The Effects of Methylphenidate on the Repeated Acquisition Performance of Children with Attention Deficit Disorder

Christopher P. Giuliano
Western Michigan University

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THE EFFECTS OF METHYLPHENIDATE ON THE REPEATED ACQUISITION PERFORMANCE OF CHILDREN WITH ATTENTION DEFICIT DISORDER

by

Christopher P. Giuliano

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This work is dedicated to my wife, Ann, who sacrificed more than any husband had a right to ask.

This work could not have been completed without the talents, time, and effort of a number of people. I am especially grateful to Bill Redmon and Jack Michael for their time, effort, and assistance in the completion of this dissertation. They have served as exemplary models of scholarly behavior.

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Christopher P. Giuliano
THE EFFECTS OF METHYLPHENIDATE ON THE REPEATED ACQUISITION PERFORMANCE OF CHILDREN WITH ATTENTION DEFICIT DISORDER

Christopher P. Giuliano, Ph. D.
Western Michigan University, 1991

The effects of methylphenidate on the repeated acquisition performance of three children between the ages of 9 and 13 were examined. The repeated acquisition task was programmed on a micro computer and daily doses of 0.6 mg/kg and 1.0 mg/kg of methylphenidate were compared with an active placebo (caffeine). There was no discernible effect for two of the subjects. One subject showed only a very slight facilitative effect at the 1.0 mg/kg dose, using trials-to-criterion as the dependent measure. Methylphenidate had no effect on errors or rate of responding for any of the subjects. Teacher ratings of behavior indicated improvement during both drug conditions for one subject, and no improvement for two of the subjects during either of the drug conditions. Parent ratings of behavior did not correspond to drug manipulations for any of the subjects.
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Attention Deficit Disorder and Its Treatment

Attention Deficit Disorder (ADD) is one of the most commonly diagnosed childhood disorders in the United States. It is characterized by "chronic hyperactivity, short attention span, marked distractibility, emotional lability, and impulsivity, all of which are likely to be characterized by cross-situational and cross-temporal variability" (Ross & Ross, 1982, pp. 1-2). Other characteristics include failure to follow through with requests of parents, sloppy school work, problems interacting within peer groups, and generally disorganized and non-goal-directed activity (American Psychiatric Association, 1980). It has been reported that between 2% and 20% of school-aged children suffer from this disorder (Barkley, 1981), and estimated that "over 1 million U.S. children will be receiving stimulant medication by the early 1990's" (Safer & Krager, 1988, p. 2258).

Barkley (1981) found that the reported estimate of prevalence varied as a function of different definitions of the disorder, differing methods of measurement, and variation in statistical cutoff scores. While there has been considerable controversy over the exact nature of the disorder, as well as the appropriate diagnostic criteria to be applied in these cases, the treatment of choice has remained stimulant medication. The stimulant most often prescribed has been methylphenidate hydrochloride (commonly known by the trade name Ritalin), because of the relative paucity of serious side effects (Safer, 1978).
With such a large number of school-aged children taking this medication, the importance of understanding the effects of methylphenidate on learning are self-evident. A plethora of studies have investigated the effects of methylphenidate; yet, despite this, what is known with certainty about the effects of this medication on children’s ability to acquire new behaviors is quite limited (Walker, 1982).

**Effects of Methylphenidate**

Methylphenidate has been shown to have a wide variety of physiological and behavioral effects including anorexia, insomnia, increased heart and respiratory rates as well as elevated blood pressure (Barkley, 1981). It has enjoyed great popularity as a treatment for ADD as a result of its effect on the activity level of children with this disorder, as well as its tendency to increase attention and task persistence for many children (Barkley, 1981). Improvements in classroom behavior, social interactions and parent-child interactions also have been reported (Barkley, 1988; Pelham, Bender, Caddell, Booth, & Moorer, 1985; Wallander, Schroeder, Michelli, & Gualtieri, 1987; Whalen, Henker, Collins, Finck, & Dotemoto, 1979). Effects have been especially marked when global rating scales, such as those developed by Conners (1973), have been used. While children may be seen as more attentive and less impulsive by their teachers and parents, the nature of methylphenidate’s effect on academic achievement, measures of cognitive performance, and learning has not been clearly established. For example, Barkley and Cunningham (1978) reviewed 17 studies examining the effects of methylphenidate and other psychostimulants on academic achievement and found that 83.6% of the 55 dependent variables utilized were unaffected by the medication. In addition, those that indicated improvement showed no consistency in terms of the
types of abilities affected. They concluded that psychostimulants had no reliable effect on scholastic achievement.

The effects of psychostimulants on other aspects of children's performance have been evaluated by many authors using a wide variety of dependent measures, for the most part also with equivocal results. One of the most common measures has been the Wechsler Intelligence Scale for Children (WISC) (Wechsler, 1949). While some investigators have found significant increases in Full Scale I.Q. (Conners, 1972; Hoffman, Engelhardt, Margolis, Polizos, Waizer, & Rosenfeld, 1974; Weiss, Minde, Douglas, Werry, & Sykes, 1971), others have reported significant changes in only the Verbal or Performance I.Q. (Epstein, Lasagna, Conners, & Rodriguez, 1968; Finnerty, Soltys, & Cole, 1971; Greenberg, Deem, & McMahon, 1972; Weiss et al., 1971; Weiss, Werry, Minde, Douglas, & Sykes, 1968). Still others found no drug effect on the performance of children on this measure (Alexandris & Lundell, 1968; Conners, Rothschild, Eisenberg, Stone, & Robinson, 1969; Conrad, Dworken, Shai, & Tobiessen, 1971; Rapoport, Quinn, Bradbard, Riddle, & Brooks, 1974; Rie, Rie, Stewart, & Ambuel, 1976). Investigators using other measures of intelligence also have reported no significant drug effects (Weiss et al., 1968). Similarly, mixed results have been reported for measures of activity level, as well as continuous performance tasks (Barkley, 1977). Thus, it has generally been thought that learning is not directly affected by stimulants, but that drugs in this class have their effects through enhanced attentional and inhibitory processes (Barkley, 1977; Fish, 1975; Sroufe & Stewart, 1973; Whalen & Henker, 1976). In reviewing the effects of stimulants on cognitive functioning Whalen and Henker (1976) summarized the situation as follows:
When broad-gauged measures of intellectual aptitude, learning, or achievement are used, the findings are contradictory and often negative. When comparisons are based on more refined measures, however, a consistent picture begins to emerge: Hyperactive children perform more poorly than normal youngsters, and psychostimulants improve their performance. (p. 1117)

Of the more "refined" measures utilized to investigate the effects of methylphenidate on learning, there have been three used frequently enough to require a brief review.

**Effects of Methylphenidate on Learning**

**Short-Term Memory Task.** One paradigm that has frequently been used to study the effects of stimulants on learning has been conceptualized as a short-term memory task, utilized by Sprague, Barnes, & Werry (1970). The task was a type of delayed matching-to-sample exercise where a matrix of pictures was presented briefly on a screen followed by a 4-sec delay when no stimuli were presented. A single test stimulus was subsequently presented and the child was required to determine if the test stimulus had been included in the previously presented matrix.

Sprague et al. (1970) utilized a triple-blind, crossover design, administering placebo, 0.25 mg/kg, and 0.35 mg/kg doses of methylphenidate to assess the effects of the drug on learning, reaction time, and activity level in emotionally disturbed children. Matrix complexity was varied by presenting one, two, or three pictures per presentation. They found that, on average, accuracy improved and response latency increased in the methylphenidate conditions as compared to placebo. They also found no significant differences between performance at the 0.25 mg/kg and 0.35 mg/kg dosages.

Werry, Aman, & Diamond (1980) utilized this same procedure to assess the effects of 0.4 mg/kg of methylphenidate compared with imipramine on learning.
Unfortunately, the task proved to be too easy and "any drug effects on memory were obscured by ceiling effects" (p. 30).

Sprague and Sleator (1977), in a study that probably has been the most frequently cited study on the effects of methylphenidate on learning, utilized the same short term memory task as their measure of learning, but made the task more difficult by presenting arrays of 3, 9, or 15 pictures. They found that performance was maximally improved at a dose of 0.3 mg/kg and somewhat impaired at 1.0 mg/kg. This dosage effect was most prominent when the task was most difficult, and not evident when the task was relatively easy. They were also able to demonstrate differential dose response curves for learning and measures of social behavior. While performance on the learning task was maximally improved at a dose of 0.3 mg/kg, teacher reports of appropriate social behavior were highest at a dose of 1.0 mg/kg.

**Paired-Associate Tasks.** One of the most frequently used procedures has been the paired-associate task where children learn to "associate" two previously unrelated stimuli. For example, a child may be presented with some symbol or geometric shape, followed by the presentation of a digit; then another symbol followed by another digit, and so on for a predetermined number of symbol-digit combinations. The task requires recall of the digit when presented with the associated symbol. Stimuli need not be restricted to digits and symbols (although this has been common), and many paired-associate tasks have utilized pairs of nonsense words, letter-digit combinations, or pictures of animals to be associated with different zoo locations (e.g., North, South, East, or West).
Swanson and Kinsbourne (1976) utilized this paradigm in order to investigate the possibility of state-dependent learning in hyperactive children taking methylphenidate. They found that methylphenidate facilitated performance when compared to placebo, both in the initial learning session and in subsequent relearning trials conducted the following day. Using similar paradigms, some have been able to demonstrate facilitative effects of methylphenidate on paired-associate tasks (Dalby, Kinsbourne, & Swanson, 1989; Douglas, Barr, O'Neill, & Britton, 1986), while others have been unable to demonstrate any clear facilitative effect (Becker-Mattes, Mattes, Abikoff, & Brandt, 1985; Conners, Eisenberg, & Sharpe, 1964; Gittelman-Klein & Klein, 1976; Sebrechts et al., 1986; Steinhausen & Kreuzer, 1981; Strauss et al., 1984). Still others have found that methylphenidate enhances initial learning on this type of task but does not improve retention (Gan & Cantwell, 1982; Rapport, Quinn, DuPaul, Quinn, & Kelly, 1989; Shea, 1982; Stephens, Pelham, & Skinner, 1984).

Matching Familiar Figures Task. The third frequently used method of evaluating the effects of stimulants on learning has been the Matching Familiar Figures Test (MFFT) (Kagan, Rosman, Day, Albert, & Phillips, 1964) which has been used to measure impulsivity. The task is a simultaneous matching-to-sample task where a sample picture is presented along with an array of six pictures, five of which are similar to the sample and one that is identical. The subject's task is to select the one picture from the array that exactly matches the sample. Unfortunately, studies utilizing this paradigm also have yielded equivocal results. Some have demonstrated effects similar to those found by Sprague and Sleator (1977) (Brown & Sleator, 1979; Brown, Slimmer, & Wynne, 1984), while others have suggested that
improvement in performance was a linear function of increased dosage (Rapport et al., 1988). Still others have been unable to document significant drug effects on accuracy when utilizing this task (Conners & Taylor, 1980; Tannock, Schachar, Carr, Chajczyk, & Logan, 1989).

Thus, the evidence that methylphenidate facilitates learning of any of these tasks is equivocal at best. Reports of facilitative effects, mixed effects, and no effects can be found throughout the literature. Further, none of these three methods of learning adequately represents the process of acquiring new behaviors. These approaches, and others that have been used to assess the effects of methylphenidate, focus on performance only (Walker, 1982) and generally represent only the simplest of learning paradigms. In spite of these shortcomings, extensive claims have been made regarding the effectiveness of methylphenidate in facilitating learning in ADD children. The present study will adopt a method that more adequately measures acquisition and exemplifies a more complex learning paradigm, thus providing a more thorough analysis of learning typical of elementary school students.

Repeated Acquisition

In order to examine the process of acquisition, repeated observations of children acquiring novel units of equivalent behavior must be made. The repeated acquisition procedure developed by Boren and Devine (1968) provides a model for this method.

Repeated acquisition procedures allow for the repeated acquisition of novel, but equivalent, behavioral chains over a relatively extended period of time. This approach has been utilized to examine the effects of instructions and rules on behavior (Boren & Devine, 1968; Danforth, 1983; Ozuzu, 1982; Vaughan, 1985), and as a method
of investigating the effects of a variety of psychotropic drugs (Delaney & Poling, 1987; Moerschbaecher, Boren, Schrot, & Simoes-Fontes, 1979; Moerschbaecher & Thompson, 1980; Picker & Poling, 1984; Poling, Blakely, White, & Picker, 1986; Thompson, 1973, 1974, 1975, 1980; Thompson & Moerschbaecher, 1979, 1981; Thompson, Moerschbaecher, & Winsauer, 1983). While the procedure has been used often in the psychopharmacological literature with non-humans as subjects, it has been virtually ignored as a method of exploring the effects of drugs on learning in children (see Walker, 1982, and Yoder, 1984, for exceptions).

First and foremost, repeated acquisition allows for an examination of the acquisition of behavior, as well as performance, over a relatively extended period of time. When utilized within a single-subject design, with each subject serving as his/her own control, the effects of a drug can be evaluated by comparing both acquisition and performance under varying drug doses with baseline levels of responding. Such an arrangement eliminates the within-group variability associated with group designs and gives a direct behavioral measure of individual performance rather than a statistically-derived measure (Boren & Devine, 1968; Sidman, 1960). This latter feature significantly reduces the variability associated with the dependent measure, and renders the complex statistical analyses associated with group designs unnecessary (Johnston & Pennypacker, 1980). A further reduction in the variability associated with the dependent measure could be achieved by automating the procedure for use with children.
Effects of Methylphenidate on Repeated Acquisition

Walker (1982) utilized a computerized repeated acquisition task that required children to complete a chain of six correct responses associated with the position of three animal shapes on a computer screen. She found that 0.7 mg/kg of methylphenidate significantly decreased errors over placebo or 0.3 mg/kg of methylphenidate, and that both dosage levels of the drug increased correct response rates as compared with placebo.

Yoder (1984) attempted to extend Walker's results utilizing the repeated acquisition procedure with children, but was unable to detect any systematic effect of methylphenidate on either learning or performance. These results should be viewed with caution however, as there were a number of procedural issues that likely influenced the results. The repeated acquisition task utilized in this study was not automated, and presented stimuli associated with all six components of the chain simultaneously (rather than sequentially as in the previous study). Additionally, variability associated with the independent variable was likely quite large. Dosages were scheduled on the basis of milligrams of drug administered and not on milligrams per kilogram of body weight. Furthermore, only the morning dose of medication was manipulated, leaving the afternoon dose constant throughout the study. It also was suggested (Yoder, 1984) that task difficulty may have been a factor, as error rates tended to be relatively low.

The Problem

The confusing array of findings with respect to the effects of methylphenidate on learning may have been the result of a number of difficulties:
1. Virtually all the studies in this area have been group designs, with either between-subject or within-subject comparisons. Rapport et al. (1989) have suggested that conflicting results in this area may be an artifact of the design utilized, with within-subject designs being more sensitive to drug effects.

2. Dosage schedule has been highly variable within the literature. Studies may utilize single doses or a range of doses. Furthermore, the dosage may be prescribed solely in terms of milligrams, or in terms of milligrams per kilogram of body weight. This situation has made comparative analyses quite difficult.

3. Many of the studies cited utilized dependent measures that have not been automated. The requirement that the subject interact with the experimenter may allow for unintended cuing, and subtle contingencies of reinforcement or punishment may inadvertently be established within the experimental session. The lack of precisely arranged contingencies may therefore add an additional source of variability.

4. The dependent measures utilized may not be the most sensitive or useful in determining drug effects in children. Rapport et al. (1989) have suggested that "trials-to-criterion" may yield a more meaningful measure of learning, and have found that this particular measure has been ignored when studying the effects of methylphenidate on learning.

5. Finally, the effects of methylphenidate on children's learning appear to be multiply determined by "what is being measured, specific task and temporal parameters, dosage, the inherent difficulty of the task, and required level of mastery" (Rapport et al., 1989, p. 687).
If a clear picture of the effects of methylphenidate on learning is ever to emerge, these sources of variability must be excluded or controlled in the experimental analysis.

Purpose of the Study

The purpose of the present study was to extend previous research by:

1. Replicating the repeated acquisition procedure with ADD children utilizing a more difficult and more complex task than has been used thus far.

2. Examining the effect of higher dosages on the repeated acquisition task.

In addition to providing a test of acquisition, the present study will include several methodological improvements over previous studies including (a) use of a single subject design, (b) an automated repeated acquisition task, (c) "trials-to-criterion" as an additional dependent measure, and (d) an "active" stimulant placebo (caffeine) condition.

Caffeine was chosen as the active placebo in order to mimic the initial stimulus effects of methylphenidate and thus help insure that subjects, parents, and teachers were truly blind to the drug conditions.
CHAPTER II

METHOD

Subjects and Setting

Subjects were two boys (ages 12 and 13) and one girl (age 9), selected from two local elementary schools, who had been diagnosed by their physicians as exhibiting ADD, and who had been prescribed Ritalin as part of their course of treatment. They were referred for possible participation in the study by teachers who were aware of the child's diagnosis and treatment status, or by physicians. No child suffering from any neurological disorder, or any other medical condition that would preclude the use of stimulant medication, was accepted for participation in the study. All subjects had demonstrated a positive response to the medication based on teacher reports and had been taking Ritalin at their current dosage for at least six months prior to the study.

Sessions for Subject 1 and Subject 2 took place at the subject's elementary school in a room designated for that purpose for the duration of the study. Sessions for Subject 3 took place in the office of the experimenter. Additional data on classroom behavior was based on teacher observations within the child's regular classroom setting, and observations of the child's behavior within the home were made by each child's mother.

Written informed consent was obtained from the mother of each subject in accordance with the guidelines of the Human Subjects Institutional Review Board (HSIRB) of Western Michigan University, Kalamazoo (Appendix D). In addition,
written assent to participate was obtained from each subject prior to their beginning participation.

Repeated Acquisition Task

For Subjects 1 and 2, the task was to select the one correct square from an array of seven identical squares arranged horizontally across the center of a computer screen. Subjects made their selection by placing the cursor within one of the squares and clicking a small button on the top of the mouse. If the subject selected an incorrect square, a buzzer sounded for a duration of 0.5 sec, and the screen went blank for a 3-sec timeout. During the timeout period, the cursor remained unavailable and responses had no programmed effect, except to reset the duration of the timeout period. At the end of the timeout period, the array of squares was presented again and the subject was given another opportunity to respond. If the subject made a correct response, a beep sound was presented three times in quick succession, the square was highlighted, and the array of squares was replaced by another array of squares. The second array was identical to the first, except that the visual pattern within the squares was distinctly different from that of the first array (see Appendix A). Again the subject had the opportunity to select the one correct square from the array of seven squares arranged horizontally across the center of the screen. An incorrect response resulted in a 3-sec timeout as described above, and a correct response resulted in another array being presented. This process was repeated seven times so that the subject was required to exhibit a chain of seven correct responses in succession in order to complete one correct trial. The subject's task was to complete five consecutive correct trials, of seven correct responses each, with no errors.
The task for Subject 3 was as described above, except that the array presented consisted of five squares and a chain of five correct responses was required in order to complete one correct trial.

After a subject completed the first trial, a counter appeared at the bottom of the computer screen. The counter was set at zero and could be advanced only by the completion of a trial with no errors. If an error did occur, the timeout procedure described above was initiated and the counter reset to zero. When the subject reached the established criterion (five consecutive correct trials) the session ended and a screen with the words "THE END" was presented (see Appendix A). At that point the subject received 25 cents for completing the task.

An intertrial interval of two seconds was programmed where a white screen was presented. The words "Your score is:" were printed at the bottom of the screen, just above the counter (see Appendix A).

The repeated acquisition task was completed twice each day, once in the morning and once in the afternoon. Each morning session constituted an acquisition session in that the subject was required to learn a new chain of responses. Each afternoon session constituted a retention session in that the subject was required to exhibit the same chain of responses learned in the morning session of that day. This pattern of morning acquisition sessions and afternoon retention sessions was maintained throughout all phases of the study.

Each day, the position of the correct square within each link of the chain was designated randomly with the following four restrictions: (1) a given position could not be represented more than twice in any given chain, (2) a given position could not be repeated in succession, (3) a given position could not be designated as correct on
consecutive days, and (4) easily recalled sequential patterns (e.g., first square, second square, third square) were eliminated.

**Equipment**

The repeated acquisition task was presented to each subject using a Macintosh SE® computer equipped with a 20 megabyte hard drive, a high density floppy disc drive, a mouse, and a 21.6 cm X 27.9 cm mouse pad. Software consisted of a computer program specifically designed for the purpose of this study (Giuliano, 1990).

**Independent Variable**

The independent variable was the Ritalin dosage administered to the subject, measured in milligrams of drug/kilograms of body weight. Subjects 1 and 2 received daily doses split in half. The first dose was administered at 8:30 a.m. and the second at 12:00 noon. Subject 3 received her daily dose split into thirds. The first dose was administered at 7:00 a.m. The second dose was administered at 10:30 a.m. The third dose was administered at 2:30 p.m.

**Active Placebo Condition**

At this level, each subject received a 7 mg/kg daily dose of caffeine that was designed to mimic the initial effects of the medication.

**Drug Condition 1**

At this level, each subject received a 0.6 mg/kg daily dose of Ritalin. This was comparable to the dose at which Walker (1982) demonstrated maximal improvement on the repeated acquisition task.
At this level, each subject received a 1.0 mg/kg daily dose of Ritalin. Dosages of 1.0 mg/kg have been shown to impair performance on a short-term memory task while enhancing social behavior (Sprague & Sleator, 1977).

Dependent Measures

Performance on the repeated acquisition task yielded the following measures for each of the two daily sessions: (a) the number of trials-to-criterion, (b) the number of incorrect responses (errors), and (c) mean response rate. Data from the initial acquisition trial were not included because responding at that point reflected random guessing with respect to the correct response.

The Conners (1973) Parent Symptom Questionnaire (PSQ) was completed by the mother of each subject at the end of each week. The PSQ has been one of the most frequently used rating scales in the assessment of ADD and has commonly been used to select children for research on ADD. It has also been used extensively in studies of stimulant drug effects on children's behavior. The PSQ is a 48-item, factor-analyzed scale that yields separate scores on the following dimensions: (1) conduct problems, (2) learning disability (inattention), (3) psychosomatic problems, (4) impulsivity-hyperactivity, and (5) anxiety. Each item is scored 0, 1, 2, or 3 based on the degree to which specific behaviors are seen as problems by the parent. A score of 0 represents "not at all," 1 represents "just a little," 2 represents "pretty much," and 3 represents "very much." High scores on this measure have been associated with a greater likelihood of academic problems and are considered predictive of a favorable response to stimulant therapy (Barkley, 1981).
The Conners (1973) Teacher Rating Scale (TRS) was completed for each subject by his/her teacher or teachers at the end of each school week. The TRS has been one of the scales most frequently used by teachers in assessing ADD children. It is a 39-item, factor-analyzed scale yielding the following five clusters: (1) aggressive conduct, (2) daydreaming-inattention, (3) anxiety-fearfulness, (4) hyperactivity, and (5) sociability-cooperation. The TRS is scored in a manner similar to that of the PSQ, with a score of 0, 1, 2, or 3 being assigned to respective ratings of "not at all," "just a little," "pretty much," or "very much" for each of the 28 behaviors included in the scale.

A Side Effect Checklist (SEC) was developed for the present experiment as a method of assessing the occurrence of side effects commonly associated with methylphenidate administration. It also was utilized to determine if parents and teachers were able to accurately judge the level of drug administered, despite the fact that they were blind to the conditions. The SEC was completed for each subject by his/her teacher or teachers at the end of each school week. Each subject's mother also completed the SEC at the end of each week.

Experimental Design

The study was a single subject, ABCA multiple baseline design across subjects. Condition A constituted a baseline where each subject received an active (caffeine) placebo and conditions B and C involved different levels of drug administration as described above (either 0.6 mg/kg or 1.0 mg/kg).

Each level of drug dosage was maintained for one week, beginning on Monday and ending on the following Friday. The order of drug administration levels for Subject 1 was as follows: (a) Placebo, (b) 0.6 mg/kg, (c) 1.0 mg/kg, (d)
Placebo. The order of drug administration levels for Subjects 2 and 3 was as follows: (a) Placebo, (b) 1.0 mg/kg, (c) 0.6 mg/kg, (d) Placebo. The order of drug administration for each subject was assigned randomly.

Procedures

Training

Training on the repeated acquisition task was conducted during the week prior to the baseline for Subjects 1 and 2, and for two weeks prior to baseline for Subject 3. All subjects remained on their clinically prescribed doses of methylphenidate, which ranged from 0.4 mgs/kg to 0.6 mgs/kg.

On the first morning of the training week, each subject was seated in front of the computer and was presented with a white screen on which the computer cursor appeared. They were instructed in the use of the equipment as follows:

I am going to show you how to use this computer and play this computer game. Do you see this? It is called a mouse. We can use it to move this little pointing hand on the computer screen. When I move the mouse to the right, the hand moves to the right. (Experimenter demonstrates.) When I move the mouse to the left, the hand moves to the left. (Experimenter demonstrates.) When I move the mouse away from me, the hand moves up. (Experimenter demonstrates.) When I move the mouse toward me, the hand moves down. (Experimenter demonstrates.) In this way you can move the hand anywhere on the screen that you like. Now you try it.

After the subject demonstrated that he/she could effectively manipulate the mouse, he/she was presented with seven boxes arranged horizontally across the center of the screen (see Appendix B). These were similar to the stimuli utilized in the repeated acquisition task, but were used only to demonstrate the consequences of selecting a correct square. Thus, selecting any square resulted in a quick succession
of three beeps and the square being highlighted. The presentation of this screen was accompanied by the following instructions:

Do you see these squares? We call these buttons. You can select any of these buttons by placing the finger of the pointing hand inside a button and pressing the button on the mouse like so. (Experimenter demonstrates.) Now you try it. (Subject demonstrates.) In this game some of the buttons make that beep sound and others make a buzzing sound like these. You try it.

The subject was subsequently presented with a screen similar to the previous one, except that it was used to demonstrate the consequences of selecting an incorrect square (see Appendix B). Thus, selecting any square on this screen resulted in a buzzer sounding for 0.5 sec and the screen going blank for three sec. After the subject selected a square, the screen associated with the first link of the repeated acquisition task was presented and following instructions were administered:

When you play this computer game, your job is to find the one correct button in a row of seven buttons like these. The correct button will beep like the others you saw and then you will get a chance to select from another set of buttons. Incorrect buttons will buzz and make the screen go blank for a few seconds. There are seven sets of buttons which I will show you now. (Experimenter presents each screen in succession.) Your job is to find the correct buttons in each of these seven sets without making an error. We will start with these buttons. (Present screen associated with the initial link.) If you pick an incorrect button you will come back to this set of buttons and start all over again. Do you have any questions? (Experimenter answers questions, if any.) If you complete the task you will get your choice of $.25 or a token for Star World.

On the initial day of training the task was presented as described in the "Repeated Acquisition Task" section above with two exceptions: (1) incorrect responses resulted in timeout followed by the presentation of the initial link in the chain (as opposed to returning to the link in which the error was made), and (2) the criterion for successful completion of the task was one trial with no errors.
The afternoon session of the first day of the training week was identical to
morning session in that the subject was required to complete the same chain of
responses as in the morning session. Incorrect responses resulted in the presentation
of the initial link in the chain and the criterion for successful completion of the task
was one trial with no errors.

On day two of the training week the task was altered so that incorrect
responses resulted in a timeout period followed by presentation of the stimuli
associated with the link in which the error was made. The criterion for successful
completion of the task was raised to five consecutive trials with no errors. Subjects
were advised of these changes prior to the morning session of the second training day,
and were advised that these conditions would remain in effect throughout the study.
After the first few days of training, it became apparent that Subject 3 was having
inordinate difficulty with the 7-link chain as she was unable to reach criterion and
became visibly upset with her poor performance. Thus, she was subsequently
presented with a 5-link chain.

**Acquisition and Retention Sessions**

Each morning session constituted an acquisition session in that each subject
was required to learn a new chain of responses. The position of the correct square
within each link of the chain was designated randomly and in the manner described
in the "Repeated Acquisition Task" section. This insured that each chain was of
equivalent difficulty, but novel enough to constitute learning.

Each afternoon session constituted a retention session in that the subject was
required to exhibit the same chain of responses learned in the morning session of that
day.
On the morning of the initial baseline session the subject was seated at the computer and was presented with a white screen having a single rectangle in the center labeled "START GAME" (see Appendix A). The subjects were advised that they were to play the game just as they had done previously, and that they could begin the game by clicking on the rectangle in the center of the screen.

After clicking on the rectangle in the center of the screen, subjects were presented with the initial link in the chain and they proceeded in the manner described in the "Repeated Acquisition Task" section.

After the last retention session of the experiment was completed, a debriefing interview was conducted with each subject. They were asked to describe what they had to do in order to perform well on the task and how they would explain the task to another youngster. The purpose of the interview was to determine if the subject was able to generate any specific strategies, or rules that may have influenced performance (see Appendix C).

**Drug Administration**

The level of drug dosage for each subject remained unknown to all individuals involved in the research, with the exception of the pharmacist who dispensed the medication, the physician who wrote the prescription, and the primary experimenter. This included the subjects, the subjects' parents, teachers, and the assistants who conducted many of the sessions. This information was disclosed only after all of the data had been collected. Each dose was prepared by the pharmacist in accordance with the requirements of the schedule described above, and was encapsulated in gelatin capsules. The daily dose for each subject was placed in a small plastic vial and a label with the date that the dose was to be taken was affixed to
the vial. This label also had a blank space where the time of each dose could be written and included the subject's name. A week's supply of medication (five vials) was delivered to the school (Subjects 1 and 2) or home (Subject 3) by the experimenter each Friday evening.

Subjects 1 and 2 received both doses at school each day. Acquisition sessions were scheduled to occur within 1.5 to 2 hours after the morning dose. Retention sessions were scheduled to occur within 1.5 to 2 hours after the afternoon dose. With only two exceptions, all doses were administered within 1 and 2.5 hours of each session.

Subject 3 received the initial dose at home and subsequent doses while at school. Acquisition sessions were scheduled to occur 1.5 hours after the initial dose. Retention sessions were scheduled to occur 1.5 hours after the afternoon dose. All doses were administered within 10 minutes of the scheduled times.
CHAPTER III

RESULTS

Trials-to-Criterion

Trials-to-criterion data for placebo and drug conditions for Subject 1 are presented in Figure 1. Performance in acquisition sessions during the initial placebo condition was quite variable and the number of trials-to-criterion relatively high compared to the other conditions. In the first drug condition (0.6 mg/kg), a decrease in trials-to-criterion in acquisition sessions was observed. Continued reductions in variability and trials-to-criterion were evident in the second drug condition (1.0 mg/kg). Returning to the placebo condition resulted in an increase in trials-to-criterion for acquisition sessions comparable to that of the first drug condition.

Performance during retention sessions also improved under the first drug condition, but was followed by a slight increase in trials-to-criterion during the second drug condition. The return to placebo did not result in substantial changes when compared with the second drug condition.

Using trials-to-criterion as the dependent measure, the performance of Subject 1 was unaffected by the 0.6 mg/kg dose of methylphenidate as performance under that condition was comparable to performance under the final placebo condition. However, there was some difficulty with Subject 1 not taking the medication as scheduled. On day 6, Subject 1 received his afternoon dose within 15 minutes of beginning the retention session. The fact that he was essentially
unmedicated for that session did not impair his performance. In fact, day 6 represented one of his best days in terms of this dependent measure during retention sessions. Similarly, on day 8, Subject 1 received his morning dose just prior to beginning the acquisition session for that day. His performance during the acquisition session on that day did not appear to be affected.

![Trials-to-Criterion for Subject 1 for Acquisition and Retention Sessions.](image)

Figure 1. Trials-to-Criterion for Subject 1 for Acquisition and Retention Sessions.

Trials-to-criterion data for Subject 2 for drug and placebo conditions are presented in Figure 2. Performance during both acquisition and retention sessions was marked by decreases in variability and number of trials-to-criterion as a function of exposure to the task rather than as a function of the drug conditions. While performance improved significantly in the first drug condition (1.0 mg/kg) when compared to the initial placebo phase, this appeared to be the result of a trend that
was evident from the beginning of data collection. Further, after performance had stabilized, no change as a function of drug condition was observed. Performance during the two drug conditions was not distinguishable from performance during the final placebo condition. Thus, it appeared that the improvements noted were the result of continued exposure to the task and not the result of the drug manipulations.

![Graph](image)

Figure 2. Trials-to-Criterion for Subject 2 for Acquisition and Retention Sessions.

Trials-to-criterion data for Subject 3 for placebo and drug conditions are presented in Figure 3. Subject 3 exhibited a steady state of responding across all conditions, for both acquisition and retention sessions. No systematic effect of either methylphenidate dose was observed on this measure when compared to the caffeine placebo.
Figure 3. Trials-to-Criterion for Subject 3 for Acquisition and Retention Sessions.

Errors

The number of errors within acquisition and retention sessions for Subject 1 are presented in Figure 4. A pattern similar to that found for trials-to-criterion was evident. Performance during acquisition was slightly enhanced in the 1.0 mg/kg condition when compared with the 0.6 mg/kg and final placebo conditions. Performance during retention however, deteriorated slightly in the 1.0 mg/kg condition when compared with the 0.6 mg/kg and final placebo conditions. In two cases, this subject received medication just prior to the session (day 6 retention and day 8 acquisition). Thus, during these sessions the medication was unlikely to have been effective. In spite of this, no changes were noted.
Error data for Subjects 2 and 3 for drug and placebo conditions are presented in Figures 5 and 6 respectively. No evidence of a systematic change in responding as a result of the drug manipulations was observed in either case.

Figure 4. Errors for Subject 1 for Acquisition and Retention Sessions.
Figure 5. Errors for Subject 2 for Acquisition and Retention Sessions.

Figure 6. Errors for Subject 3 for Acquisition and Retention Sessions.
Rate of Responding

Responses per second during acquisition and retention sessions for Subjects 1, 2, and 3 are presented in Figures 7, 8, and 9 respectively. No systematic drug effects were observed in any case. Subject 1 maintained a stable rate of responding across all conditions. Subjects 2 and 3 showed a trend toward more rapid responding as a function of continued experience with the task.

Figure 7. Responses/Second for Subject 1 for Acquisition and Retention Sessions.
Figure 8. Responses/Second for Subject 2 for Acquisition and Retention Sessions.

Figure 9. Responses/Second for Subject 3 for Acquisition and Retention Sessions.
Conners Ratings and Dose Estimates

Teacher ratings on the TRS and parent ratings on the PSQ for Subject 1 are presented in Table 1. Also included in Table 1 are the estimates made by teachers and parent regarding the drug conditions thought to be in effect during each week of the study.

Table 1
Conners Ratings and Dose Estimates for Subject 1

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>0.6 mg/kg</th>
<th>1.0 mg/kg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teacher 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conners</td>
<td>31</td>
<td>9</td>
<td>11</td>
<td>25</td>
</tr>
<tr>
<td>Estimate</td>
<td>Placebo</td>
<td>Drug</td>
<td>Drug</td>
<td>Placebo</td>
</tr>
<tr>
<td>Teacher 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conners</td>
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<td>0</td>
<td>0</td>
<td>21</td>
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<td>Placebo</td>
<td>Drug</td>
<td>Drug</td>
<td>Drug</td>
</tr>
<tr>
<td>Parent</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conners</td>
<td>22</td>
<td>12</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>Estimate</td>
<td>Placebo</td>
<td>Drug</td>
<td>Drug</td>
<td>Drug</td>
</tr>
</tbody>
</table>

Teacher ratings were considerably higher during placebo conditions (indicative of more problems) when compared with either drug condition. Both teachers also were able to estimate the drug conditions in effect each week with some accuracy. Teacher 1 accurately estimated the drug condition in effect during each week of the study (100%). Teacher 2 accurately estimated the drug condition for three out of the four weeks of the study (75%). Chance levels of 50% accuracy would be expected.
Parent ratings reflected a trend toward improved performance across conditions. Ratings were highest during the initial placebo condition and lowest during the final placebo condition. Parent estimates of which condition was in effect during each week of the study were somewhat more accurate than chance at 75% accuracy.

Neither parent nor teacher ratings were useful in differentiating between the 0.6 mg/kg and the 1.0 mg/kg conditions.

Teacher ratings on the TRS and parent ratings on the PSQ for Subject 2 are presented in Table 2. Also included in Table 2 are the estimates made by teachers and parent regarding the drug conditions thought to be in effect during each week of the study.

Table 2

<table>
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<tr>
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<th>0.6 mg/kg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teacher 1 Conners</td>
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<tr>
<td>Teacher 2 Conners</td>
<td>15</td>
<td>6</td>
<td>1</td>
<td>9</td>
</tr>
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<td>Parent Conners</td>
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<td>34</td>
<td>31</td>
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<td>Teacher 1 Estimate</td>
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<td>Drug</td>
<td>Drug</td>
</tr>
<tr>
<td>Teacher 2 Estimate</td>
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<td>Drug</td>
<td>Drug</td>
<td>Drug</td>
</tr>
</tbody>
</table>
No systematic effect of the drug manipulations on these ratings was observed. In addition, teacher estimates with respect to drug conditions were accurate only 50% of the time reflecting chance levels of accuracy.

Teacher ratings on the TRS and parent ratings on the PSQ for Subject 3 are presented in Table 3. Also included in Table 3 are the estimates made by the teacher and parent regarding the drug conditions thought to be in effect during each week of the study.

No systematic effect of the drug manipulations on these ratings was observed. In addition, both teacher and parent estimates with respect to drug conditions were accurate only 25% of the time reflecting levels of accuracy somewhat below chance.

<table>
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<th>Teacher Conners</th>
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<tbody>
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<td>Drug</td>
<td>Drug</td>
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<tr>
<td>Parent Conners</td>
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<td>3</td>
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<td>0</td>
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<td>Estimate Drug</td>
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<td>5</td>
<td>3</td>
<td>5</td>
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</table>

Table 3

Conners Ratings and Dose Estimates for Subject 3

Side Effects

The number of side effects reported by parents and teachers for each subject are displayed in Table 4. No systematic relationship between dose levels or drug conditions and reported side effects was observed. No consistency between
individual teacher reports was observed, except in the case of Subject 2 where side effects were virtually absent. Similarly, no consistency between parent and teacher reports was observed.

Table 4

Number of Side Effects Reported by Parents and Teachers

<table>
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<tr>
<th></th>
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<th>0.6 mg/kg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
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<td>Subject 1</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Teacher 1</td>
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<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Teacher 2</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Parent</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Subject 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teacher 1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Teacher 2</td>
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<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Parent</td>
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</tr>
<tr>
<td>Subject 3</td>
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<tr>
<td>Parent</td>
<td>2</td>
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<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>
CHAPTER IV

DISCUSSION

In summary, little evidence was found to indicate that methylphenidate enhances learning in the repeated acquisition task at the dose levels examined. Only one of the three subjects demonstrated any facilitative effect, and that effect was so slight that it might be considered negligible for all practical purposes. Changes in performance appeared to be more a function of exposure to the task rather than the drug manipulations. Teacher ratings for Subject 1 were sensitive to both levels of the drug, but parent ratings were not. Neither parent nor teacher ratings were sensitive to the drug manipulations in the cases of Subjects 2 and 3. Teacher and parent estimates of the drug conditions in effect during each week of the study were more accurate than chance levels for Subject 1, and at or below chance levels for Subjects 2 and 3.

The present findings disagree with those of Walker (1982) who found that performance on the repeated acquisition task was enhanced at a dose level of 0.7 mg/kg for children between 10.6 and 12.6 years of age. The present findings also stand in contrast to many other studies that have reported facilitative effects of methylphenidate on learning. However, Walker (1982) utilized mean errors/session as her dependent measure and conducted analyses on group data rather than analyzing each subject's performance individually. This has also been the case with virtually all of the studies examining the effects of methylphenidate in children. Such procedures can obscure significant individual effects and the present findings may simply reflect differences in methodology.
The present findings with respect to response rate also disagree with Walker's (1982) findings. She found that rate of responding increased as a result of both 0.3 mg/kg and 0.7 mg/kg doses. The present findings suggested no systematic drug effect on response rate. Rather, when increases in rate occurred, they appeared to be a function of exposure to the task. This difference may be explained by a procedural difference between the two studies. Walker's (1982) findings were based on subjects' performance during two sessions within each of three experimental conditions for a total of six sessions. In the present study, subjects had significantly more exposure to the task. Thus, increases in response rate were likely the result of a practice effect that was unlikely to be evident given the procedures used by Walker (1982).

This procedural difference may also render the repeated acquisition task, as utilized in the present study, less sensitive to the effects of methylphenidate. Rapport et al. (1989) have shown that, with a paired-associate task, the facilitative effects of methylphenidate diminish as a function of how well the subject has learned the task. Given that subjects typically become more effective on the repeated acquisition task as a function of experience with the task, it may be the case that any facilitative effects will have diminished by the time a steady state of responding has been reached.

The present findings extend those of Yoder (1984), who utilized similar procedures but examined the effects of a lower range of doses. He concluded that methylphenidate neither enhanced nor impaired acquisition or performance on the repeated acquisition task at doses between .17 mgs/kg and .72 mgs/kg. He also was unable to detect any systematic effect on response rate. In addition, the present findings were consistent with Rapport et al. 1989, who suggested that the effects of methylphenidate are multiply determined by "what is being measured, specific task
and temporal parameters, dosage, the inherent difficulty of the task, and required level of mastery" (p. 687), and who recommended the use of trials to criterion as a dependent measure that might be sensitive to the drug's effects.

The present findings, particularly the TRS data, also support the notion that children may be described as "responders" or "non-responders" to methylphenidate. Subjects 2 and 3 showed no systematic drug effect on any of the dependent measures administered, whereas the TRS data for Subject 1 showed a clear drug effect. This is consistent with the findings of McBride (1988) who found that as many as 30% of ADD children may be "non-responders."

Despite the fact that Subject 1 would be classified as a "responder," the drug did not have a pronounced effect on his performance on the repeated acquisition task. This may be explained, in part, by ceiling effects. In the 1.0 mg/kg condition Subject 1 consistently completed acquisition sessions in six or seven trials where five trials represented the best possible performance.

A number of other issues also need to be considered. One possible explanation for the lack of a facilitative effect is that the active placebo had a facilitative effect much the same as methylphenidate. Because caffeine is a stimulant, and has many effects similar to methylphenidate, such a possibility is not out of the question. However, there have been no reports of caffeine facilitating repeated acquisition learning and this possibility seems unlikely. In addition, the similarity of the present findings to those of Yoder (1984), who utilized an inactive placebo, also suggests that this notion is doubtful. Nonetheless, the addition of an inactive placebo condition could have provided more definitive data in this regard. However, the performance of Subject 1 during the retention session on day 6 and the acquisition session on day 8 was not affected by the fact that during these sessions he was
essentially unmedicated. These sessions represented brief no-drug conditions and the lack of any systematic effect on performance adds additional support for the notion that neither the medication nor the active placebo enhanced performance.

Statements with respect to the effect of specific doses of methylphenidate on learning are made difficult by the fact that procedures and drug administrations were not identical for all subjects. Subject 3 received the same daily dose as the other subjects, but the drug was administered three times a day rather than two times a day. Also, repeated acquisition testing was not conducted at the school but rather in the office of the experimenter. Subject 3 also received a somewhat easier version of the repeated acquisition task. Despite these differences, the performance of Subject 3 was in many respects quite similar to that of Subject 2. Once behavior had stabilized, both subjects rarely exceeded 10 trials-to-criterion and errors remained between zero and 10 for Subject 2 (with one exception) and between zero and eight for Subject 3. Their performance was different, however, in that Subject 3's performance stabilized within the first placebo condition, due to her extended training. This was not the case for Subject 2 whose performance did not stabilize until the first drug condition was implemented. Again, one must consider the possibility of ceiling effects given this level of performance.

Further research with the repeated acquisition task as a means of assessing drug effects in children should focus on methods of dealing with ceiling effects. The repeated-acquisition task could be made more difficult as the subject becomes more proficient. The chain could be lengthened and the number of components within each link of the chain increased so that a stable number of errors or trials-to-criterion could be obtained, but at a level that would allow any facilitative effect to be evident. Another way to deal with this issue would be to utilize a tandem schedule as opposed to
the chain schedule utilized in the present study. Arranging the schedule so that there is no distinctive stimulus associated with each component (in contrast to the present study where each component was associated with a distinctive stimulus) would make the task more difficult to master and perhaps make it more sensitive to the presumed facilitative effects of methylphenidate.

Given the apparently idiosyncratic effects of methylphenidate on children's behavior, perhaps it is more important to ask which children will benefit rather than searching for uniform effects of the medication. In this vein, McBride (1988) has recommended that double blind trials become a routine part of the assessment process for children suspected of ADD so that non-responders are not needlessly placed on medication. The possible role of the repeated acquisition task in assessing an individual child's responsiveness to medication might also be a fruitful avenue for further research.

Lastly, it is possible that the effects of methylphenidate on children's learning are far less dramatic than its widespread use would suggest. In view of the present findings, as well as the degree of confusion surrounding the issue of methylphenidate's effects on learning, the caveat issued by Conners et al. (1964) seems as appropriate today as it did then: "Drug enthusiasts are likely to be only too willing to attribute obtained effects to pharmacology when the effects might be due to basic demand properties of the experiment" (p. 21).
Appendix A

Screens for Repeated Acquisition Task
Appendix B

Demonstration Stimuli
Appendix C

Debriefing Interview Form
DEBRIEFING INTERVIEW

CHILD: ________________________________
DATE: __________________

1) WHAT DID YOU HAVE TO DO IN THIS GAME IN ORDER TO DO WELL?

2) IF YOU HAD TO EXPLAIN THIS GAME TO A FRIEND; WHAT WOULD YOU TELL HIM?

3) DID YOU ENJOY THE GAME OR WAS IT JUST O.K.?

4) WAS THIS GAME LIKE ANYTHING ELSE YOU HAVE DONE?

5) DID YOUR PARENTS OR TEACHERS TELL YOU ANYTHING ABOUT THE GAME?
Appendix D

HSIRB Approval
Date: June 6, 1990

To: Christopher P. Giuliano

From: Mary Anne Bunda, Chair

This letter will serve as confirmation that your research protocol, "The Effects of Ritalin on Repeated Acquisition Learning by Children with Attention Deficit Disorder", has been approved as full by the HSIRB. The conditions and duration of this approval are specified in the Policies of Western Michigan University. You may now begin to implement the research as described in the approval application.

You must seek reapproval for any change in this design. You must also seek reapproval if the project extends beyond the termination date.

The Board wishes you success in the pursuit of your research goals.

xc: W. Redmon, Psychology

HSIRB Project Number __________ 90-04-20 __________

Approval Termination __________ June 6, 1991 __________


