisons showed that the ACH treatment phase resulted in less halitosis than the baseline phase ($P < .01$); the difference from the equivalent phase was marginally significant (approximate $P = .07$). The 40% decrease in rhinitis from baseline and equivalent phases was marginally significant (approximate $P = .10$). Headache was less frequently reported during the ACH phase than the equivalent phase ($P < .05$) but not less than the baseline phase and thus did not seem to be affected by dietary manipulation.

Nutritional Status

Blood was drawn from each child during each laboratory visit, for a variety of analyses. WBC, RBC, hemoglobin, MCV, MCH, platelets, calcium, magnesium, and phosphorous values were within normal limits for all of the children and did not change significantly as a function of experimental intervention. Copper, zinc, and lead levels were also analyzed, and no treatment effects were found. One amino acid was analyzed (tryptophan) because of prior theories regarding the possible significance of serotonin in sleep disturbances,[11] and, again, there was no significant change as a function of dietary intervention. Finally, serum folate, RBC folate, and serum vitamin B_{12} levels were examined, and no meaningful treatment effects were found.

Psychometric Tests

For many of the sessions, the children proved to be untestable. This was, in part, predictable, because of the nature of attention deficit disorder with hyperactivity and the extremeness of the present sample which averaged more than 3 SD above the mean on the ASQ Hyperactivity Index. In part, however, it was because of the difficulty in selecting tests acceptable to such young children. Only one child had a complete set of data available for paired associate learning, and only five children had complete data sets for the other eight tests. This problem of missing data precluded the possibility of doing any meaningful statistical tests; graphed scores suggested no trends.

Correlated Changes

Because of our small sample size, it was not possible to ask statistical questions of prediction to

determine what variables predicted behavioral response to the ACH diet. Consequently, we selected the five variables that appeared from our earlier work[6,7] to best discriminate boys with attention deficit disorder with hyperactivity from boys without the disorder, and also to change with dietary intervention in the present study, and we correlated each of these with behavioral change due to ACH diet. Of the five variables (rhinitis, halitosis, headache, sleep latency, and night awakenings), only one (night awakenings) showed a modest correlation ($r = .42$, $P = .055$) with change in behavior as measured by the home ASQ, part 1. This means that as attention deficit disorder with hyperactivity behavior decreased, so did night awakenings.

Responders: Behavior, Sleep, Physical Signs and Symptoms, Psychometric Tests

For the subgroup of 14 responders and mild responders, the mean home ASQ score was 14.9 (SD 4.7) during the baseline phase, 14.04 (SD 4.3) during the equivalent phase, and 9.7 (SD 4.5) during the ACH phase. These values are similar to the whole sample of 24 children, except they perhaps indicate less of a placebo effect. The analyses of variance and multiple comparisons indicated results that were identical with the group as a whole: behavior on the ASQ (parts 1 and 2) improved during the ACH phase relative to both baseline ($P < .001$) and equivalent phases ($P < .001$).

For sleep variables, the results for the subgroup of responders mirrored precisely the results for the whole sample: sleep latency, getting out of bed prior to sleep, and night awakenings showed predicted significant treatment effects.

For physical signs and symptoms, once again, halitosis and rhinitis were the variables that tended to change, although the 30% improvement in rhinitis during the ACH phase did not reach statistical significance in this small subsample.

For the psychometric tests, three of the five children who had complete data sets were in the responder group, but this was too few to do a meaningful test for eight dependent variables.

Bias

Two sets of analyses addressed the question of whether attitudes toward food might have biased our results. As a result of other research,[6,7] we had a pool of 115 boys with attention deficit disorder with hyperactivity (of whom the 24 in the current study were a subset) and 89 boys without the disorder, all of whom were 3 to 6 years of age, with whom we could compare the present sample. Parents of all 204 boys completed the Food Attitude Questionnaire, prior to participating in any studies. There was no difference in scores between these two groups (t (95.32 df) = 0.87). Thus, the presence of a child with attention deficit disorder with hyperactivity in the home did not appear to have affected parental attitudes toward food. The second analysis divided the 24 children in the current study into two groups, responder and nonresponder, according to the criteria mentioned before. Again, there was no difference in parent Food Attitude Questionnaire score (t (20 df) = −1.52). Thus, the parents whose children subsequently responded to the ACH diet did not differ from parents of nonresponders.

DISCUSSION

Approximately 42% (n = 10) of the children exhibited approximately 50% improvement in behavior as a result of the ACH diet (Fig 2); an additional 16% (n = 4) exhibited a 12% improvement with no placebo effect. The remaining 42% (n = 10) of the children were unresponsive to dietary intervention. Overall, this is evidence of a much larger effect of dietary intervention than the 15% behavioral improvement noted by Conners et al,[2] but it is consistent with the home-based evaluations by Harley et al[1] who showed behavioral improvement in 13/36 school-aged children and 10/10 preschool-aged children (the magnitude of which was unspecified), resulting in an overall rate of 50% of the subjects studied. Results of replacement studies indicate larger response rates than challenge studies (with the possible exception of Swanson and Kinsbourne[12]). Challenge studies make up the vast majority of the research literature, and their results generally indicate that 0% to 10% of the subjects studied exhibit a response to a challenge substance.[4] In the present study, significant treatment effects of the ACH diet were also noted with respect to some of the same sleep variables and physical signs and symptoms that have discriminated children with and without attention deficit disorder with hyperactivity in our laboratory in other studies.[6,7] The relationship between these variables and the behavioral data is not clear, however, because only one (night awakenings) changed consistently with behavior.

The fact that replacement diets (which are broad interventions) result in more of a behavioral change than challenge studies (which focus on individual classes of substances) suggests that individual differences in responsivity to various food substances are of major importance in this area. It is possible that, if we had tested only a single type of substance (eg, sugar or dyes) in this same sample, then the usual 0% to 10% of the children would have exhib-

ited a behavioral response. By testing a broader dietary intervention, we have demonstrated the phenomenon that perhaps should have preceded the various studies of the 1970s: food substances can improve the behavior of 45% to 60% of these children (depending on the criterion of a response). Moving from the general phenomenon to the more specific tests of individual substances can stimulate further research which is theory driven.

Even though it appears that our ACH diet was broad, it, too, can be criticized for ignoring many possible individual differences in responsivity to food substances. After the current research was already underway, one report[13] appeared in which behavioral changes were demonstrated with challenges of a wide variety of foods which were not excluded in our ACH diet: oats, peanuts, wheat, grapes, and bananas, etc. Perhaps exclusion of these other items would have resulted in even greater changes in behavior, but it would have been more difficult to conceal the treatment conditions.

A number of explanations for the present findings were considered in the data analyses. First, given that the ACH diet was nutritionally enhanced, serum levels of various nutrients were examined for treatment effects, but none was found. Thus, our hypothesis that poorly nourished children might be the ones most likely to be susceptible to nutrition-behavior effects was not supported. Because blood biochemistry values of all of the children were within normal limits, perhaps we had an insufficient range during the baseline phase to test this hypothesis. It should also be noted that our definition of nutritional status was limited, relative to those used elsewhere.[14] Second, we considered the possibility that the negative behaviors of children with attention deficit disorder with hyperactivity with somatic complaints might be partially due to physical discomfort. If this were so, then one might have expected a correlation between change in behavior and change in physical signs and symptoms. In fact, only night awakenings correlated modestly with behavioral change, but a larger sample is required to explore this issue. Third, in light of the finding that night awakenings decreased during the ACH diet, and because of research that demonstrates the effect of tryptophan in sleep,[11] tryptophan levels were examined for treatment effects, and none was found.

Given that the positive effects of the ACH diet were obtained in the home setting (parent ASQ scores, sleep variables, physical signs and symptoms), it could be argued that the parents or the children themselves were not really unaware of the study design. However, the debriefing interviews demonstrated that no parent was aware of the timing or nature of the dietary manipulation. Also, demonstration that parents of responders were nc more biased about nutrition-behavior relationship than parents of nonresponders (or, indeed, parent of boys without attention deficit disorder witl hyperactivity) enables us to rule out parental bia as a source of the treatment effects. We had in tended to provide data from another setting (da cares) in support of any treatment effects tha occurred, but the high turnover rates of day-car staff and the difficulties encountered with the observational data precluded this possibility. As with other studies,[1] there was no demonstration of treatment effects in laboratory tests either. Thus, confidence in our ability to conceal the treatment conditions is essential in interpreting the treatment effects obtained in this study. In spite of our best efforts to minimize bias, one can never be certain that the parents were truly unaware, because perfectly matched placebos are not possible with the dietary replacement method.

One issue of great concern in nutrition-behavior research has been the frequent occurrence of a treatment order effect, in which an elimination diet has been associated with a greater treatment effect when it follows the placebo control diet.[1,2] Although such order effects may, indeed, be indicative of large expectancy effects, they may also be due to nonreversible treatment effects.[15] In other words, perhaps the beneficial effects of an elimination diet do not reverse in the few weeks allocated for a placebo control diet. Although we found no statistically significant order effects on any of our dependent variables, it is interesting that nine of our 14 responders were in the baseline-equivalent-ACH group. As Kinsbourne[15] has pointed out, the treatment order effect has been used by the food industry and others to minimize the significance of possible nutrition-behavior effects. Perhaps the consistency of the direction of these order effects suggests, instead, that it is a problem that warrants further investigation.

There was a sharp discrepancy between Conners Rating Scale scores obtained during screening (when the 24 boys averaged 3.37 SD above the mean) and the comparable ASQ score obtained during the baseline phase (when they averaged less than 1 SD above the mean). This unexpected decline increased the difficulty of obtaining treatment effects. In discussing the tendency of ASQ scores to drift downward after repetition, Zentall and Zentall[16] concluded that regression toward the mean is an insufficient explanation when the overall mean changes, and that the drift is due to a true, or psychologically based, practice effect. Their description fits the current situation: the initial ratings were retrospective and were probably heavily influenced by recall of severe negative behaviors,

whereas the daily observations permitted the parents to balance their evaluation with "many less memorable, appropriate behaviors."[16] In the present study, practice effects were inconsequential because the treatment orders were counterbalanced.

This study in conjunction with our previous ones[6,7] seems to provide converging lines of evidence that five of the sleep variables and physical signs and symptoms may be clinically relevant: halitosis, rhinitis, headache, night awakenings, and sleep latency. In the current study, not all of these variables exhibited significant treatment effects (eg, halitosis improved significantly during ACH relative to baseline phase, but the change relative to the equivalent phase was only marginal), and in the earlier work not all of the variables consistently discriminated boys with and without attention deficit disorder with hyperactivity; however, of the 16 nonbehavioral variables we have evaluated in several experiments, it has been these five that have tended to be the ones sensitive to group and treatment effects. Their cooccurrence with attention deficit disorder with hyperactivity and their partial amelioration with the ACH diet is worthy of further study.

Finally, the nature of the impact of our dietary intervention should be emphasized. On the one hand, a much larger percentage of children responded to dietary intervention than found in previous studies. On the other hand, only half of the children who completed the study exhibited behavioral improvement, and it is safe to say that not a single parent believed that participation in this study had transformed their child into an easy to manage person. We removed everyday obstacles to compliance which practitioners regularly face: we determined the menus and provided the food at no cost to participants. Our research provides some clues as to where further work should proceed (ie, the examination of the physical basis of adverse reactions, cf Bock[17]), and it also demonstrates a larger potential impact of diet than previously reported. These results suggest that pediatricians and other practitioners might consider dietary modifications worth trying, particularly in younger children.

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