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ABSTRACT

Fifteen hyperkinetic children (6-12 years old) were involved in a pilot study to test B. Feingold's hypothesis that hyperkinesis may be caused by artificial flavors and colors in food. Prior to treatment, parents and teachers completed bi-weekly questionnaires regarding each Ss' behavior both on medication (pretreatment period) and when medication was discontinued (baseline period). Ss were randomly assigned to either the experimental (K-P) diet which eliminates artificial flavors, colors, and natural salicylates or a control diet for 4 weeks. The following month, each S was placed on the alternative diet. Following each diet condition, parents were interviewed, school reports were examined, and a judgment was made using the Clinical Global Impressions scale without knowledge of diet condition. Results showed that both parents and teachers reported fewer hyperkinetic symptoms on the K-P diet as compared to pretreatment baseline; that teachers noted a highly significant reduction of symptoms on the K-P as compared to the control diet but the parents did not; and that control diet ratings did not differ from the baseline period for either parents or teachers. Although findings suggested that the K-P diet may reduce hyperkinetic symptoms, results should be viewed cautiously until further research is completed. Concluded in a critique of the pilot study by the National Institute of Education was that the behavioral outcome measures were "soft" and pharmacology uncertain; that the experimental design was subject to certain problems; and that the sample size did not allow for much further analysis. (SB)

NIE STAFF CRITIQUE OF CONNERS, ET AL., "FOOD ADDITIVES AND HYPERKINESIS: A CONTROLLED DOUBLE BLIND EXPERIMENT"

This is a pilot study and, as such, is a preliminary attempt to discover empirically whether, under certain specified conditions, there is statistical justification for the assertion that food additives, as characterized by Dr. Ben F. Feingold, are causally related to hyperkinesis in children.

Despite the title of the study, it is not, nor was it intended to be, a test of the effects of food additives per se. Rather it is a test of two diets -- the Feingold diet which contains no artificial colors or flavoring and the control diet which does in amounts commonly found in the marketplace.

As a test of two diets it is the investigators' conclusion that the results should be viewed with caution. As the investigators observe, the Feingold diet not only differs from the control diet with respect to certain food additives, but also with respect to the amount each diet contains of several common and essential nutrients, e.g., carbohydrates, vitamin C, niacin, thiamin and others. Thus, it is difficult to tell whether the behavior of the children on the Feingold diet changed because of food additives or because of nutritional differences. There is reason to believe such a distinction may be important. For example, the investigators call attention to the observed association of hyperkinesis and hypoglycemia, and indicate that hypoglycemia is dietarily regulated by, among other things, reducing carbohydrate intake. Since the Feingold diet has fewer carbohydrates than the control diet, the investigators note that part of

the observed reduction in hyperkinesis attributed to reduced food additives could as well be attributed to the attenuated effects of hypoglycemia. The possibility of other uncontrolled effects due to dietary differences cannot be discounted.

Two other significant sources of uncertainty in the study are its small sample size (15 children), and the uncertain control of the information and expectations held by the parents. In the first instance a review of the literature and statistical considerations suggested that a sample size of 80 children would be large enough to permit reliable estimates of statistical differences. That a significant effect is shown with just 15 children does not take away from the desirability of a larger sample in order to ensure and expand the generalizability of the results to children of diverse social and demographic characteristics.

A larger sample might also shed light on the unexplained finding that the behavioral effects of the diets are evidently related to the order in which they are administered to the children (Figure 2, p. 25 of report). That is, when the Feingold diet is given first, followed by the control diet, the difference in the children's behavior between the two diets is not significant, and there is only trivial amelioration of behavior due to the Feingold diet. But when the Feingold is administered after the control diet, there appears to be a significant different between the two diets, and a marked reduction of hyperkinetic symptoms of those children using the Feingold diet. The investigators indicate that "order effects" of this kind are not an uncommon finding in other drug-related "double blind" research. Nonetheless, one would expect that if the observed effects were entirely or even largely due to dietary differences, then there would be consistent effects regardless of the order of presentation of the diets.

That effects are not consistent opens the possibility of alternative and competing interpretations of the data. One such alternative is that the parents and/or teachers are influenced through their awareness of differences between the diets, or some other uncontrolled exposure to information, and subsequently bias their own ratings of the children's behavior or, possibly, directly influence the behavior of the children. The study does not permit confident selection among the alternatives and thus it simply shows that while this particular formulation of the Feingold diet may reduce hyperkinetic behavior, it is also possible that the observed reduction is an artifact of the parents and teachers' belief that it will.

In addition to the foregoing primary concerns, there are a number of secondary issues which also have been exposed by the study and which will need consideration before embarking on further research or establishing policy with regard to food additives. These issues are largely methodological or questions of study design which might exert influence on the findings and which must be better understood in the assessment of the validity of these and future results. The issues are as follows:

1. Why should the control diet produce an increase in hyperkinetic behaviors reported by teachers and not by parents?
2. What are the pharmacological and behavioral implications of using subjects, some of whom, as in the pilot study, were on medication prior to the experiment, and some of whom were not?

3. What effect would the variation in prior dietary habits of the children have on the findings? Is there reason to suspect long term carry-over effects of pre-treatment diets?

4. How many and what types of related factors must be taken into account in defining and studying hyperkinesis? There are presumed associations between hyperkinesis and such factors as age, residential location, hypoglycemia, etc., each of which will limit the determinacy of future results unless we have sufficient awareness of their incidence, etiology, and effect to permit appropriate assumptions and controls.

5. What is the reliability and validity of the 10-item hyperkinesis index used, given that it is a short version derived from a much longer scale?

6. Although the analysis of variance has an "order of diet" term in the model (mislabeled as "group" in the report), Figure 2 p. 25 illustrates that the order effect may be worth investigating further.

7. The report and this figure use "baseline-corrected scores", which are the differences between the ratings of the children before and after they were placed on the diets. There are disadvantages in using difference scores for such analyses (including variance, unclear interpretive meaning, etc.,). Are there other, more effective ways to correct for initial differences in behavior of the children?

CONCLUSION

The pilot study concludes that findings should be reviewed with caution and this seems to be a fair statement. The behavioral outcome measures are "soft" and the pharmacology uncertain. The experimental design is subject to certain problems as the authors point out. The sample size does not allow for much further analysis. The question is whether or not to correct the design for stronger inferences, get more data, and continue this research. This does not seem to be a question that can be answered by statistics or analysis. Rather it is a question which must be addressed within and between the many relevant subject-matter areas, whose members, armed with theory and method, can objectively continue the exploration of this complex phenomenon.

Acknowledgements

The authors wish to express their thanks to Bernard Levy, M.D., Director of the Human Resource Institute of Boston who originally permitted the senior author to begin this study at the Institute, and to Richard Sarle, Administrator, for facilitating contract arrangements. David Boesel of the National Institute of Education was responsible for many helpful arrangements and patiently encouraged the continuation of the study after the senior author moved to the University of Pittsburgh.

Alan Cohen, M.D. and Janice Hubka, M.A. assisted during pilot phases of the program in Boston. Joanna Dwyer, D.Sc. was instrumental in providing much useful advice in the early phases of the study regarding dietary and design aspects of the investigation.

Benjamin Feingold, M.D. served as a consultant and advisor on the project, and of course provided the initial impetus to open up the entire field of investigation for study.

Food Additives and Hyperkinesis: A Controlled Double-Blind Experiment

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Introduction. In June of 1973 a preliminary report was presented by Benjamin F. Feingold, M.D., professor emeritus of the Kaiser-Permanente department of allergy, in which it was proposed that hyperkinesis in childhood is associated with the ingestion of salicylates, of compounds which cross-react with salicylates, and with common "food additives", i.e. artificial flavors and colors. Other oral presentations, including a popular book and testimony in the Congressional Record, have served to popularize the hypothesis that this common childhood behavior disorder may be caused by artificial flavors and colors in food.

The medical literature shows that urticaria and asthma can be induced by food additives and dyes (Chafee & Settipane, 1967), and that strong allergic reactions occur to some dyes in patients with aspirin hypersensitivity (Juhlin, et. al., 1972). Feingold noted (1973) that an adult patient with aspirin hypersensitivity showed remission of psychiatric disturbances when the patient

was placed on a diet free of natural salicylates, food colors and artificial flavors. Because of the supposed cross-reactivity of salicylates and dyes (especially tartrazine, the yellow FD&C #5 dye), Feingold treated hyperactive children with a diet free of so-called natural salicylates (found in many fruits) and all artificial colors and flavors.

A number of criticisms were immediately raised against Feingold's claims (many of these are summa ized in the National Advisory Committee on Hyperkinesis and Food Additives Report to the Nutrition Foundation, based on a conference held in January, 1975). Included among the criticisms are that: (1) the patients reported upon were not described by any standard methods, nomenclature or measurements; (2) no controls were utilized to compare changes against those in the children treated with the elimination diet (hereinafter referred to as the K-P diet); (3) no objective measures of change were employed; (4) the observer of change was not blind to the treatment being evaluated and had a vested interest in confirming the hypothesis; (5) alternative explanations based on commonly accepted placebo phenomena were not considered; (6) no measures of the actual dietary habits of the patients were presented to rule out the possibility of unintended harmful dietary effects or that changes in the diet other than artificial flavors and colors could cause the effect; (7) claims of percentage improvement varied from one presentation

to another, and no hard statistical numbers were ever employed. In short, the claims were strictly impressionistic, anecdotal, and lacking in objective evidence.

Because of the wide public interest aroused by the claims, however, and because of the public health implications of the hypothesis, the National Institute of Education (NIE), of the Department of Health, Education and Welfare (HEW), solicited contract proposals for the study of the hypothesis. An initial contract was awarded to the Human Resource Institute of Boston, with C. Keith Conners as Principal Investigator. Since the contract was awarded in May of 1974, only a small pilot study was completed before the end of the school year. In the subsequent October Dr. Conners took up a new position as Associate Professor at the University of Pittsburgh Medical School's Department of Psychiatry where the bulk of the present work was undertaken.

Method

Subjects. In order to be eligible for the study, children had to be between the ages of 6 years and 12 years and 11 months. The children were examined by a child psychiatrist who utilized a standardized examination and rating scale, and had to agree that the child fit the criteria for hyperkinetic reaction of childhood (308.0 of the APA DSM II) based upon the medical and

social history, parent and teacher symptom ratings, and the psychiatric rating scale. Demographic, history, physical and mental status examination, neurologic evaluation and rating scales were all forms adopted by the National Institute of Mental Health Psychopharmacology Research Branch for conducting scientific trials in pediatric populations with drugs and related types of studies (Appendix I). The purpose of these instruments was to record in an objective and standardized manner the entire set of data available on each child.

Central to this study was the use of two symptom rating scales filled out by parents and teachers (Conners, 1969, 1970). The teacher scale is a 39-item list of common behavioral problems found in school age children. The parent scale is a 93-item symptom list covering a wide variety of behavioral reactions in children. Both scales have been demonstrated to have satisfactory reliability and validity. Most of the present report will deal with data from a 10-item subscale ("hyperkinesis index") which measures the cardinal symptoms of the hyperkinetic syndrome. The 10 items are identical for parents and teachers. Since each item is scored 0, 1, 2, or 3, scores may range from zero through 30. It should be emphasized that these scales do not diagnose hyperkinesis; diagnosis is a complex judgment based upon all of the data available to the

clinician; but studies have shown that a cut-off score of 15 on the 10-item scale is an efficient discriminator between diagnosed patients and classroom controls (Sprague, et.al., 1975), and that the scale is sensitive to changes brought about by other therapies.

Table 1 shows that of 37 children referred for the study, 15 completed the entire program, with the other children largely having dropped out prior to the actual start of the experiment itself.

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Table 1 here

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In addition to symptoms of moderate to severe degree, the children had to have a history of at least two years duration of the major symptoms of the hyperkinetic syndrome. Most had in fact been seen as problems by parents from a relatively early age.[1] Table 2 shows the distribution of ages in the children completing this study, and Table 3 summarizes the selection criteria.

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Tables 2 and 3 here

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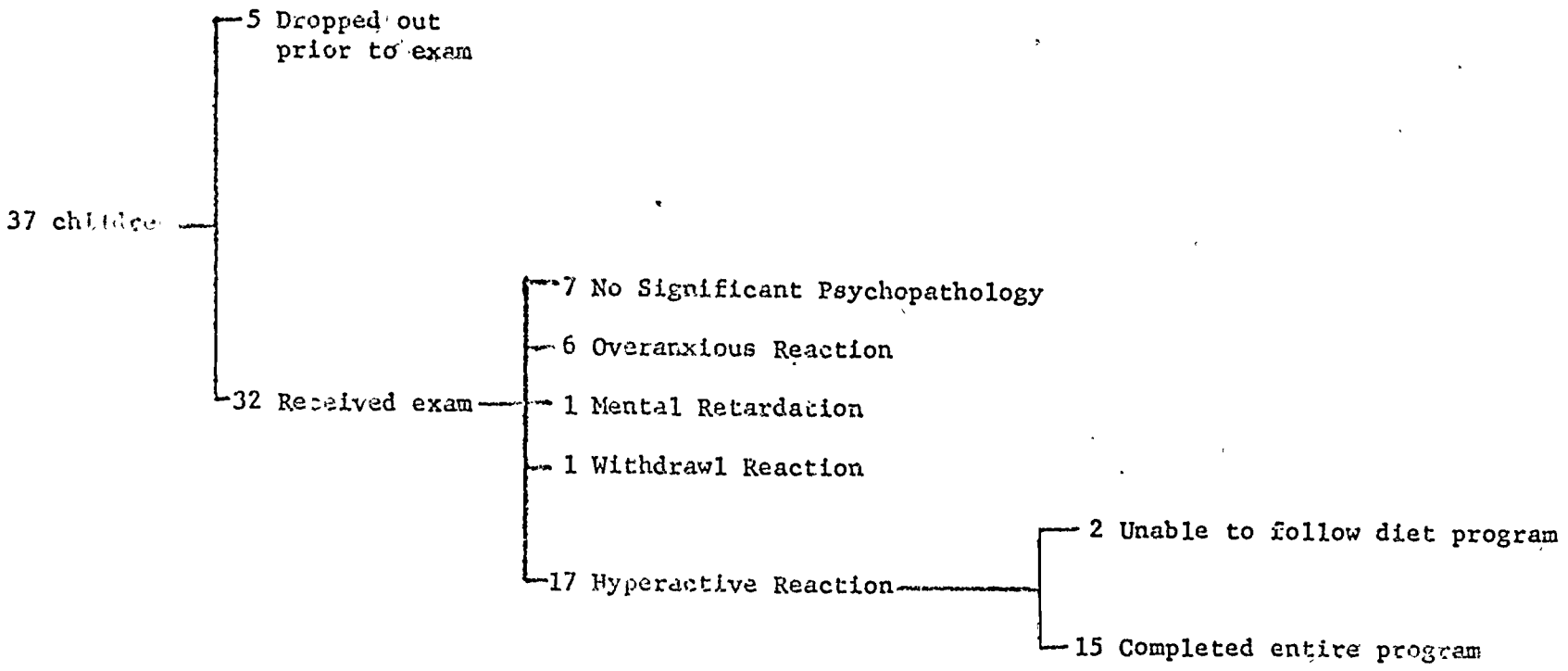
12

[1] A more complete description of the subjects, including [illegible] history, demographic status, physical characteristics and [illegible] details will be provided in a final report, based upon more complete analysis of the NIMH forms by the Biometrics Laboratory of George Washington University.

Table 4

FOOD ADDITIVES AND HYPERKINESIS SAMPLE FLOW SHEET



Referral	Psychiatric exam	Diagnosis	Diet program results

Table 2

Age Distribution of Sample

Age in Months*	%	N
61-84	6.7	1
85-108	53.3	8
109-132	33.3	5
133-156	6.7	1

*Mean Age = 105.4 months (8.78 years)

Table 3

selection criteria

1. *AGE:* 6 YEARS - 12 YEARS, 11 MONTHS
2. *INTELLIGENCE:* LOW NORMAL (85 IQ) OR ABOVE
3. *DIAGNOSIS:* HYPERKINETIC REACTION OF CHILDHOOD (308.0)
   - *a.* PARENT QUESTIONNAIRE
   - *b.* TEACHER QUESTIONNAIRE
   - *c.* PHYSICIAN PSYCHIATRIC JUDGEMENT
4. *SEVERITY:* MODERATE TO SEVERE
5. *DURATION OF SYMPTOMS:* 2 YEARS MINIMUM
6. *PREVIOUS TREATMENTS:* DRUG THERAPY NOT CONTRAINDICATED

Design. Prior to treatment parents and teachers independently completed bi-weekly questionnaires regarding the child's current behavior, utilizing the abbreviated 10-item symptom scale ("pre-treatment period"). These measures were collected for two weeks, and then if the child was on medication, the medication was discontinued and the ratings continued for another two weeks ("baseline period"). If the child was not on medication, the ratings were similarly collected for the two-week baseline period.

At this point the children were randomly assigned to either the experimental (KP) diet, or a control diet. Parents and teachers continued to observe the children with weekly symptom ratings for four weeks. At this point the parents were interviewed by the principal investigator, the school reports were examined, and a judgment was made without knowledge of the diet condition as to overall global improvement, using the Clinical Global Impressions (CGI) scale. The same procedure was then followed for the next one month while the child was on the alternative diet. A summary of the experimental procedure appears in Table 4, and Table 5 lists the instruments used to document the trial.

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Tables 4 and 5 here

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[illegible] the various forms used for data collection.

Table 4

Experimental design

1. PRE-TREATMENT

a. PARENTS AND TEACHERS COMPLETE BI-WEEKLY BEHAVIORAL QUESTIONAIRES BASED ON CHILD'S BEHAVIOR

b. DURATION: 2 WEEKS

2. BASELINE

a. MEDICATION DISCONTINUED IF PREVIOUSLY PRESCRIBED

b. PARENTS AND TEACHES CONTINUE TO COMPLETE BI-WEEKLY BEHAVIORAL QUESTIONAIRES

c. DURATION: 2 WEEKS

experimental design: (cont.)

3. DIET 1

a. CHILD RANDOMLY ASSIGNED TO EITHER EXPERIMENTAL OR CONTROL DIET

b. PARENTS AND TEACHERS COMPLETE WEEKLY BEHAVORIAL QUESTIONAIRES

c. PRINCIPAL INVESTIGATOR INTERVIEWS PARENTS AT CONCLUSION OF DIET TO ASSESS DEGREE OF IMPROVEMENT (CGI)

d. DURATION: 4 WEEKS

experimental design: (cont.)

4. DIET 2

a. CHILDREN CROSSED OVER TO SECOND DIET

b. PARENTS AND TEACHES COMPLETE WEEKLY BEHAVIORAL QUESTIONAIRES

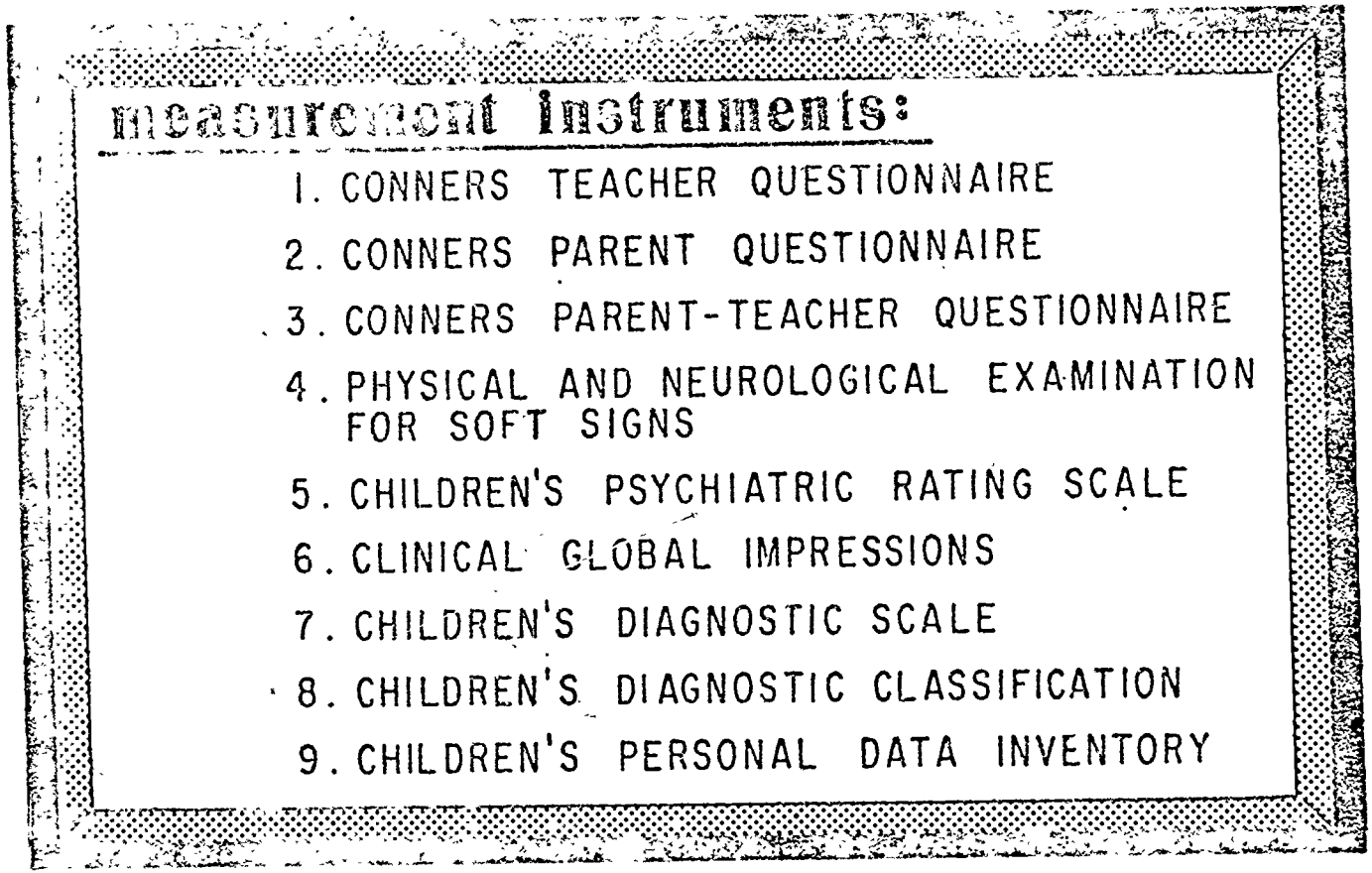
c. PRINCIPAL INVESTIGATOR INTERVIEWS PARENT AT CONCLUSION OF DIET. TO ASSESS DEGREE OF IMPROVEMENT (CGI)

d. DURATION: 4 WEEKS

5. FOLLOW-UP:

a. PARENTS CONTACTED IN 6 MONTHS TO DETERMINE PRESENT STATUS OF CHILD

Table 5


Measurement Instruments:
1. CONNERS TEACHER QUESTIONNAIRE
2. CONNERS PARENT QUESTIONNAIRE
3. CONNERS PARENT-TEACHER QUESTIONNAIRE
4. PHYSICAL AND NEUROLOGICAL EXAMINATION FOR SOFT SIGNS
5. CHILDREN'S PSYCHIATRIC RATING SCALE
6. CLINICAL GLOBAL IMPRESSIONS
7. CHILDREN'S DIAGNOSTIC SCALE
8. CHILDREN'S DIAGNOSTIC CLASSIFICATION
9. CHILDREN'S PERSONAL DATA INVENTORY

Experimental and control diets. Prior to the start of the diets the parents met with the nutritionist (D.A.S.) who explained the particular diet the child was assigned to, giving the parent a list of items to be excluded, as well as a list of acceptable items. Procedures regarding compliance were discussed and general matters regarding food selection, preparation and recording were outlined.

The control diet was devised with the following criteria in mind: (1) The diet should involve the same degree of time in preparation, shopping and monitoring as the K-P diet; (2) the items in the control diet should be drawn from the same food groupings and categories where possible as the K-P diet; (3) the two diets should be nonoverlapping; i.e. items on the control diet should allow for eating of items excluded on the K-P diet, and vice versa; (4) the control diet should be as palatable and easy to follow as the K-P diet; (5) the control diet should appear plausible and reasonable as a possibly effective treatment.

With regard to this last point, care was taken in the instructions to parents to make each diet seem worthwhile and as likely to provide benefit as the experimental diet. At no times were the words K-P, Feingold diet, experimental diet, or control diet used. Instead, parents were told that their child

would try both diets, that either might produce improvement, and that it was necessary to have both diets to compare with each other. They were told we were studying dietary factors in behavior problems, and that there might be a number of separate food items that could cause behavioral difficulties, and that only by systematically comparing different approaches could we be sure which diet(s) might be effective for their child. The two exclusion diets and suggested items available on each diet are provided in Appendix II.

Assessment of Prior Dietary Status. A nutritionist collected dietary information on each child using a dietary questionnaire, 24-hour recall, and food frequency measure.

Dietary Questionnaire - Parents supplied information pertaining to the food habits of their child -- number of meals and snacks per day, foods eaten for meals and snacks, meal times, food likes and dislikes, problems at the meal table, food allergies and other medical complications (See Appendix II).

24-hour Recall - Parents were asked to recall everything consumed by the child during the previous day. The time, place, a description of preparation and judged amount for each food item were also recorded. Food models were used to assist in assessing the amount.

Food Frequency Measure - Given a list of foods, parents were asked to indicate the number of times or frequency each food is usually consumed by their child during a "typical" week (See Appendix II).

The twenty-four hour recall, frequency and questionnaire were used together to determine the adequacy of prior dietary habits of the children (Adelson, 1960; Beal, 1967; Burke, 1947; Stefanik, et. al., 1962; Chalmers, et. al., 1952). Data from recall and frequency were grouped according to the basic four food groups, and with the data from the questionnaire, judged for adequacy and appropriate dietary patterns which would be conducive to sound nutritional practices. Problems or poor eating habits were discussed with the parents.

Dietary Compliance and Nutrient Monitoring. During the 12 week program, parents kept diet records, recording everything their child consumed, for 6 days each month. The time, place, food, a detailed description and the method of preparation, and the weighed or measured amount consumed were to be recorded. Three to seven day diet records have been shown to give reliable dietary information for nutrient analysis (Beal, 1967; Chalmers, et. al., 1952). In addition, parents maintained a list of infractions that occurred during each of the diet periods, and completed a dietary degree of difficulty questionnaire at

the conclusion of each diet period to assess the comparability of the difficulty in following the control and experimental diets (see Appendix II).

Determination of Nutrient Intake. Diet records were coded using the USDA Home & Garden Handbook, No. 72, Nutrient Value of Foods, and analyzed with the Diet Research Program for calories, protein, carbohydrate, fat, calcium, iron, Vitamin A, thiamin, riboflavin, niacin, and Vitamin C. Averages for the nutrients were calculated for each individual based on the 6 day diet records (representing one month) for the three month periods, i.e., 3 sets of averages for each individual. Group averages were tabulated for each month period.

The computed nutrient intake data reported the contribution in gram units and percent made by meals (breakfast, lunch, dinner and snack) for individuals and group. Percentages of the Recommended Dietary Allowances were calculated for breakfast, lunch, dinner and snack; total for each individual average intake; and for the group intake during baseline, K-P diet and control diet.

Recommended Dietary Allowances. The Recommended Dietary Allowances (RDA) are the levels of intake of essential nutrients considered, in the judgement of the Food and Nutrition Board on the basis of available scientific knowledge, to be adequate

to meet the known nutritional needs of practically all healthy persons.

In order to meet these needs, the levels of nutrients listed in the RDA have an added margin of safety to cover individual variation. The RDA was established as a standard for populations. When dealing with individuals or small groups, 2/3 of the RDA is, by convention, taken as a cut-off point in assessing adequate or poor diets.

Levels of nutrients listed by the RDA have been categorized by sex and age groupings. Thus, the percentages of the RDA tabulated from the dietary records in the present study have incorporated both sex and age of the subjects studied.

Appendix III contains a detailed flow sheet of the different types of contact with the parents, teachers, and patients.

Results

Clinical Global Impressions. Table 6 shows the principal investigator's judgement of improvement based upon interview with the parents, the parent symptom ratings, and the teachers' symptom ratings. The project coordinator (C.H.G.) met with parents prior to each of the two final interviews following each diet, and reminded parents not to mention any specific

foods involved in the diet. The Principal Investigator (C.K.C.) also reminded the parents at the start of the interview not to reveal which diet their child had been on. Then a semi-structured interview was conducted in which the parents' view of overall changes, somatic changes, peer and family changes, the child's reaction to the diets and any knowledge of changes in school were elicited. At this point, if the interview was following the first diet, regardless of what changes the parent noted or failed to find, the parent was strongly exhorted to give the other diet a fair try, to be scrupulous in following and monitoring it, and to encourage the child to follow the new diet. If the child had improved, parents were told he conceivably could improve even more on the second diet, and if unimproved, the second diet might offer hope of more change. In this way an effort was made to have the second diet uninfluenced by results from the first diet.

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Table 6 here

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Table 6 shows that significantly more of the K-P diet trials were rated as improved than the control diet, using a Wilcoxon signed ranks test ($p < .01$).

Teacher and parent ratings. Table 7 presents the summary of hyperkinesis index scores for the two raters, together with

Table 6

Clinical Global Impressions

Control Diet \ Feingold Diet	0	+1	+2	+3	
0	4	4	3	0	11
+1	1	1	0	1	3
+2	0	0	1	0	1
+3	0	0	0	0	0
	5	5	4	1	15

Note: 0 = Unchanged or Worse
+1 = Minimal Improvement
+2 = Moderate Improvement
+3 = Marked Improvement

Wilcoxon Matched-Pairs Signed-Ranks Test:

$p = 0.01$ (one-tailed)

a summary of statistical analyses. Table 8 presents hyperkinesis index scores broken down by the order in which each treatment was received. The data indicate that the K-P diet is significantly more effective than the control diet for the teachers ($p < .005$), but not for the parents, while for both teachers and parents the K-P diet is significantly better than the baseline period, ($p < .05$), whereas the control diet does not differ from the baseline.

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Tables 7 and 8 here

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Figure 1 shows that both parents and teachers note approximately a 15% reduction in symptoms on the K-P diet, relative to a 3% or smaller reduction on the control diet. Figure 2 shows the same data broken down by order of treatment, where it may be seen that the bulk of the improvement on the K-P diet was noted when it <u>followed</u> the control diet (although the order effect was not quite significant ($p = .07$).

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Figures 1 and 2 here

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Figures 3 and 4 show the average hyperkinesis index scores for all patients across the 12 weeks of the study, for parents and teachers, respectively. Figures 5 and 6 present data from

PARENT AND TEACHER RATINGS OF HYPERKINETIC BEHAVIOR ACROSS TREATMENT

MEAN HYPERKINESIS INDEX SCORES		
	RATERS	
TREATMENT	PARENTS	TEACHERS
BASELINE	16.30	16.48
CONTROL DIET	15.72	17.18
K-P DIET	13.77	13.93

LEVEL OF SIGNIFICANCE BETWEEN TREATMENTS (ANALYSIS OF VARIANCE)

DIET COMPARISON	PARENTS	TEACHERS
K-P vs BASELINE *	<0.05	<0.05
CONTROL vs BASELINE	NS	NS
K-P vs CONTROL *	NS	<0.005

NS = NOT SIGNIFICANT AT THE 0.05 LEVEL

* ALL DIFFERENCES IN FAVOR OF K-P DIET

Table 7

Table 8

Rater	Pre-treatment	K-P Diet	Control Diet
Parent reports			
K-P 1st (N=9)	16.83	16.11	16.28
Control 1st (N=6)	15.50	10.25	14.87
Combined	16.30	13.77	15.72
Teacher reports			
K-P 1st (N=9)	16.22	15.53	18.22
Control 1st (N=6)	16.88	11.54	15.63
Combined	16.48	13.93	17.18

Figure 1

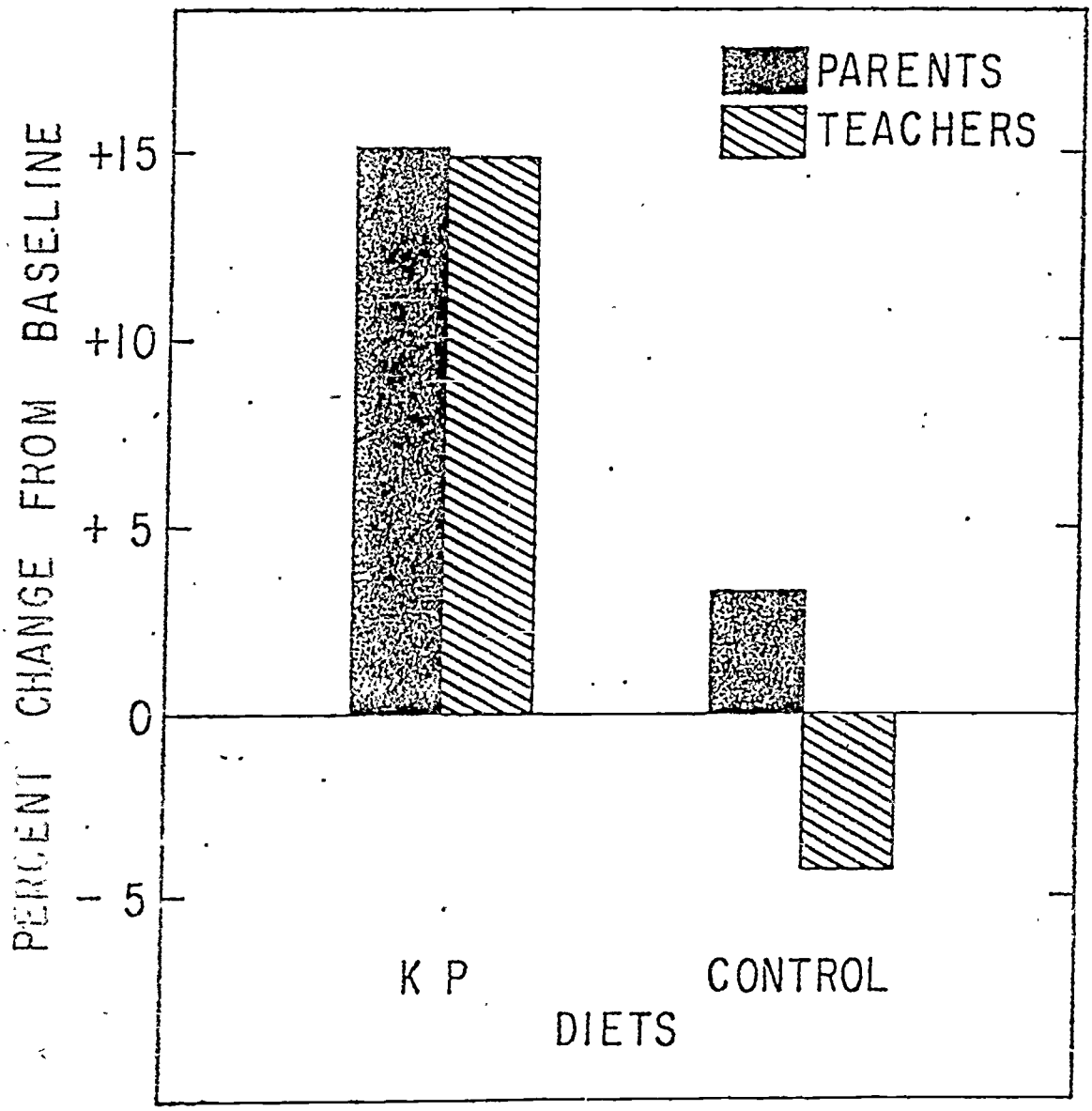
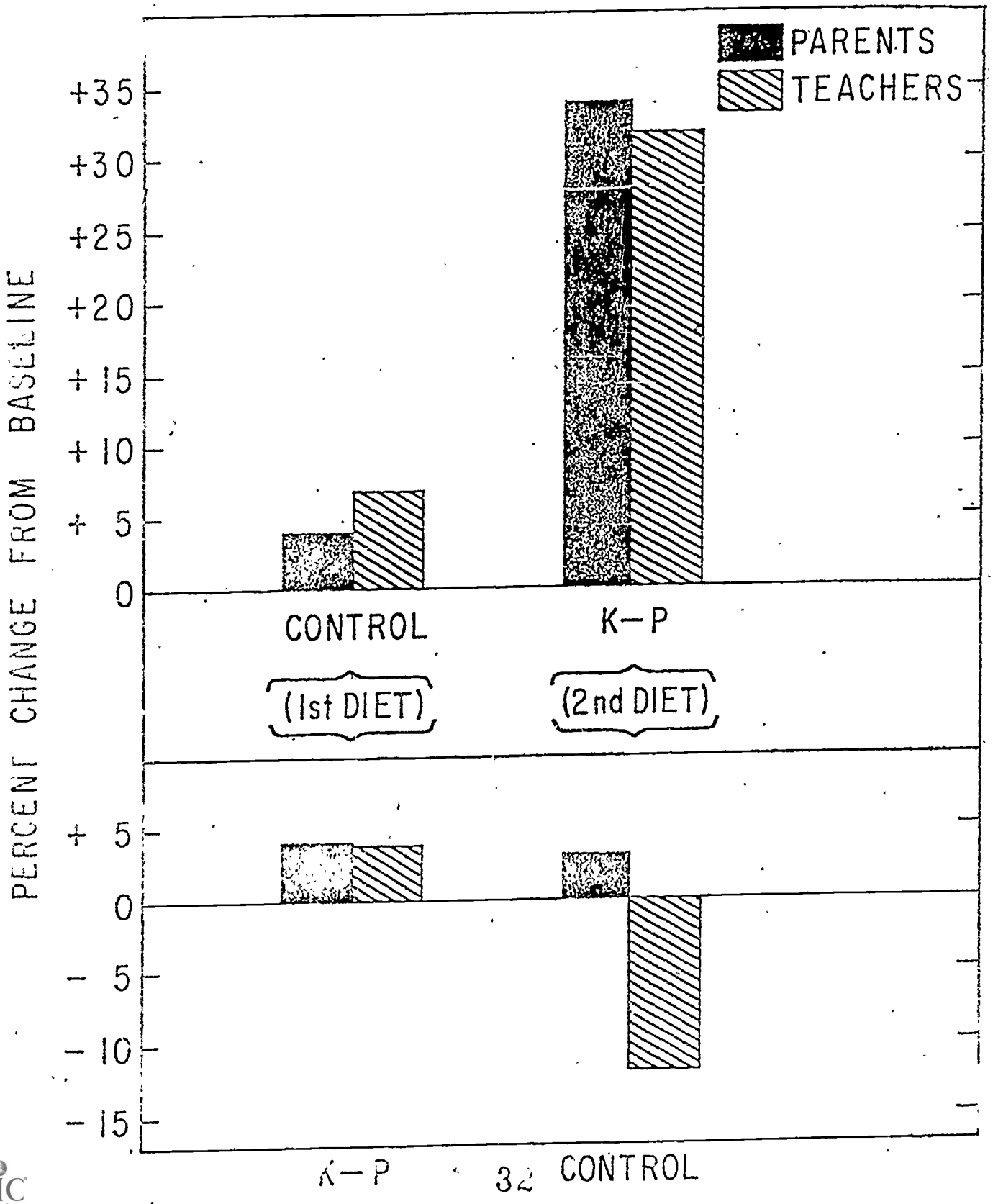

PARENTS
TEACHERS
PERCENT CHANGE FROM BASELINE
+15
+10
+ 5
0
- 5
K P
CONTROL
DIETS

Figure 2


PARENTS
TEACHERS
PERCENT CHANGE FROM BASELINE
+35
+30
+25
+20
+15
+10
+5
0
CONTROL
(1st DIET)
K–P
(2nd DIET)
+5
0
–5
–10
–15
K–P
CONTROL

two individual subjects which illustrate the remarkably close agreement between changes in behavior noted by parents and teachers at different points in the experiment. The congruence of these ratings provides assurance that the fluctuations are probably reflecting real behavioral changes and not idiosyncratic rating errors or unreliability of the scales.

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Figures 3 - 6 here
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Tables 9 and 10 show the analyses of variance for the teacher data for raw scores and baseline-corrected (difference) scores. In the latter procedure, the mean of the baseline scores was subtracted from the mean of the scores for each diet period to correct for initial starting level of symptoms prior to treatment. Similar analyses for the parent data are presented in Tables 11 and 12.

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Tables 9 - 12 here
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The raw scores for each of the periods of the study, for the different treatments and treatment orders for parents and teachers are presented in Appendix IV. Appendix V presents the informal comments of teachers as these were noted on the symptom questionnaires filled out at the end of the two diet periods.

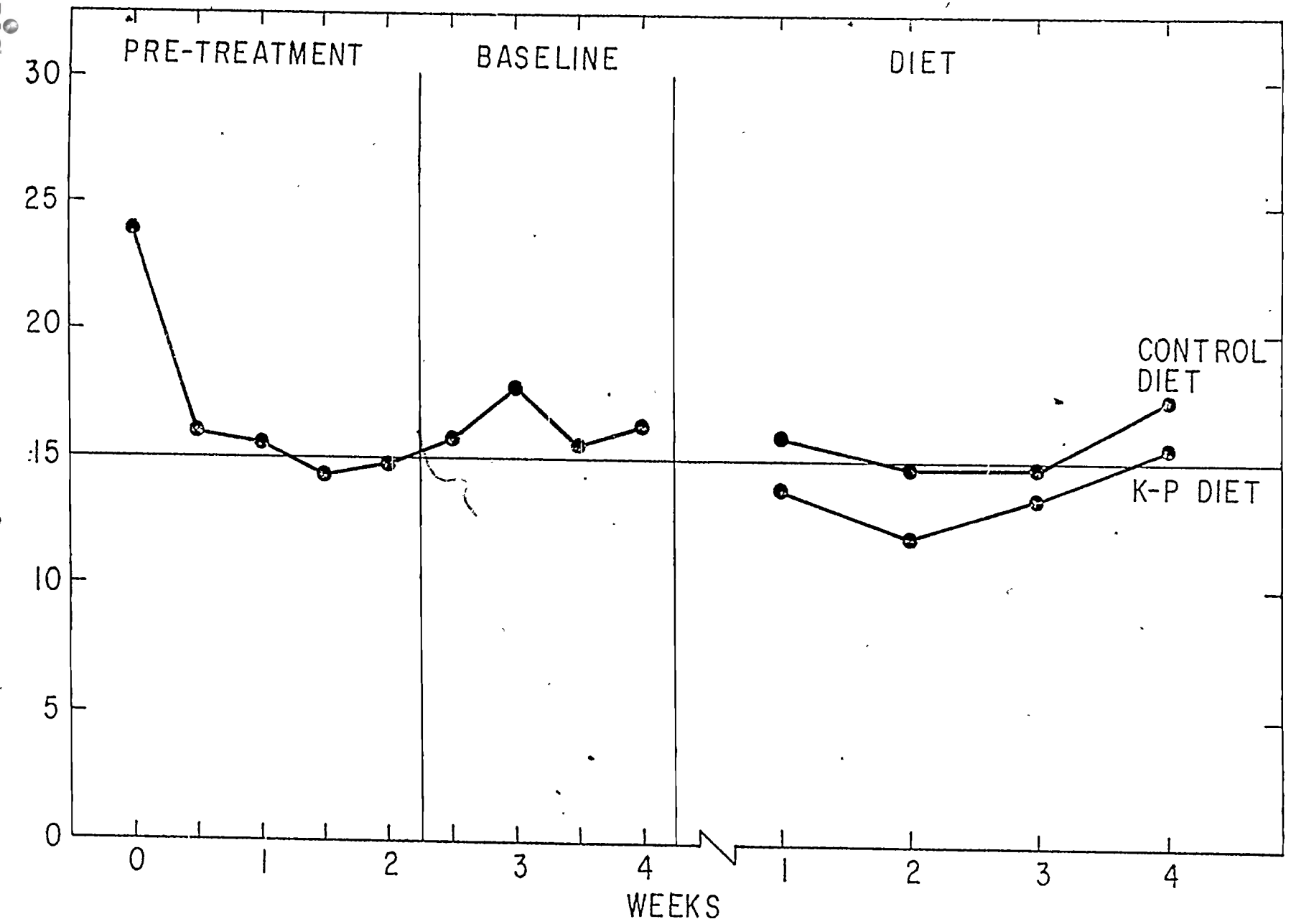
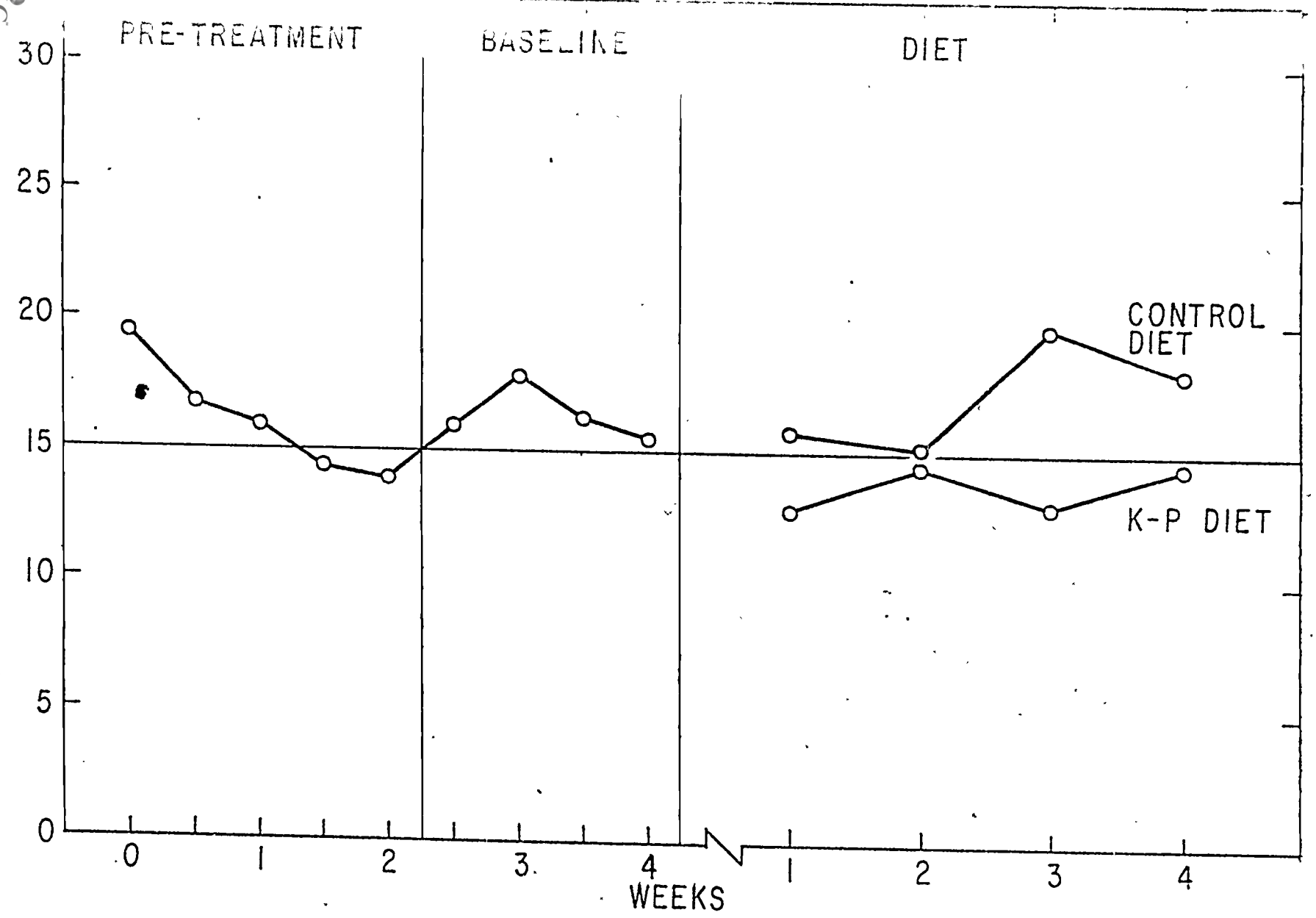


Figure 3

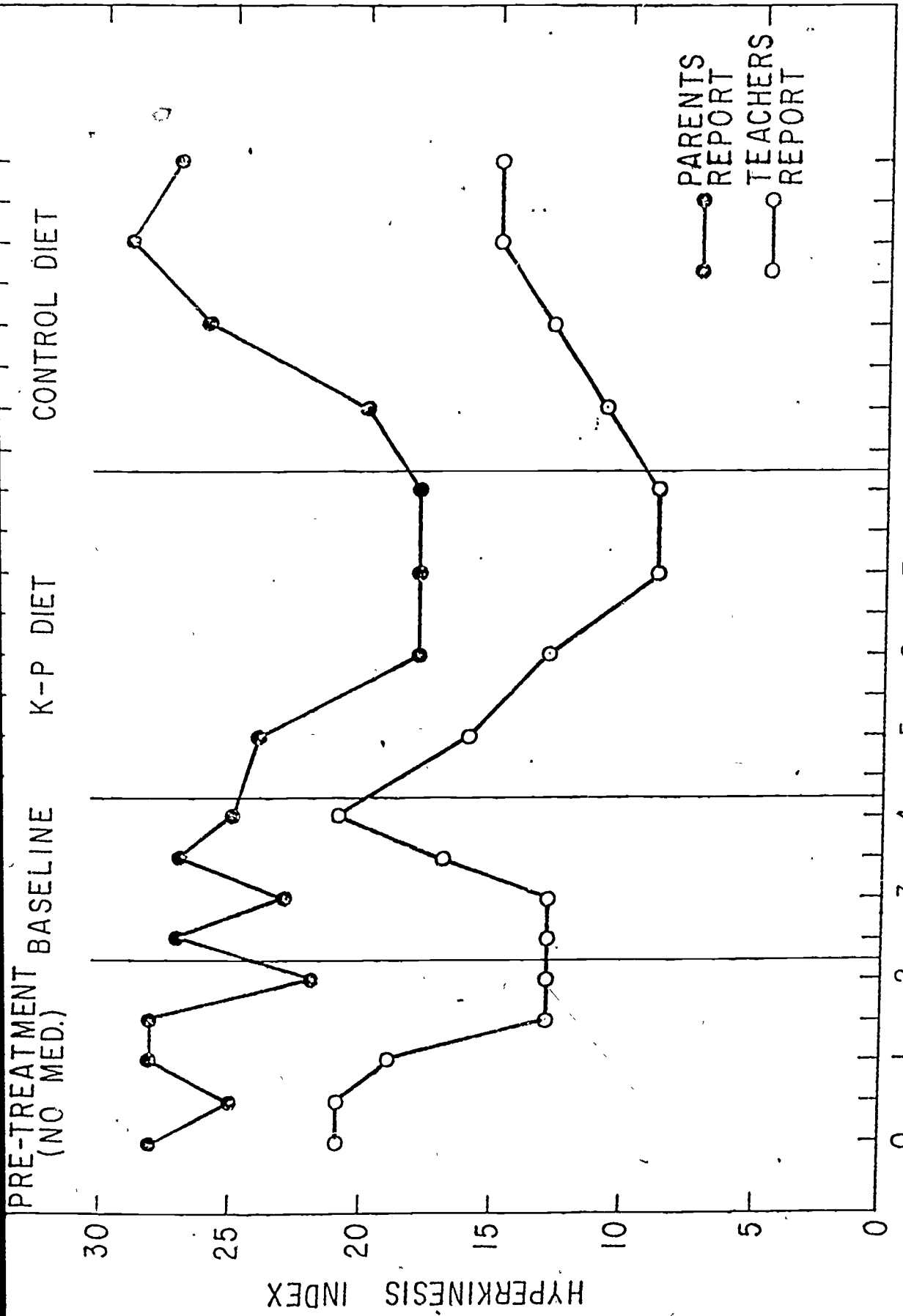
PARENT SYMPTOM REPORT FOR 15 PATIENTS AT PRE-TREATMENT, BASELINE (OFF MEDICATION) AND CONTROL OR KP DIET (EACH S HAD BOTH DIETS ASIGNED IN RANDOM ORDER)



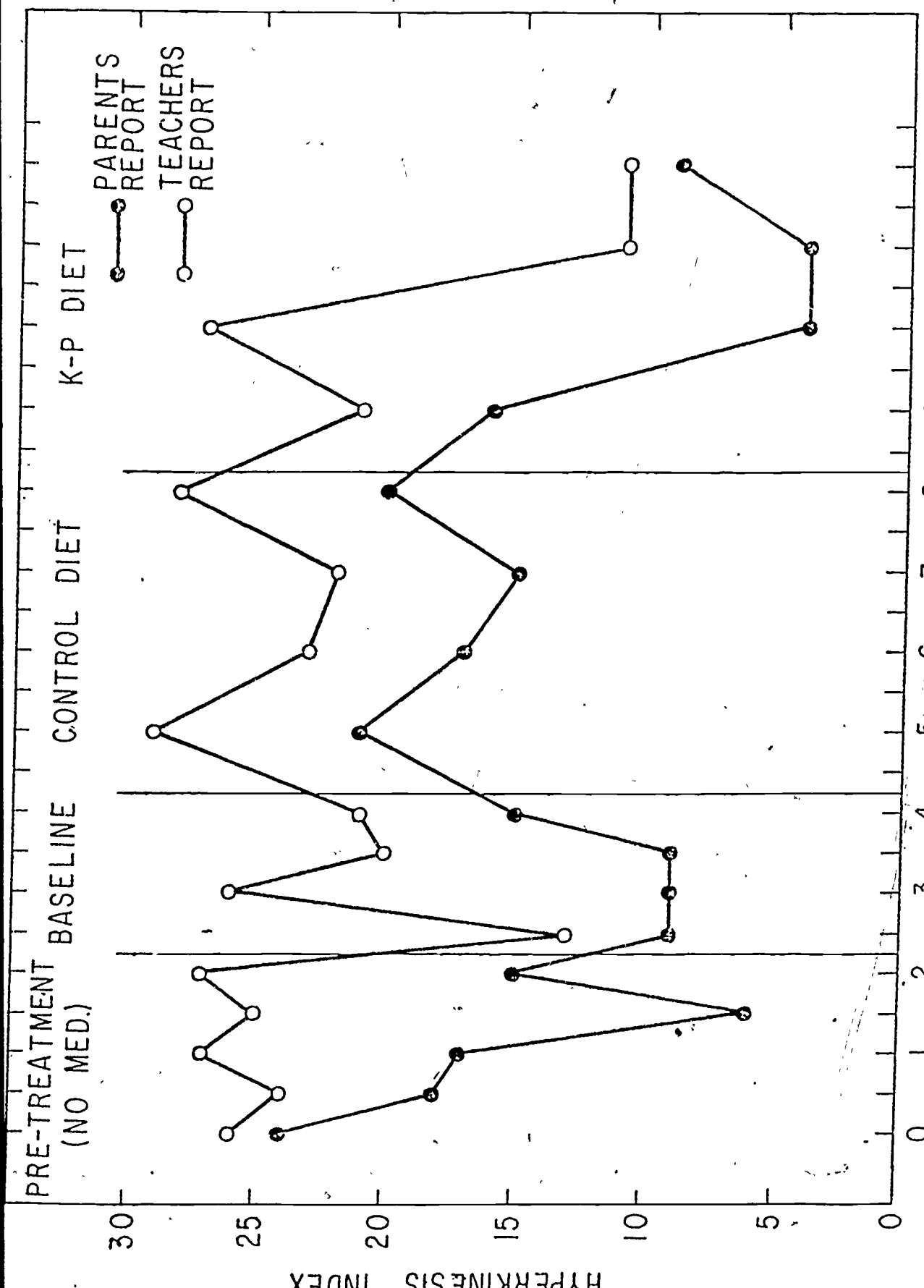
SCHOOL TEACHER SYMPTOM REPORT AT BASELINE AND ON EACH DIET

Figure 4

Figure 5



Graph showing individual case over 12 week treatment period. Lower score indicates improvement on hyperkinesis index



Graph showing individual case over 12 week treatment period

Table 9

ANALYSIS OF VARIANCE: BASELINE VS KP DIET TEACHERS

SOURCE OF VARIANCE	SUMS OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	P
BETW. SUBJ	1444.604	14			
GROUPS	20.000	1	20.000	0.183	0.6786
ERROR	1424.604	13	109.585		
WITHIN SUBJ	228.539	15			
BASELINE-KP	65.401	1	65.401	6.834	0.0204
GP. X BASELINE-KP	38.735	1	38.735	4.048	0.0629
ERROR	124.403	13	9.569		
TOTAL	1656.510	29			

ANALYSIS OF VARIANCE: KP DIET VS CONTROL DIET TEACHERS CORRECTED

SOURCE OF VARIANCE	SUMS OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	P
BETW. SUBJ	533,363	14			
GROUPS	112,022	1	112,022	3,456	0,0830
ERROR	421,340	13	32,411		
WITHIN SUBJ	166,001	15			
KP-CONTROL	82,689	1	82,689	13,464	0,0031
GP X KP-CONTROL	3,472	1	3,472	0,565	0,5286
ERROR	79,840	13	6,142		
TOTAL	695,894	29			

Table 11

ANALYSIS OF VARIANCE: BASELINE VS KP DIET PARENTS

SOURCE OF VARIANCE	SUMS OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	P
BETW. SUBJ	494,779	14			
GROUPS	93,168	1	93,168	3,016	0,1031
ERROR	401,611	13	30,893		
WITHIN SUBJ	276,880	15			
BASELINE-KP	64,201	1	64,201	4,748	0,0462
GP X BASELINE-KP	36,901	1	36,901	2,729	0,1195
ERROR	175,778	13	13,521		
TOTAL	755,592	29			

ANAYLSIS OF VARIANCE: KP DIET VS CONTROL DIET PARENTS CORRECTED

SOURCE OF VARIANCE	SUMS OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	P
BETW. SUBJ	522.242	14			
GROUPS	38.042	1	38.042	1.021	0.3322
ERROR	484.200	13	37.246		
WITHIN SUBJ	281.153	15			
KP-CONTROL	41.328	1	41.328	2.633	0.1257
GP X KP-CONTROL	35.778	1	35.778	2.279	0.1522
ERROR	204.047	13	15.696		
TOTAL	790.585	29			

Prior Dietary Habits. Inspection of the 24-hour recall, dietary questionnaire, and food frequency measure indicated profound individual differences in the 15 children participating in the study. Two children had dietary habits which could be considered poor in most respects and which would likely worsen on restrictive diets without close supervision: one child had a good appetite, but did not like and rarely ate fruits and vegetables -- this child's diet consisted mainly of cereal with milk, crackers and cheese, and bread; the second child was reported to have a poor appetite and be a picky eater who would not eat anything he did not like, particularly vegetables -- he would not eat anything if one of his food dislikes was among the foods served.

Six children had some dietary habits which, though presently not a problem, could develop in the future into various forms of malnutrition. Two of these six children were reported by the mother to be overweight, and four were "picky" eaters and usually avoided foods they did not like - notably fruits and vegetables.

The remaining seven children were reported to be good eaters with no apparent nutritional problems.

Nutrient Analyses of Diet Records.

Pretreatment-Baseline - Nutrient analysis from diet records kept during pretreatment-baseline seemed to indicate that the nutrient intake for the group was good to adequate. Table 13 reveals the percentage of the RDA of calories and 8 nutrients for the group's average period intake. During this period, all nutrients exceeded 66% of the RDA with protein, calcium, Vitamin A, riboflavin, and Vitamin C exceeding 100% of the RDA. However, large individual variation existed as can be seen from the magnitude of the standard deviations also presented in this table. Thus although there did no apparent nutrient deficiencies in the nutrients analyzed, the possibility that certain individuals may have undesirable intakes does exist (Note: the nature of the RDA is such that evaluation of individuals should not be made on analysis of intake alone [e.g., individual needs vary and may not compare clearly to a standard]; for this reason individual comparisons will not be discussed further).

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Table 13 here

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Adequacy of Intake on Trial Diets - Nutrient intake during K-2 and control diet periods are also presented in Table 13. As was the case with the pretreatment-baseline

Table 13

Percentage RDA and Standard Deviation of Group's Intake during Pretreatment-Baseline, Control and K-P Diets

	Pretreatment-Baseline		Control		K-P	
	%RDA	s.d.	%RDA	s.d.	%RDA	s.d.
Calories	80.4	24.8	82.1	29.1	76.6	30.4
Protein	204.7	62.3	206.3	64.2	194.3	58.5
Fat (gm)	(79.5)	(27.4)	(75.5)	(33.7)	(77.6)	(33.5)
CHO (gm)	(228.5)	(68.9)	(242.6)	(71.5)	(215.3)	(80.5)
Calcium	127.9	59.1	120.9	60.7	105.7	46.9
Iron	99.3	35.5	99.6	36.6	92.9	28.6
Vitamin A	128.5	137.7	123.7	85.7	107.3	122.8
Thiamin	95.8	43.5	91.9	47.6	83.4	36.4
Riboflavin	157.5	65.0	151.1	67.8	133.8	48.8
Niacin	84.2	38.6	78.3	35.7	94.3	48.2
Vitamin C	221.2	182.4	239.5	204.9	140.9	110.4

period, the nutritional intake during both trial diets was good to adequate, with all nutrients exceeding 66% of the RDA.

Treatment Differences - Statistical analyses comparing nutritional intake while following the K-P diet vs. pretreatment-baseline indicated lower calcium, riboflavin and Vitamin C on the K-P diet (similar trends were observed with all other nutrients with the exception of niacin). Comparisons between K-P and control diets revealed only two statistically significant differences: carbohydrate intake was less on the K-P diet, but niacin intake was greater. No differences were observed between the control diet and pretreatment-baseline.

Contribution of Breakfast - Reports have been made that the consumption of breakfast has a direct bearing on a person's activities during the morning. It is generally suggested that breakfast supply 1/3 of the days calories and nutrients. Table 14 shows the percent contribution made by selected nutrients to breakfast during the three periods. For this group, most nutrients are considerably less than 33%. Apparently breakfast was a small meal consisting of dairy food, grain food and a source of Vitamin C. The K-P diet severely reduced the Vitamin C sources taken at breakfast.

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Table 14 here

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Table 14

Percentage Contribution made by Breakfast to Group's Average Daily Intake during Pretreatment-Baseline Control and K-P Periods

	Pretreatment-Baseline	Control	K-P
Calories	17	16	15
Protein	15	14	14
Calcium	22	20	23
Iron	17	18	15
Vitamin A	14	15	11
Thiamin	22	26	20
Riboflavin	20	21	21
Niacin	11	15	10
Vitamin C	30	31	18

Dietary Degree of Difficulty and Dietary Compliance Measures. The dietary degree of difficulty questionnaires were converted to numerical scores (See Appendix) and averaged for each diet (possible score of 0 to 25, 25 being very difficult to follow). The mean dietary degree of difficulty score, as reported by parents, was 8.27 for the control diet and 9.53 for the K-P diet, indicating that the K-P diet perceived to be slightly more difficult to follow than the control diet.

The mean number of infractions reported per week for each of the diet periods was 1.50 for the control diet and 1.33 for the K-P diet, indicating close adherence to both diets. Viewed in conjunction with the dietary degree of difficulty questionnaire results, these data indicate a high degree of correspondence between diets on measures of overall dietary difficulty.

Discussion

The results of this study strongly suggest that a diet free of most natural salicylates, artificial flavors and artificial colors reduces the perceived hyperactivity of some children suffering from hyperkinetic impulse disorder. Teachers who observed the children over a 12-week period without knowledge

of the fact that there were two diets which were employed, rated the children as less hyperactive while the children were on the diet recommended by Feingold. The difference obtained between the ratings when the children were on the K-P diet and when they were on the control diet would have occurred by chance only 5 times in one thousand. Similarly, the teachers rated the children as significantly improved over the baseline period at the beginning of the study while on the K-P diet but not while on the control diet.

The results from ratings by parents are slightly different in that parents do not detect a difference in behavior between the K-P and control diets, although they note the effect as compared with the baseline period. The fact that the parents do not detect a difference between the two special diets could mean that subjective factors associated with a change in diet of any kind mask whatever therapeutic effect might be present in the K-P diet. This interpretation is supported by the fact that whereas the baseline means for parents and teachers are very similar (16.3 and 16.5, respectively), the control diet means are somewhat different (15.7 vs. 17.2).

Another possibility is that the children are in fact not noticeably different at home, but are observed to respond better

in a more structured situation where task expectations are clearly established, and where the teacher has a long baseline of comparison of the same children over many months. Similar findings of weak or marginal effects on behavior as rated by parents in contrast to clear effects noted by teachers has been found in drug studies with hyperkinetic children. It has been generally assumed that the demands on the child's attention and goal-oriented behavior are greater in the classroom, and therefore that any improvements in these areas will be more evident.

It was found in this study that the bulk of the positive changes noted by both parents and teachers occurred in the group that started with the control diet and then switched to the experimental diet. Such an effect could be due either to the fact that the more responsive children happened, by chance, to fall into the sequence involving the control diet first; or the results could be due to the fact that the observers have a clearer basis on which to judge improvement after the control diet has failed to produce any noticeable changes. Although this finding weakens the argument that the obtained differences are reflecting the K-P diet rather than some nonspecific factors, it should be noted that such findings are quite common in psychopharmacologic research involving crossover designs. For

example, in a double-blind crossover study involving dextroamphetamine and hyperkinetics, (Conners, Eisenberg and Barcai, 1967), the following results were obtained on the teacher questionnaire (using a somewhat different set of items):

	Pre-Treatment	Dexedrine	Placebo
Drug 1st (N=28)	29.1	20.6	26.00
Placebo 1st (N=24)	22.6	12.8	21.2
Combined	25.6	16.7	23.6

It is clear that the drug effect is much more pronounced in the group which received placebo first. Thus, even when objective measures substantiate improvement in behavioral functioning in the first period of evaluation, the teachers may be less aware of the improvement until they see the lack of improvement on another treatment.

Inspection of the individual ratings of children in the study shows that only four or five of the children were seen as improved by both parents and teachers. This fact is apparent from inspection of the clinical global impressions which took into account both parent and teacher effects. The findings suggest that there may be a small subgroup of hyperkinetic children who are showing the changes induced by the K-P diet. Further research will be required to determine if such children are physiologically different from non-improvers. Another possibility needing further evaluation is that somehow the

blind of the experiment, the bias of the parents, or communication between parent and teacher regarding the diets served to bias the results in the children rated as improving. It seems unlikely on the face of it that teachers would detect a significant effect when they are unaware that two diets are involved. On the other hand, if enthusiastic parents communicated to teachers when the diets were changed, the obtained results would be entirely spurious.

It is important to note that dietary compliance and degree of difficulty following the diets were comparable for the control and K-P diets. The K-P diet may have been slightly more difficult to follow, but there were also slightly fewer infractions, suggesting that the effects are unlikely to reflect any real difference in the difficulty of maintaining the child on the diets.

It would be hazardous at this point to draw too many conclusions from this experiment, given the small size of the sample and the lack of complete consistency in the results. Any thoughtful observer will understand that a major intervention into dietary habits of a family will produce behavioral effects, regardless of the specific diets, a phenomenon well understood in the management of such conditions as juvenile diabetes. The results would have been substantially clarified

if it had been possible to have objective measures of function uncontaminated by the psychological factors which are bound to operate in the family-school-child system. At this point the results point to the need for considerable further investigation.

One of the difficulties in testing the Feingold hypothesis is that the independent variable--the foods being varied in the experiment--is so nonspecific. We cannot say whether the natural salicylates, food colors, food flavors--or indeed unsuspected nutritional factors--might not be responsible for the results. For example, we found that, among other things, carbohydrate intake was significantly less on the K-P diet. In view of a commonly held argument that many hyperkinetics suffer from hypoglycemia, it is conceivable that such an unintended effect of the diet is producing the improvement seen by parents and teachers.

A matter of some concern is the extent to which the K-P diet reduced the nutrient intake of the children. As a group the children still had intakes above the recommended daily allowances, but dietary problems could arise for certain individuals over a prolonged period of time. Dietary counseling and/or careful monitoring by a physician should be considered until the long-term effects of the diet can be evaluated more

thoroughly. It was particularly notable that the children as a whole were poor in terms of the contribution of breakfast to the total recommended daily allowance of nutrient intake, and the fact that vitamin C is substantially reduced on the K-P diet makes the role of breakfast potentially more of a problem in this group of children.

The higher values of Niacin on the K-P diet has no ready explanation. Considering the number of comparisons examined statistically, this may be a chance finding of dubious significance from a practical point of view.

Summary and Recommendations

A double-blind crossover trial involving a control diet and a diet eliminating artificial flavors, colors and natural salicylates as recommended by Feingold was conducted on 15 hyperkinetic children. Teachers and parents observed the children for one month prior to treatment, using standardized rating scales. Both parents and teachers reported fewer hyperkinetic symptoms on the K-P diet as compared to the pre-treatment baseline ($p < .05$). The teachers noted a highly significant reduction of symptoms on the K-P diet as compared to the control diet ($p < .005$) but the parents did not. The control diet ratings did not differ from the baseline period ratings for either parents or teachers.

It is concluded that the K-P diet may reduce hyperkinetic symptoms, though this result is put forth with caution in view of several features inherent in the present study which need further evaluation, including objective measures of change, manipulation of the independent variable and reducing the independent variable to more specific components.

The K-P diet produced consistently poorer nutrient intake than the control diet or baseline period, especially for vitamin C. However, the effects were not nutritionally serious inasmuch as the children were still having nutrient intake above the recommended daily allowances. Long-term consequences of the diet would have to be followed with caution.

The following recommendations are made:

(1) Further studies employing objective measures, challenge testing of the putative harmful agents, and other controls are required before definitive recommendations are made on any large scale basis;

(2) Careful monitoring of nutritional status and dietary habits are recommended before children are placed on the K-P diet.

(3) Food intake at breakfast needs especial care in hyperkinetic children;

(4) Biochemical and clinical testing to determine the possible mechanisms involved should be undertaken, especially on clearly defined subjects who improve on the K-P diet, but further validation of the basic clinical effects is still required.

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THE NIE EXPERIMENT ON FOOD ADDITIVES AND HYPERACTIVITY

Background and Summary

In 1973 NIE researchers interested in finding alternatives to drug treatment for hyperactive elementary school youngsters became aware of the work of Dr. Ben Feingold of the Kaiser-Permanente Medical Center in San Francisco. Dr. Feingold's clinical experience with hyperactive children had led him to believe that food additives, especially artificial colors and flavors, were an important contributing factor in the disorder and that dramatically favorable results could be achieved with some hyperactive youngsters by putting them on a diet free of these additives.

After a visit with Dr. Feingold and conversations with other doctors who had tried the diet, it was concluded that there was enough plausibility to the hypothesis to warrant its being investigated systematically. In the spring of 1974, then, NIE requested proposals for a controlled experiment to test the hypothesis. A $60,000 contract for the study was awarded to Dr. Keith Conners, currently Professor of Psychiatry at the University of Pittsburgh and since the early 1960's a researcher eminent for his work in this field.

In this experiment Dr. Conners first determined the pre-diet levels of hyperactivity among 15 hyperactive children and then randomly assigned them to experimental and control groups. Those in the experimental group were placed on a diet free of artificial colors and flavors, those in the control group, on a diet containing the usual complement of food additives. The diets were comparable in terms of nutritional value and the degree of difficulty likely to be encountered in their implementation. The parents kept track of the food their children consumed and noted any dietary in-

fractions.

Each week parents and teachers filled out a standard hyperactivity rating scale for the children in the experimental and control groups, and after one month Dr. Conners interviewed the parents and reviewed parent and teacher ratings in order to make a global judgment about each child's improvement, or lack of it. Parents were not told which diet was being tested, and neither the teachers nor Conners (at the time of the interviews) were told which diet any particular child was on.

At the end of the month the children on the experimental diet were placed on the control diet and vice-versa. Once again parents, teachers and Dr. Conners rated them on the hyperactivity scales.

Based on the teachers' ratings, traditionally the most reliable of the three, there was a statistically significant difference between the experimental and control treatments. Both parents' and teachers' ratings during the experimental diet indicated a significant improvement over the pre-diet period, whereas the control diet showed no such improvement. Further, according to Dr. Conner's global assessments, the children on the experimental diet did significantly better than those on the control diet. However, a comparison between parents' ratings for the experimental and control treatments showed no significant difference.

Dr. Conners concludes that the Feingold diet "may reduce hyperkinetic symptoms," though he urges caution in interpretation of the results and emphasizes the need for further research on the subject before any definitive recommendations are made.