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Effects of Pemoline on Hyperactive Boys[1]

ROBERT M. KNIGHTS[2] AND CELIA A. VIETS

Department of Psychology, Carleton University

and

Department of Pediatrics, Ottawa Civic Hospital, Ottawa, Canada

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KNIGHTS, R. M. AND C. A. VIETS. *Effects of pemoline on hyperactive boys.* PHARMAC. BIOCHEM. BEHAV. 3(6) 1107–1114, 1975. – Thirty boys rated as hyperactive by their teachers and parents received pemoline or placebo in a double blind design. A variety of measures were taken during the nine week blind period. Behavior ratings were made on the Conners scale at 4 time intervals showing that a significant improvement in the drug group was observed by the teachers, but no significant change occurred in the ratings by the parents and physician. No toxic or grossly abnormal results were obtained from pediatric examinations which included blood, urine and stool samples as well as height, weight and cardiovascular data. Psychological tests, including the WISC, yielded no significant findings over the 9 weeks although initial differences existed between the drug and placebo groups. These measures were also administered during the 18 month long-term phase for 14 of the children which led to the conclusion that pemoline is an effective agent for improving the general behavior and school performance of some of the hyperactive boys.

Hyperkinesis Hyperactivity in children Pemoline Stimulant medication

THE effects of stimulant medication such as dextroamphetamine and methylphenidate in the treatment of childhood hyperkinesis has been investigated in a number of studies. Recently there has been interest in another mild CNS stimulant, pemoline (Cylert). This drug is reported to reduce symptomatology and to produce positive cognitive, achievement and perceptual changes with fewer side effects in children exhibiting symptoms of minimal brain dysfunction (5). The present study is concerned with a further evaluation of pemoline in hyperactive boys. This study was designed and included as part of the project described by Page, Bernstein, Janicki and Michelli (8). The present study includes a more detailed and extensive data analysis and discussion of the results.

METHOD

Subjects

The investigation included children referred to the authors in the 3 months prior to the study for hyperactivity, behavioral and/or learning problems.

A group of examinations made in the initial period served as a selection guide by which children were included in the study. The major criterion was that each child be diagnosed as hyperkinetic due to minimal brain dysfunction as indicated by the presence of one or more of the following: a significant history of pre- or perinatal complications, abnormal developmental milestones, onset of hyperkinetic behavior within the first few years of life, presence of soft neurological signs, abnormal EEG, or visual or auditory perceptual impairment. As well as a diagnosis of minimal brain dysfunction, the following criteria were met by each child selected: age between 6 and 12 years; at least one WISC IQ score (full scale, performance or verbal) above 90; laboratory tests within normal limits; visual acuity and pure tone audiogram screening; no psychoactive drugs, seizure medication or other analeptic therapy during the course of the study; and an absence of psychopathology in the family.

Behavioral questionnaires completed by the parent and teacher were also used for subject selection. These questionnaires were a modification of those used by Conners [1,2] although they contained the same 10 critical items reported as the abbreviated questionnaire in the pemoline study by Conners *et al.* [5]. The child was required to score a minimum of 18 points out of 30, or an average of 18 between the parent and teacher rating on the critical items in order to participate in the study. Critical problem items included such behavioral descriptions as impulsivity, restlessness, excitability, distractibility, low frustration tolerance and immaturity.

Global evaluations of each child were made by the physician, parents, teachers and the psychologist on a five-point rating scale from categories of "much worse" to "much better". Most children were rated as being worse in overall behavior than their peers in the initial evaluations. The most frequent diagnosis was that of hyperkinesis, while 2 children were thought to have primarily an emotional

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[2] Send reprint request to Robert Knights, Psychology Department, Carleton University, Ottawa, Ontario, K1S 5B6 Canada.

disturbance and 2 children to have a learning problem. The most common secondary diagnoses were emotional disturbance and specific learning problem.

The 30 boys that were selected to be subjects ranged in age from 6 years to 12 years 10 months with a mean age of 9 years 1 month. The mean WISC Full Scale IQ was 102.6, the scores ranging from 77 to 130 with a standard deviation of 10.7.

Seventy-five percent of the boys came from middle class socioeconomic backgrounds and the mean parental education level was 11.0 years for the mothers and 12.3 for the fathers.

As a group the children had a high incidence of abnormal characteristics in their development. Previous abortions, still births and deaths were reported by 26 percent of the mothers and other abnormal conditions of pregnancy by 16 percent. Short or long gestation periods and complications of delivery were experienced by 42 percent. During the postnatal period 11 percent of the neonates had jaundice, anoxia, seizures or abnormal sleep patterns. As youngsters 10 percent had seizures and 33 percent had a negative reaction to drugs or vaccine. The development of the children was unusual in that 23 percent were said to need less than normal sleep, 23 percent showed abnormal emotional response and 26 percent were slow in reaching development milestones. Seventeen percent of the boys were left-handed.

Procedure

The children were randomly assigned to the Drug or Placebo groups on the basis of consecutive precoded numbers. Pemoline was administered in 18.75 mg tablets that looked identical to the placebo tablets. The procedure was to begin administration with 2 tablets each morning and to increase the daily dosage by 1 tablet at weekly intervals until a notable improvement in behavior occurred, or until a maximum of 6 tablets was administered. Dosage was decreased if undesirable side effects were reported. The number of tablets taken by the 2 subject groups was similar for the first 3 weeks after which the Drug group received a mean of 3.9 per day and the Placebo 4.8 per day.

The measures taken before the child began medication and at the end of the 9 weeks are listed in Table 1. Physical measures included weight, blood pressure and pulse; the laboratory examination included hematology (hemoglobin, hematocrit, WBC, differential and platelet estimate), chemistry (BUN, uric acid, alkaline phosphatase, SGOT, SGPT, LDH and bilirubin) and urinalysis; and the neurological exam was a standardized examination procedure for children. Physical measures, as well as parental and teacher questionnaires and global ratings were taken at 3 week intervals, the neurological examination was administered in mid-study and telephone reports were made weekly.

The length of time each of the children continued in the study is presented graphically in Fig. 1. The medication code was broken for 7 children before the end of the 9 week blind period. It was found that 4 of these children had been receiving pemoline. Two of these 4 children had previously been under the care of one of the authors and had shown a good response to methylphenidate; the lack of a rapid response to pemoline (a common occurrence in relation to the short time for methylphenidate response) was a significant factor in breaking the code. The mother of the third child exhibited a high level of anxiety after the study began and an adequate evaluation of the effects of the drug did not seem possible. The fourth child was doing well on pemoline but was discontinued at the sixth week because of a slow heart rate. This was subsequently shown to have no relation to the drug. The 3 children taking the placebo had exhibited continued deterioration of school performance and increased aggressiveness. These 3 children had been taking methylphenidate prior to 2 weeks before the study. One was continued on methylphenidate at the request of the parents while the other two began the pemoline therapy and continued with it for 11 and 34 weeks.

When the code was broken at the end of the 9 weeks, 9 of the 11 children taking pemoline had shown substantial improvement on the basis of the behavioral ratings and were continued on the medication. Of the 15 children initially on placebo, 13 began pemoline therapy in the long-term phase of the study. After 70 weeks 14 children were still taking pemoline when the long-term follow up study was terminated. Physical, neurological and laboratory

TABLE 1

MEASURES USED BEFORE AND DURING MEDICATION

Medical and Physical	
History	
Physical examination	
Laboratory – blood, urine, stool	
Standardized neurological exam	
Ratings	
Parent	48 item behavioral rating global rating
Teacher	24 item behavioral rating global rating
Physician	global rating
Psychologist	global rating
Psychological Tests	
Weschler Intelligence Scale for Children (WISC)	
Wide Range Achievement Tests (WRAT)	
Porteus Maze	
ITPA Visual Sequential Memory Subtest	
Wepman Auditory Perception	
Lincoln Oseretzky Motor Performance	
Bender Gestalt	

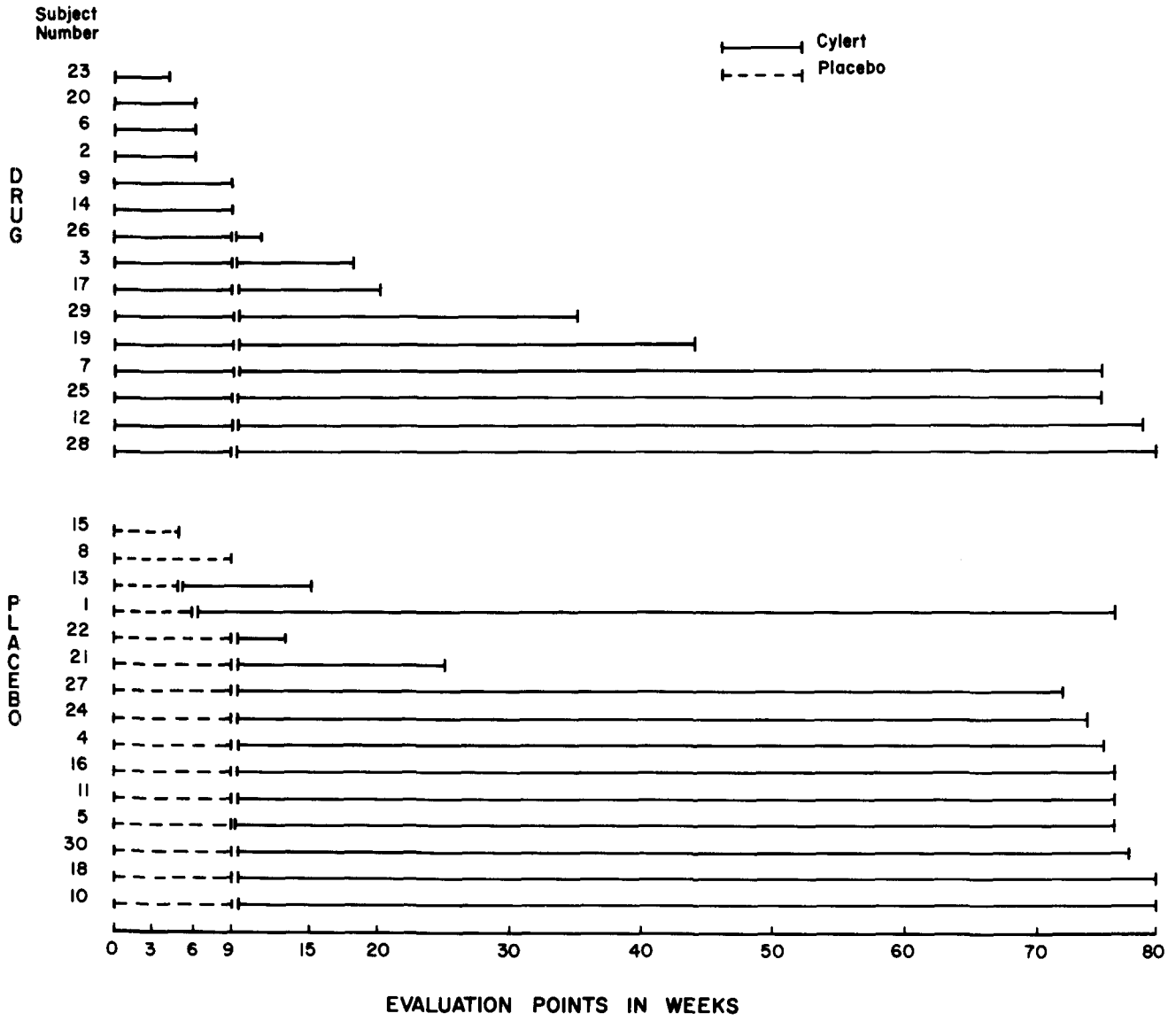

FIG. 1. Length of drug and placebo administration for each child.

examinations, as well as parent and teacher questionnaires were completed at 5 intervals throughout the long-term and the psychological test battery was readministered before the medication was terminated at 70 weeks.

RESULTS

At the end of the 9 week period the children were tested and the drug code broken. The statistical analyses of the results included data from 11 children in the Drug group and 12 in the Placebo group. Long-term analyses included data from the 14 children who were still taking pemoline at the end of 70 weeks.

Initial Group Differences

Table 2 presents the mean results of some of the measurements taken in the initial testing session. In spite of the random assignment procedure for placing subjects into the Drug and Placebo groups it is apparent from these scores that some significant differences existed initially between these two groups. These differences may have acted as confounding variables especially since the Drug group showed fewer instances of abnormal development and a higher mean score on the IQ measure.

Physical and Laboratory Measures

The physical measures recorded during the 9 week period and in the long-term study are presented in Table 3. In the initial 9 week phase the children in the Placebo group showed a normal mean weight increase due to growth, whereas, the mean weight for the children in the Drug group did not change significantly over the 9 weeks. In the long-term study the Drug group (n = 4) again showed a slight decrease in weight and maintained this level until an increase occurred after Week 20. The group originally on

TABLE 2

CHARACTERISTICS OF CHILDREN RANDOMLY ASSIGNED TO DRUG AND PLACEBO GROUPS

	Drug	Placebo	
Instances of abnormal developmental history	68	121	$p<0.01$
Mean age of hyperactivity onset	3.1	2.9	NS
Prior medication	9	13	NS
Mean activity rating – global	1.8	2.3	NS
Mild or moderate neurological abnormality	11	14	NS
WISC Full Scale IQ	106.5	98.7	$p<0.05$

TABLE 3

PHYSICAL MEASURES: WEIGHT, PULSE AND BLOOD PRESSURE FOR DRUG AND PLACEBO GROUPS OVER THE NINE WEEK PERIOD AND IN THE LONG-TERM PHASE

		Nine Week Phase (n = 23)				Long-Term Phase (n = 14)				
		Week 0	Week 3	Week 6	Week 9	Week 0	Week 9	Week 20	Week 45	Week 70
Weight	Drug	29.8	29.3	29.5	29.6	27.8	27.3	27.2	28.1	31.8
	Placebo	27.7	28.9	29.3	29.8	28.1	30.3	29.1	30.6	33.1
Pulse	Drug	77.7	76.9	80.9	74.4	71.0	76.0	80.0	83.0	89.0
	Placebo	77.6	85.3	83.3	80.7	77.7	80.4	78.0	87.0	79.0
Blood Pressure										
Systolic	Drug	102.3	104.5	108.1	105.9	100.0	100.0	102.5	100.0	97.5
	Placebo	105.4	107.5	106.7	105.8	104.0	105.5	107.5	103.0	103.5
Diastolic	Drug	70.8	70.5	71.4	71.4	71.3	70.0	68.8	67.5	67.5
	Placebo	74.2	73.3	74.2	72.1	73.5	71.5	71.5	69.0	72.5

Placebo (n= 10) showed a normal growth increase in weight until they began taking the pemoline after Week 9. Weight then dropped slightly and the Placebo group did not surpass their nine week weight until Week 45. Analysis of variance of both the initial and the long-term data showed an overall significant increase in weight as would be expected for normal growth (initial phase, $F(3,63) = 8.88$, $p<0.05$; long-term phase, $F(9,108) = 16.67$, $p<0.001$).

Similar analyses of variance of the data for pulse revealed no significant effects in the initial 9 week period, however, there was a statistically significant increase in the long-term phase from 79.0 to 83.6 beats per minute, $F(9,108) = 2.29$, $p<0.05$). No significant effects were observed in the blood pressure measures, the neurological examination or the laboratory measures. Although occasionally various laboratory measures exceeded the normal limits for some children, there were no consistent findings that could be related to the drug.

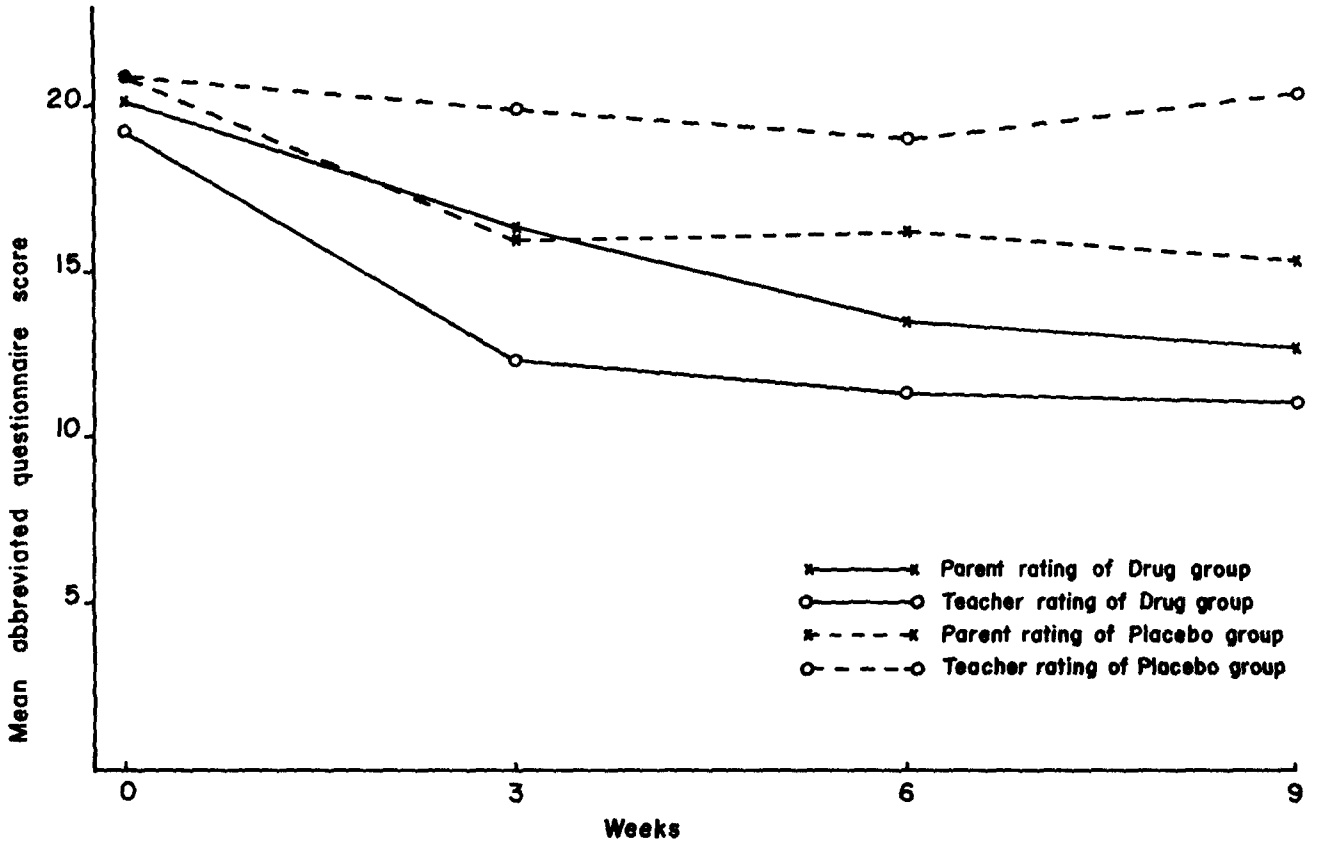

FIG. 2. Parent and teacher ratings of the drug and placebo groups.

Parent and Teacher Questionnaires

Parents and teachers completed the behavioral rating scales at 4 intervals in the 9 week study and 5 intervals in the long-term phase. In the initial 9 weeks, no differences occurred between the Drug and Placebo group of boys in the parent rating scores. But there was a significant decrease in scores for all children indicating that parents of both the Drug group and the Placebo group felt there was an improvement in behavior over the 9 weeks, $F(3,63) = 10.32$, $p<0.001$.

A different pattern was observed with the teacher ratings throughout the first 9 weeks. Like the parent ratings, teachers felt there was significant improvement in the behavior of both groups of boys, $F(3,63) = 3.97$, $p<0.05$. But in contrast to the results of the parent ratings, teachers observed a significant difference between the Drug and Placebo groups, $F(1,21) = 4.75$, $p<0.05$. The drug effect was also significant, $F(3,63) = 2.60$, $p<0.05$, indicating that the teachers recorded a greater improvement in behavior of the children in the Drug group than those in the Placebo group. The pattern of behavior improvement rated by the teachers is of interest. The Placebo group of boys improved only slightly (although significantly) over the 9 weeks, whereas ratings for the boys in the Drug group showed a large improvement in the first 3 weeks and then remained relatively constant throughout the rest of the initial study.

Analysis of variance was also completed for the abbreviated questionnaire scores from both the parent and teacher ratings. This abbreviated version includes the ten critical items which served as part of the criterion for admission into the study. These items deal with the problem behaviors most related to hyperactivity. Mean scores for the Drug and Placebo groups appear in Fig. 2. (It should be noted that a decrease in score denotes improvement in the child's behavior as judged by parents and teachers) Analysis confirmed that there was an overall significant decrease in scores for all children, $F(3,63) = 17.28$, $p<0.001$; but the boys in the Drug group showed a pattern of greater improvement in behavior than those in the Placebo group, indicating a significant effect of the pemoline, $F(3,63) = 2.95$, $p<0.05$. The pattern of improvement in the hyperactive problem behaviors illustrated in Fig. 2, demonstrates that both parents and teachers noted initial improvement in these target behaviors for the boys in the Drug group. Improvement was great initially and tended to level off somewhere between 3 and 6 weeks into the drug therapy. According to teacher ratings of the Placebo group, hyperactive problem behaviours improved slightly until Week 6 and then regressed to their initial levels. But parents tended to see improvement in these behaviors for the Placebo boys throughout the 9 weeks.

Parents and teachers continued to answer the same questionnaires for all the boys taking pemoline in the long-term study. Both parents and teachers noted significant overall improvement of general behavior, $F(8,88) = 7.89$, $p<0.01$; $F(8,88) = 4.33$, $p<0.01$; respectively, as well as continued progress in the hyperactive problem behaviors measured by the 10 critical items, $F(8,96) = 11.9$, $p<0.01$.

At the termination of the study, about two weeks after medication was discontinued, the parents completed the same questionnaire to determine if there was an immediate change in behavior. Parent ratings continued to decrease indicating that at least two weeks after termination of the pemoline, behavior was rated as continuing to improve, $F(9,90) = 11.7, p<0.01$.

The teacher questionnaire also included a rating of academic achievement as well as the behavioral items. The school subjects Reading, Writing, Arithmetic and Spelling were rated by the teacher on a scale from 1 indicating very good, to 5, failing. There was a trend for all scores to improve over the initial 9 weeks but this improvement was significant only for Reading, $F(1,15) = 4.35, p<0.05$. Also, although the Drug group of youngsters consistently achieved better scores at the end of Week 9 than the Placebo boys in all 4 school subjects, this difference showed a significant effect of the drug only for Writing Achievement, $F(1,15) = 5.4, p<0.05$.

Global Ratings

Global ratings of each child were made at intervals in the initial 9 weeks and in the long-term phase by parents, teachers, the pediatrician and the psychologist. These ratings were based on a 1-to-5 scale from "much worse", through "about the same", to "much better". In the initial 9 weeks analysis of variance demonstrated that all raters noted a significant improvement for both subject groups, $F(3,63) = 43.35, p<0.001$. A significant rater effect was also noted in that parents tended to give the highest ratings and teachers gave the lowest scores; psychologist and pediatrician ratings were generally at levels between those of the parents and teachers, $F(2,42) = 12.3, p<0.001$. It was also evident that for each of the raters the boys in the Drug group were rated with higher scores than the Placebo group, but this difference did not reach statistical significance ($p = 0.08$). A comparable pattern of results was evident in the long-term ratings. The overall improvement was significant, $F(2,20) = 62.6, p<0.001$, as was the difference between the four raters, $F(3,30) = 12.8, p<0.01$.

Psychological Measures

The battery of standardized psychological tests was administered in the beginning of the study, during the ninth week and at Week 70 of the long-term phase. A total of 28 analyses of variance were performed on total scores for each test and on the subtests of the WISC and the WRAT. Results of the analyses of the initial 9 weeks showed that in 9 cases there was a significant ($p<.05$) difference in scores between the initial and final testing. Mean scores for both groups of children increased on the Full Scale IQ, Information, Object Assembly and Block Design of the WISC and also on WRAT Spelling scores, the ITPA Visual Association, Wepman Auditory Discrimination x Factor, Lincoln Oseretzky Factor 11 and the Bender Gestalt.

There was a significant difference on the initial scores between the Drug and Placebo groups on 5 scores; the Drug group achieved higher scores on Verbal IQ, Information, Arithmetic and Digit Span of the WISC, while the boys in the Placebo group achieved higher mean scores on the Lincoln Oseretzky Factor 11. Also the Drug group showed greater WISC Full Scale IQ scores than the Placebo group and this difference was approaching significance at the $p<0.05$ level.

The absence of a significant interaction effect from the analyses of these measures indicated that the Drug had no differential effect on any of the psychological measures.

For the children involved in the long-term study, there were no changes in WISC IQ levels over the 70 weeks; final IQ scores for Drug and Placebo groups respectively are 107 and 102 for Full Scale, 105 and 95 for Verbal and 107 and 110 for Performance. Little change was observed in the WISC subtests although there were some overall increases in scores on the Porteus Mazes. Also, as would be expected for normal development over a period of 70 weeks, there was an overall increase in achievement as measured by the Wide Range Achievement Test.

Dosage and Side Effects

Dosage levels were prescribed by the physician and adjusted according to the child's behavior. At the end of the 9 week period the boys in the Drug group were taking doses ranging from 37.5 mg to 112.5 mg of pemoline per day. The mean dosage level was 69.9 mg. Dosage levels for the 14 boys who completed the long-term study yielded a mean of 44.5 mg per day. Eight children were taking 37.5 mg, 3 were taking 56.25 mg, 2 were taking 75 mg and 1 was taking only 18.75 mg. The average mg/kg drug dose was 1.61 and the range was from 0.65 to 2.41 mg/kg.

Side effects were determined from problems noted by the parents, and to a lesser extent, the teachers of the youngsters. These problems included appetite loss, stomachache or headache, drowsiness or daydreaming behavior, excitable or aggressive behavior and sleeping problems. In the initial 9 weeks both the Drug and Placebo groups of children exhibited a similar incidence of side effects. The only side effect that may be related to the Drug is the sleeping, as 6 of the children in the Drug group, but only 2 of those in the Placebo group had problems with sleeping.

Side effects in the long term phase occurred less frequently than in the initial 9 week period. There was one problem with loss of appetite, one with drowsiness and daydreaming, one with aggressive and more excitable behavior and two cases of sleeping problems. No child was discontinued because of side effects in the long-term study.

DISCUSSION

The results of this study are comparable to those reported by Conners *et al.* [5]. These observations indicate that pemoline was effective in improving the behavior of hyperactive boys, a conclusion based primarily on the ratings made by the parents and teachers. The ratings showing the most distinctive drug effects were concerned with hyperactive problem behaviors related to distractibility, impulsivity, and attention span. Although the psychological tests results were not significant in the present study, both Conners *et al.* [5] and the larger study reported by Page *et al.* [8] (of which this research is a part) have found significant pemoline effects on some psychological assessments as well as through the parent and teacher ratings.

Figure 2 illustrates the effects of pemoline on behavior as indicated by the pattern of parent and teacher ratings on the abbreviated questionnaire (the ten critical hyperactivity items) in the initial nine week experimental period. A comparison of these ratings with those of Conners *et al.* [5] shows great similarity. When graphed, the mean rating curves show almost indentical beginning and ending points, as well as a comparable rate of improvement. The rating

curve demonstrates that the maximum effectiveness of the drug did not occur until sometime after the third week of administration. This is in contrast to methylphenidate in which behavioral effects occur within hours.

In addition, Fig. 2 demonstates that the teachers noted the drug effects sooner than parents and their ratings showed a greater difference between the Drug and Placebo groups of children than did the parents.

It is also interesting to note that for the original Placebo group the pattern of parent and teacher ratings at the beginning of the long-term phase shows a parellel initial improvement and subsequent levelling off to that of the original Drug group. Both groups showed a slight improvement in behavior, according to the ratings, near the end of the long-term phase.

A substantial Placebo effect was illustrated in the initial period as parents, and to a much lesser extent teachers, rated improvement in the behavior of the boys who were taking the Placebo tablets. The fact that teacher ratings showed a greater differentiation between the Drug and Placebo groups of boys than the parents, may be due to the greater motivation by the parents to have their children show a change in behavior. Parents understood that some of the boys in the study would draw the Placebo, whereas teachers were informed only that the child was participating in a drug study and would be receiving medication for his attentional problems. The teacher's ratings which demonstrated only a slight Placebo effect, also showed greater differentiation between the Drug and Placebo groups. These findings, plus the fact that they reported larger Drug effects before they were noticed by the parents, suggests that the teacher questionnaire is a more sensitive measuring tool of drug effects on behavior.

The results of the global ratings made by teacher, parent, physician and psychologist were generally similar and consistent with the questionnaire ratings. The maximum ratings, however, did not appear until the sixth week. At the end of the nine week period the teachers' global ratings classified 36 percent as better or much better for the Drug group and 17 percent in the same category for the Placebo group. The parents were more positive in their reporting and placed 73 percent of the Drug group and 42 percent of the Placebo group in the better or much better category. The physician reported improvement at a level similar to that of the teachers, and the psychologist at comparable levels to the parents. These global ratings show a high agreement with the parent and clinician ratings in the other pemoline studies [5,8]. But both of these studies report higher percentages of improvement for children taking pemoline as rated by the teachers; Conners *et al.* [5] reported that 63 percent of the pemoline group and 30 percent of the Placebo group were rated as improved by their teachers, while in the Page *et al.* [8] study 68 percent of the Drug group and 32 percent of the Placebo group improved in the eyes of their teachers. It is apparent that the teacher ratings in the present study are not only a sensitive measure of drug effects, but in this case are also quite conservative.

Although the scores on the psychological tests did not show significant drug related effects over the initial 9 week period, there was a trend for the Drug group to obtain better scores than the Placebo group. In this study the random assignment of subjects to each of the groups may have influenced the results. Table 2 shows that the initial mean Full Scale IQ of the Placebo group was nearly 8 points lower than the Drug group. It may be that it was easier for the Placebo group to improve their scores, because they started lower. The data show that the Placebo group increased by a mean of 4.1 IQ points while the Drug group increased 2.4 IQ points. This confounding factor may have hidden any possible drug effects. The risk of using random placement in drug studies with small samples has been discussed in the literature [4]. It is suggested that data obtained for subject selection be reviewed prior to group assignment and that a matching procedure be used rather than blind and random placement of subjects into groups.

Another general point related to the finding of group differences on psychological tests in drug studies with children is the ratio of the number of test variables that are significant compared to the number of variables on which significance tests were conducted [6]. In this study 27 variables were examined and only one showed a group over time interaction in the long-term study, although the children improved on many scores. Conners *et al.* [5] obtained a significant drug effect of pemoline verses placebo on five of 35 psychological test variables and Page *et al.* [8] found significant differences on five of 27 psychological test variables.

Looking at data as a percentage of significance obtained over the many analyses conducted is a more conservative interpretation of the results. Rather than assuming that pemoline affects certain of the psychological subtests, it is suggested that pemoline may affect overall behavior differentially in each child.

In view of the recent interest in the effects of stimulants on children's growth a detailed review of height and weight data was conducted. Examination of the children's height measurements showed no significant differences between groups over the 9 week period. Initially the children were slightly below normal in height at 131.3 cm and gained only 3.6 cm in a year in contrast to normative data [7] which indicate an increase of 4.8 cm between 9 and 10 years of age. Although this difference is substantial it was not statistically significant.

The analysis of weight data produced similar trends although the differences between the Drug and Placebo group were statistically significant. It is of interest to note that in the first 9 week period the group taking Cylert lost 0.2 kg while the group on Placebo gained 2.1 kg. The data for the long-term study also showed that when the children on Placebo began to take pemoline they lost 0.9 kg within the first 5 weeks. An overview of the data indicate the children weighed slightly less than average at the beginning of the study and gained slightly less than the expected 4.0 kg in the 70 week period.

A similar pattern of initial weight loss and subsequent slow gain was noted in the study by Page *et al.* [8] but no effect of the pemoline on weight was observed in the study by Conners *et al.* [5]. Conners's study however did not extend past the initial 8 week period and therefore any effect on long-term weight gain would not be apparent.

These observations suggest that at least these samples of hyperactive children are initially smaller in height and weight than the norm. Pemoline was associated with an initial weight loss, but these children were smaller to begin with and it is difficult to determine if the subsequent slow rate of weight gain is a drug related effect or related to their generally small physical size.

A related hypothesis formed during the study was that the smaller children reacted more positively to pemoline

than the larger boys. A review of these data showed no significant differences in comparison of the good versus poor responders although the trend was present. The good responders averaged 131.7 cm in height and 28.7 kg in weight while the poor responders averaged 134.0 cm in height and 30.3 kg in weight.

An attempt was made to determine other characteristics or variables which were associated with either a positive response or an absence of response to the medication. Similarly the children on Placebo who responded were also examined carefully for some type of predictive characteristic. Neither of these attempts was successful and individual prediction of drug response remains to be an unknown in the area of stimulant medication for children [3,9].

During the study there were very few side effects due to pemoline and this observation has also been noted elsewhere [5]. Some of the children who took up to 112.5 mg did have trouble eating and sleeping but when the medication was reduced these side effects disappeared. In terms of statistical comparisons there were no significant side effects. Clinically the side effects were difficult to evaluate. One child seemed confused and dazed while on a large amount of pemoline but there was also one child in the Placebo group who exhibited the same symptoms and was terminated from the study. Pemoline's relative lack of side effects would suggest its usefulness as a substitute for other stimulants.

The clinical impression of the personnel involved in this study, in agreement with parent and teacher behavioral ratings, was that the onset of the effectiveness of the pemoline was slower than other stimulants used with children. It took 3 to 4 weeks before maximum effect was noted. There was the odd instance in the long-term study of children forgetting to take their medication and it was often immediately noticed by the teacher. If one considers a box score in terms of the number of children who stayed on the drug for the 70 weeks, approximately 50 percent benefited enough to be maintained in the study by the authors and the parents. Within this group of 14 it is estimated that about 10, on the basis of clinical observation, showed obvious improvements in problem behaviors related to hyperactivity in both the home and the classroom environments. Pemoline has the advantage of being effective when given in a single daily dose and could be a useful drug in the management of children who are hyperactive or have specific learning disabilities.

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