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Dose–Response Effects of Methylphenidate on Ecologically Valid Measures of Academic Performance and Classroom Behavior in Adolescents With ADHD

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The effects of methylphenidate on the academic performance and classroom behavior of 45 adolescents with attention deficit hyperactivity disorder were studied. During a 6-week, placebo-controlled medication assessment in the context of a summer treatment program, participants received a double-blind, crossover trial of 3 doses of methylphenidate. Dependent measures included note-taking quality, quiz and worksheet scores, written language usage and productivity, teacher ratings, on-task and disruptive behavior, and homework completion. Group data showed positive effects of methylphenidate on academic measures; however, the greatest benefit came with the lowest dose. Although additional benefit did occur for some participants with higher doses, the largest increment of change usually occurred between the placebo and 10-mg dose. Many adolescents did not experience added benefit with increased dosages, and in some cases they experienced deterioration. Guidelines for assessment of medication effects are discussed.

Attention deficit hyperactivity disorder (ADHD) is a mental health disorder that presents a major public health problem (National Institutes of Health Consensus Development Panel Members, 2000). ADHD children suffer from serious impairment in relationships with parents, teachers, peers, and siblings, as well as difficulties in academic functioning. Although it has been well established that such difficulties continue into young adulthood for individuals with ADHD, there has been very little research directed at the nature of these impairments in adolescents with ADHD. The great majority of children with a diagnosis of ADHD continue to meet diagnostic criteria when they reach adolescence (Barkley, Fischer, Edelbrock, & Smallish, 1990; Biederman et al., 1996). Furthermore, adolescents with a diagnosis of ADHD continue to demonstrate significant impairment when compared with their peers (Weiss & Hechtman, 1993), perhaps even more than when they were children. Investigators have reported that these youth demonstrate dysfunction in many areas of adaptive functioning, including self-esteem, school performance, and family relations (Barkley, Anastopoulos, Guevremont, & Fletcher, 1992). The problems that are reported as most frequent and severe by parents of adolescents with ADHD have to do with school functioning (Robin, 1990). As a group, adolescents with a diagnosis of ADHD tend to have more suspensions, poorer achievement, greater off-task behavior, higher rates of fidgeting and out-of-seat behavior, and less productivity than their nondiagnosed peers. Given these findings, it is not surprising that they also are more likely to be in special education placements and be retained in grades than their peers, and they are more than 10 times more likely to fail to graduate from high

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school than peers (Barkley, Anastopoulos, Guevremont, & Fletcher, 1991; Mannuzza, Klein, Bessler, Malloy, & LaPadula, 1993).

Despite the fact that most children with ADHD do not remit, there is a dearth of research on the treatment of ADHD in adolescents (Smith, Waschbusch, Willoughby, & Evans, 2000). Whereas stimulant treatment for children with ADHD is arguably the best studied treatment in child psychiatry and psychology, only a handful of studies have assessed the effectiveness of stimulant medication with adolescents (Spencer et al., 1996). This lack of research is especially salient given that the number of adolescents who receive stimulant treatment for ADHD has increased dramatically in recent years (Safer & Krager, 1994). The few studies that have examined stimulant effects in adolescents have been small and have focused on aggressive behavior, teacher ratings of behavior, or both (Brown, Jaffe, Silverstein, & Magee, 1991; Kaplan, Busner, Kupietz, Wassermann, & Segal, 1990; Klorman, Brumaghim, Fitzpatrick, & Borgstedt, 1990), and have generally reported positive effects of stimulants. We (Smith, Pelham, Evans, et al., 1998) recently examined stimulant dose–response effects on social behavior in a large study[1] and reported effects of stimulants on adolescent social behavior that were comparable to stimulant effects that have been reported in children with ADHD. In contrast, there is a near total absence of information regarding the effects of stimulants on the classroom academic functioning of adolescents with ADHD.

Many of the measures used in these previous studies have primarily addressed the dichotomous question of whether stimulant medication helps adolescents with ADHD. Rating scales addressing impulsive, inattentive, and disruptive behavior have been the primary tools of choice. Although these scales serve as good global measures of medication response, they do not provide specific information necessary to determine the effectiveness of stimulants in treating the particular behaviors that correspond to an individual adolescent's presenting problems. Objective measures of behavior and academic performance that are ecologically valid indicators of presenting problems are thus needed to assess medication response.

Early studies of stimulant effects on academic functioning in children used laboratory cognitive tasks as proxy measures of academic functioning (e.g., Swanson, Kinsbourne, Roberts, & Zucker, 1978). However, research showing little correspondence between performance on such tasks and classroom academic performance caused a shift toward evaluating drug effects on actual classroom tasks in classroom settings. Since 1985 (Pelham, Bender, Caddell, Booth, & Moorer, 1985; Rapport, Stoner, DuPaul, Birmingham, & Tucker, 1985), a series of studies from a number of laboratories have documented the effects of stimulant drugs on daily measures of academic productivity (i.e., "seatwork") in classroom settings in elementary-aged ADHD children (see Carlson & Bunner, 1993, Rapport & Kelly, 1991; Swanson, McBurnett, Christian, & Wigal, 1995, for reviews). These measures have typically included daily measures of completion and accuracy on arithmetic, reading, and language tasks typically assigned to grade school children, and have in large part been conducted in summer treatment program or laboratory classroom settings. However, these well-documented gains in daily academic work have not translated into gains in long-term academic achievement (MTA Cooperative Group, 1999; Swanson et al., 1995). It is possible that this lack of long-term effects is related to the fact that the school tasks in which children and adolescents typically engage are dramatically different (i.e., individual seatwork or teacher-supervised worksheets vs. note-taking during lectures, subsequent independent studying, and quizzes and tests). Stimulants may not affect the classroom activities in which adolescents engage on a daily basis in the same way that drugs benefit children's daily performance.

As was the case 2 decades ago with ADHD children, attempts have been made to evaluate stimulant response in adolescents on laboratory measures or cognitive tasks that are thought to relate to academic performance (e.g., Klorman, Brumaghim, Fitzpatrick, & Borgstedt, 1991); stimulants have improved performance on such tasks. However, the correspondence between improvement on these laboratory tasks and actual classroom performance is yet to be tested, and there is no reason to think that it will be better than in childhood. Indeed, there have been very few studies of the relationship between performance on information-processing tasks in the laboratory and corresponding measures in the natural environment, and the existing studies have not shown much evidence for such a relationship (Kupietz & Richardson, 1978; Lovejoy & Rasmussen, 1990). For example, Pelham and colleagues have obtained only minimal correlations between laboratory and natural measures of attention, particularly when the question is whether drug effects on the laboratory tasks correlate with drug effects in the natural environment (Pelham & Milich, 1991; Pelham, Schneider, Evans, & Carlson, 1992). Furthermore, such tasks do not reflect the academic setting in which adolescents with ADHD are typically involved—a classroom in which they are required to attend to a lecture, take notes, study independently, and take quizzes and tests.

One small study has examined stimulant effects on such tasks in young adolescents with ADHD. Evans and Pelham (1991) reported significant stimulant effects for classroom behavior and direct measures of academic performance in 9 adolescents. Data were collected over a 6-week period in a summer treatment program (STP) during a lecture-format history class. Quiz scores, assignment scores, test scores, behavior observations, and teacher ratings were collected daily in a double-blind, placebo-controlled, randomized stimulant trial. There were significant improvements due to stimulant medication on all of the measures except rule violations and teacher ratings of oppositional and defiant behavior. Although there appeared to be considerable individual differences in response to medication, the small sample size and the design of the trial (weekly medication

[1] This article reports on the classroom performance and behavior of the same adolescents as reported in Smith, Pelham, Evans, et al. (1998).

changes) prevented us from examining individual differences on either global indices of response or on the specific dependent measures involving daily academic functioning.

To increase the likelihood that clinicians and physicians will adjust their prescribing and assessment practices on the basis of research findings, it would be beneficial to present data in a manner that allows for the interpretation of practice guidelines. Rapport, Denney, DuPaul, and Gardner (1994) developed a pictorial representation of the data from a study on the effects of methylphenidate (MPH) in children with ADHD. The authors presented response data in a format that allows the reader to determine the probability that increasing the dose of medication will have on improving scores on specific measures. For example, the authors reported that 77% of the participants experienced no change on an academic task when they received 5 mg of MPH as opposed to placebo. Of the 77% that did not respond to 5 mg, slightly more than a third of them showed significant improvement when the dose was increased to 10 mg. Another quarter of the nonresponders showed significant improvement when the dosage was increased to 15 mg. However, if a child had not responded to 15 mg, going to 20 mg was unlikely to produce a benefit on this measure: only 13% of the nonresponders at 15 mg improved at 20 mg. These findings suggest that simply increasing medication dose because of nonresponse may be beneficial when starting with relatively low doses, but that after reaching a moderate dose of medication, it is unlikely that continuing to increase the dose will provide incremental benefit. No comparable analyses of stimulant effects on academic tasks have been reported for adolescents.

We used a variety of naturalistic measures of classroom performance in a summer program setting approximating a secondary school history classroom. Double-blind, placebo-controlled medication assessment procedures were used to assess the effectiveness of MPH on academic achievement and behavior in an adolescent population. Dependent measures included a variety of dimensions of achievement and behavior that are frequently reported as presenting problems for adolescents with ADHD, including note-taking, study hall assignment scores, quiz scores, grades on essays, and disruptive and off-task behavior. The findings are reported in statistical terms for the group, as well as in a format that affords examination of individual differences in response. This article provides academic class data for the same adolescents on whom we reported about stimulant effects on social behavior in our companion article (Smith, Pelham, Evans, et al., 1998).

Method

Participants

The 45 participants (40 male and 5 female) took part in the 8-week, 1993, 1994, or 1995 Summer Treatment Program for Adolescents (STP) conducted by the ADHD Program at the Western Psychiatric Institute and Clinic at the University of Pittsburgh Medical Center. All participants had chronic problems both at school and at home, and all had a primary *Diagnostic and Statistical Manual of Mental Disorders* (third edition, revised; *DSM-III-R*; American Psychiatric Association, 1987) diagnosis of ADHD. Structured parent interviews, in combination with standardized parent and teacher rating scales (e.g., Loney & Milich, 1982; Pelham, Gnagy, Greenslade, & Milich, 1992), were used to arrive at the final diagnosis. Participants were required to (a) meet *DSM-III-R* diagnostic criteria for ADHD, (b) have had their 12th birthday before the protocol began, (c) have a Verbal IQ higher than 80, and (d) have no conditions that precluded full participation in the STP activities or a trial of stimulant medication. According to *DSM-III-R* criteria, all of the participants were diagnosed with ADHD; 23 (50%) of the participants were diagnosed with comorbid oppositional defiant disorder, and 7 (15%) were diagnosed with comorbid conduct disorder. Approximately 85% of the participants were Caucasian. The median family income was $38,500 (range = $8,300 to $500,000). Participant characteristics did not differ by year recruited. Table 1 presents descriptive information for the participants.

Procedures

STP overview. Adolescents participated in STP activities from 7:45 a.m. until 5:00 p.m., Monday through Friday for 8 weeks. Daily activities included the classroom periods described below, therapeutic recreation activities, social skills and problem-solving groups, and a period during which adolescents performed age-appropriate jobs (e.g., office aide, counselor assistant). A behavior management procedure was in effect throughout the day that involved individualized, negotiated behavioral contracts and other basic rules and contingencies. When adolescents met the criteria of these contracts and basic rules they achieved increases in levels of privileges and weekly monetary payments. The nonclassroom program and medication effects on variables measured outside of the classroom are reported elsewhere (Smith, Pelham, Evans, et al., 1998).

Table 1
Participant Information

Measure	*M*	*SD*
Age in years	13.8	1.2
Full-Scale IQ[a]	101	15.3
Achievement, Reading[b]	98	15.1
Achievement, Math	101	15.0
Achievement, Written Language	95	17.7
Disruptive Behavior Disorder Parent Rating Scale[c]		
ADHD factor	1.8	0.6
ODD factor	1.7	0.7
CD factor	0.4	0.4
IOWA Conners Teacher Rating, Inattention/Overactivity[d]	8.6	4.9
IOWA Conners Teacher Rating, Oppositional/Defiant	6.0	5.2
Disruptive Behavior Disorder Teacher Rating Scale[c]		
ADHD factor	1.6	0.8
ODD factor	1.3	0.9
CD factor	0.5	0.6

Note. ADHD = attention deficit hyperactivity disorder; ODD = oppositional/defiant disorder; CD = conduct disorder.
[a] Wechsler Intelligence Scale for Children—Revised. [b] Achievement cluster standard scores for the Woodcock–Johnson Psychoeducational Battery. [c] Pelham, Gnagy, Greenslade, and Milich (1992); possible scores range from 0 to 3. [d] Loney and Milich (1982); Pelham, Milich, Murphy, and Murphy (1989); possible scores range from 0 to 15.

Classroom periods. Each Monday through Thursday morning, adolescents participated in a 60-min class formatted as a junior high school American history course that required the participants to listen to a lecture and take notes.[2] The class was staffed by a teacher (the same teacher for all cohorts) and an aide and included 10, 18, and 21 adolescents, respectively, for each of the 3 years of the study. The classroom period was divided into segments during which adolescents listened to lectures and took notes, received assignments, and completed a written language task. The classroom procedures remained constant over the course of the three summer programs.

Over the course of the STP, the teacher taught the participants a set of study skills (Evans, Pelham, & Grudberg, 1995; Spires & Stone, 1989). During the first 2 weeks of the STP (prior to the medication trial), the teacher modeled note-taking skills during the lecture period. The effectiveness of this intervention for adolescents with ADHD is reported elsewhere (Evans et al., 1995). For the 6 weeks of the medication assessment, the teacher gave lectures and daily feedback regarding assignments, but did not provide note-taking instruction.

After the lecture period, adolescents completed a creative writing assignment in which they were instructed to spend 15 min writing a story on their own topic or a suggested topic (if they could not think of a story, they could write anything they chose). Productivity and content were evaluated (see *Dependent Measures* below).

Directly following the morning classroom period, the adolescents had a 30-min study hall that was supervised by two staff members. Monday through Thursday, participants were given a 15-question history worksheet to be completed in study hall. The worksheets were fill-in-the-blank questions on simple facts from the morning's lecture. After they completed their assignments, adolescents were to spend time studying their notes for the daily quiz. The teacher provided no texts or other written material for the participants during study hall; thus, the adolescents had to rely on their notes to complete the assignments and to study. The teacher collected notebooks at the end of the study hall period and returned them at the beginning of the next day's class to ensure that the participants did not review the material at any time other than during the classroom period and study hall.

After lunch, the adolescents had a second classroom period. During this period the students completed a 20-question, fill-in-the-blank quiz that covered the material from the morning lecture (see Footnote 1). At the end of the classroom period, the adolescents were given homework assignments to complete for the following day. Homework was completed in the evening hours, when the third dose of medication (half of the daily condition, as described below) was in effect.

Behavior management. A set of rules was established for behavior within the classroom and study hall, including such behaviors as respecting others, obeying the teacher, using materials appropriately, and working quietly (Pelham et al., 1993). When a student violated a rule, the teacher issued a verbal warning. If an adolescent violated a rule after receiving two warnings, the teacher assigned a 5-min time-out that was served outside the classroom. Time-outs were extended in length or restarted if the adolescent behaved inappropriately. Several contingencies were used to provide incentives for appropriate behavior in the classroom. First, if an adolescent served more than one time-out in any of the classroom periods or did not serve the time-out appropriately, he or she was required to serve 15 min of detention, up to a maximum of 60 min, during which he or she completed academic assignments rather than attending the job period (and thus losing the opportunity to earn money for job performance). In addition, monetary fines were levied for serving time-outs from the classroom, and adolescents earned monetary bonuses for behaving appropriately. These monetary consequences were part of a weekly salary system that adolescents earned on the basis of academic performance and behavior during the week.

Medication procedures. During the first 2 weeks of the STP, participants were unmedicated. Beginning in the 3rd week of the STP and lasting for 6 weeks, the adolescents underwent a double-blind, placebo-controlled, clinical medication assessment. The randomization and dosing procedures were similar to those that we have reported in many STP medication studies with children (e.g., Pelham et al., 1993, 1999). Participants took placebo, 10-mg MPH, 20-mg MPH, or 30-mg MPH at 7:45 a.m. and at 11:45 a.m. A third daily dose, which was half of the morning and noon dose (i.e., 5 mg, 10 mg, or 15 mg), was administered at 3:45 p.m. These doses translate into mean (standard deviation) mg/kg of body weight doses of 0.18 (0.17), 0.36 (0.17), and 0.54 (0.17), respectively. Medication conditions were randomized on a daily basis within-week so that each adolescent received each drug condition in random order within each week. Therefore, each participant received each dose for approximately 6 days, with absences or program holidays accounting for reductions in the number of days per condition. The classroom periods were scheduled so that they fell within peak medication hours—1 to 3 hr after ingestion.

Dependent Measures

Daily measures were taken in the classroom setting and were used as dependent measures. The measures came from four general areas: academic performance, writing productivity and quality, observed behavior, and teacher ratings. For all measures, results were averaged over days within drug condition. As measures of academic performance, percentages of main ideas and details that adolescents recorded in their notebooks from history lectures were scored. These scores indicated the degree with which the adolescents correctly recorded information presented in the lecture into their notebooks. In addition, the daily history worksheet and quiz were scored and percentages correct were used. The number of words written in the creative writing period served as a measure of productivity in the area of written language. The stories were then scored for grammatical structure. Research assistants read the stories and identified the grammatical errors. Each story was divided into segments of grammatically correct words (Parker, Tindal, & Hasbrouck, 1991). The number of words between errors constituted a segment of grammatically correct words. The mean length of these segments was calculated and served as a measure of correct usage. Finally, independent raters scored each writing assignment in terms of story idea (characterization, originality, detail) as a measure of quality of the ideas presented. Scores on these ratings ranged from 1 (*poor*) to 5 (*superior*) and were derived from the Resource Consultant Training Program scoring system (Jentzsch & Tindal, 1991).

Behavioral measures included observed on-task and disruptive behavior from the history lecture classroom period. Percentages of the intervals during which adolescents were observed as exhibiting disruptive behavior or being on task were computed (Pelham et al., 1993). In addition, the number of minutes that each adolescent was

[2] The teacher also gave a second lecture on science, and the adolescents completed a worksheet from the afternoon lecture material. The results obtained in the afternoon class were identical to those of the morning; in the interest of brevity, the results for the afternoon class are not reported herein.

Table 2
Means (and Standard Deviations) for Each Drug Condition

Measure	Placebo	10-mg MPH	20-mg MPH	30-mg MPH	$F(3, 132)$	Effect
History worksheet correct[a]	53.2 (31.1)	70.2 (25.8)$_p$	79.8 (19.8)$_{p,d}$	78.5 (20.9)$_p$	38.52***	L,Q
History quiz correct[a]	46.6 (29.6)	63.8 (22.2)$_p$	71.0 (18.5)$_{p,d}$	72.1 (20.1)$_p$	51.08***	L,Q
History notes						
Main ideas recorded[a]	69.8 (28.8)	77.3 (23.5)$_p$	85.1 (17.7)$_{p,d}$	83.2 (18.8)$_p$	12.42***	L,Q
Details recorded[a]	41.1 (26.5)	52.8 (24.7)$_p$	58.9 (21.3)$_{p,d}$	60.0 (24.6)$_p$	35.82***	L,Q
Written language						
Words written	58.8 (47.6)	82.6 (53.4)$_p$	96.9 (49.4)$_{p,d}$	102.0 (54.5)$_p$	32.76***	L,Q
Sequence length	7.4 (7.6)	9.8 (8.5)$_p$	10.7 (7.9)$_p$	11.7 (10.6)$_p$	11.25***	L
Story idea[b]	2.2 (1.1)	2.6 (1.1)$_p$	2.9 (1.0)$_{p,d}$	3.0 (1.1)$_p$	20.74***	L,Q
Disruptive behavior[a]	5.2 (10.0)	3.9 (8.0)$_p$	2.7 (5.1)$_p$	2.5 (5.1)$_p$	6.94**	L
On-task behavior[a]	83.9 (15.3)	88.9 (11.8)$_p$	90.1 (9.3)$_p$	90.0 (11.6)$_p$	7.86**	L,Q
IOWA Conners I/Q Scale	4.4 (3.5)	2.7 (2.7)$_p$	1.7 (2.2)$_{p,d}$	1.2 (1.5)$_{p,d}$	41.01***	L,Q
IOWA Conners O/D Scale	2.5 (3.4)	1.3 (2.2)$_p$	0.9 (1.8)$_p$	0.6 (1.2)$_{p,d}$	19.51***	L,Q
Time-out minutes	10.6 (20.0)	3.7 (7.4)$_p$	2.0 (3.9)$_{p,d}$	1.7 (3.8)$_p$	11.53***	L,Q
Homework completed[c]	33.0 (26.1)	37.7 (26.5)	39.3 (29.3)	42.5 (27.5)$_p$	3.07*	L

Note. [a] Percentage. [b] Qualitative rating: Scale 1 (*poor*) − 5 (*superior*). [c] Percentage of days in each drug condition that homework was 100% complete. A subscript of *p* indicates a significant difference from placebo. A subscript of *d* indicates a significant difference from the next lowest dose (e.g., 10 mg and 20 mg). MPH = methylphenidate; L = significant linear effect; Q = significant quadratic effect; I/O = Inattention/Overactivity factor; O/D = Oppositional/Defiant factor.
$^{*}p < .05$. $^{**}p < .001$. $^{***}p < .0001$.

sent out of class to serve time-outs was recorded daily and was used as a measure of inappropriate behavior in the classroom.

Each day, the teacher completed IOWA Conners rating scales for each adolescent (Loney & Milich, 1982; Pelham, Milich, Murphy, & Murphy, 1989). The Inattention/Overactivity score and Oppositional/Defiant scores were computed and used as dependent measures.

Adolescents were assigned homework each evening, Monday through Thursday. Homework was completed in the evening hours, when the third dose of medication (half of the daily condition, as described above) was in effect. Preliminary investigation of data frequencies showed that the adolescents typically did either all of the assignment or did not complete any of the assignment. Therefore, the dependent measure used was the percentage of days in each drug condition in which the adolescents completed all of their homework assignments.

Results

Group Effects

To determine the effects of MPH on the classroom measures, a repeated measures multivariate analysis of variance (MANOVA) was performed using four levels of drug (placebo, 10 mg, 20 mg, 30 mg) on the classroom measures described above. The results of the MANOVA were significant, $F(36, 9) = 4.95$, $p < .01$. Follow-up univariate analyses of variance with orthogonal decomposition were performed on each independent variable; all univariate tests were highly significant. Means and standard deviations for each dependent variable along with univariate statistics are presented in Table 2.[3]

Examination of the means in Table 2 shows clear improvement on all measures in all medication conditions relative to placebo. The pattern of means indicates a large improvement from placebo to the 10-mg dose, with smaller increments of improvement from the 10-mg dose to the 20- and 30-mg doses. These diminishing gains with increasing dose are reflected in the significant quadratic components of the orthogonal decompositions and are depicted in Figures 1 and 2.

The measure of homework completion was analyzed in a separate, repeated measures analysis of variance with orthogonal decomposition. The effect of drug was significant ($p < .05$), as illustrated in Table 2, but the effect was very small compared with the other dependent measures.

Individual Differences

To examine individual differences in the effects of increasing doses of medication, standard effect sizes (ESs) were computed for each adolescent, comparing each of the three doses with placebo. ESs were calculated for each measure by subtracting each adolescent's placebo mean from each of his or her drug treatment mean and dividing the result by the adolescent's placebo standard deviation (see Evans & Pelham, 1991; Pelham et al., 1993; Smith, Pelham, Evans, et al., 1998). If there was no placebo standard deviation (e.g., the adolescent received a score of 0% on every placebo day), the difference was divided by the 10-

[3] As Table 2 shows, medication significantly decreased the number of minutes of time-out served, and thus increased the time spent in class. It was therefore necessary to rule out the possibility that the medication effects seen on the classroom measures were secondary to the effect on time-out minutes—that is, that the adolescents' work did not improve merely because they were in the classroom longer. Therefore, the MANOVA was repeated using time-out minutes as a covariate. Drug continued to have a significant effect, $F(27, 360) = 4.58$, $p < .0001$. The only measure for which the univariate test became nonsignificant after covarying time-out minutes was that of observed disruptive behavior in the morning classroom, $F(27, 360) = 1.3$. Presumably, this is because the behaviors for which adolescents were required to serve time-outs were directly related to the disruptive behavior categories.

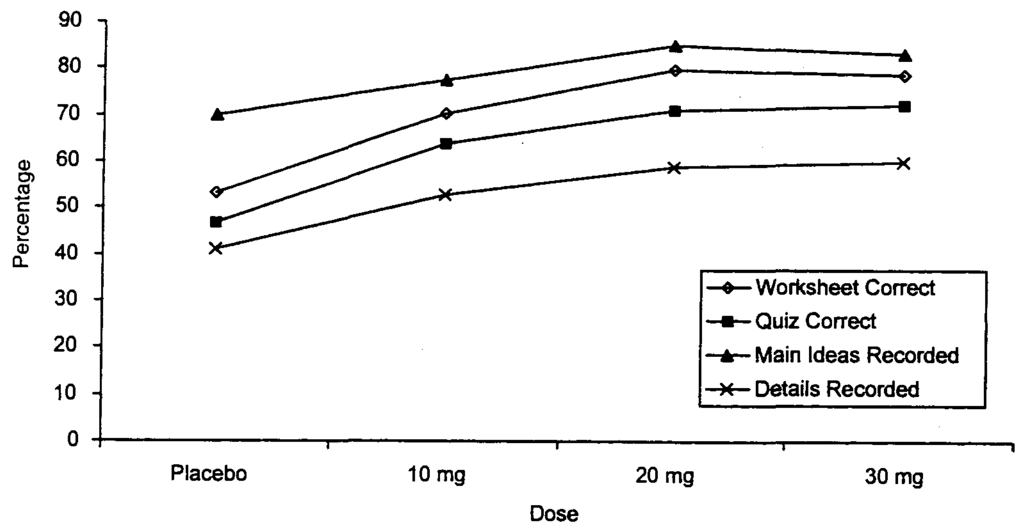

Figure 1. Dose response for academic measures.

mg standard deviation to estimate the ES. In cases where the mean was expected to decrease with treatment (e.g., disruptive behavior, IOWA Conners ratings), the treatment mean was subtracted from the baseline mean. Thus, a positive ES always indicated a beneficial response to treatment.

We then examined the ESs to determine at what medication dose each adolescent reached a meaningful positive ES, defined as 0.5. Results for a representative sample of dependent measures are summarized in Table 3. For all dependent measures, the vast majority of the adolescents who experienced a meaningful positive effect of medication reached that level at the 10-mg dose; a smaller, though substantial, percentage reached this threshold at the 20-mg dose; there were few adolescents who reached threshold at the 30-mg dose. It should be noted that most adolescents had very low rates of disruptive behavior on placebo (see Table 2) and therefore had no room for improvement on this measure. Similarly, most of the adolescents who showed no effect of medication on other measures were functioning at an appropriate level on placebo and thus had no room for improvement.

ESs were then examined to provide information regarding how many adolescents continued to benefit from increasing doses of medication and how many experienced maximal effects on lower doses. First, ESs were recalculated to compare each dose with the preceding dose (i.e., 10 mg with placebo, 20 mg with 10 mg, and 30 mg with 20 mg). ESs were then categorized into deterioration from the previous dose (ES < -0.5), no change (ES between -0.5 and 0.5), moderate improvement (ES between 0.5 and 1.5),

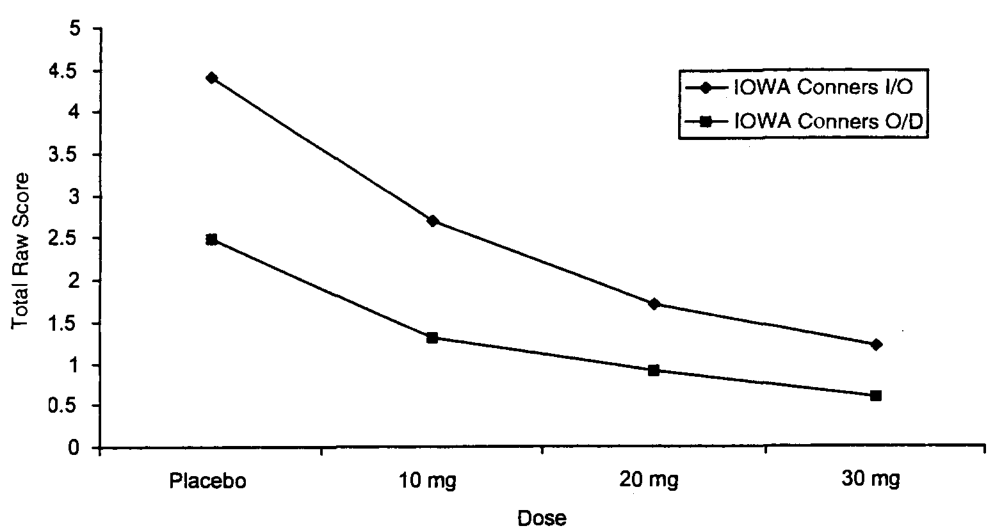

Figure 2. Dose response for teacher ratings. I/O = Inattention/Overactivity factor; O/D = Oppositional/Defiant factor.

Table 3
Percentage of Adolescents Reaching Effect Sizes of 0.5 or Greater at Each Level of Drug

Measure	10 mg	20 mg	30 mg	Never reached
History worksheet	66	13	11	9
History quiz	67	20	4	9
Words written	49	27	2	22
Sequence length	49	16	4	31
Story idea	42	24	4	29
Disruptive behavior	22	11	7	60
On-task behavior	47	9	9	36
Iowa Conners I/O Scale	53	13	11	22

Note. I/O = Inattention/Overactivity factor.

and large improvement (ES > 1.5). Figure 3 depicts, for five major classroom measures, the number of adolescents who fell into each category at each drug level. As the figure shows, there was variability across participants such that some reached the peak of effects at 10 mg, whereas others required higher doses to experience maximal improvement. The patterns of response also differed across variables.

Finally, the data from Figure 1 are summarized in Table 4. The data in the table indicate the number and percentage of participants who deteriorated or improved at each dosage of medication. In addition, ratios were calculated to indicate the likelihood that increasing dosages are likely to improve response versus deteriorate performance. In other words, the likelihood of achieving improvement across these five variables when we increase a dosage from 10 mg to 20 mg is much greater than the likelihood of causing deterioration. However, deterioration is more likely than large improvements if we increase a dosage of 20 mg to 30 mg.

Side Effects

Each day, the classroom teacher completed ratings of the major side effects associated with MPH. The teacher reported few side effects as a whole in the context of the classroom setting. Table 5 illustrates the percentage of participants for whom side effects were reported on at least 1 day and, at an average, as being moderate or severe. As Table 5 shows, similar to studies in children (e.g., Pelham et al., 1999), most side effects dissipated with repeated administration of medication or placebo. Very few side effects were reported at the average level, and none of the symptoms appeared to increase in frequency with increasing dose. Side effect ratings for counselors and parents are reported in Smith, Pelham, Evans, et al. (1998) for these same participants and were completely consistent with these data.

Discussion

This study represents the first large trial of the effects of multiple doses of MPH on the behavior and performance of young adolescents on ecologically relevant measures in a classroom setting. The results replicate and extend our previous pilot study (Evans & Pelham, 1991), demonstrating that MPH had clear positive effects on the adolescents' classroom behavior and academic performance. Analysis of the group data showed statistically significant improvement due to MPH on every dependent variable. Furthermore, the individual effects in Table 3 showed that with the exception of disruptive behavior, on which there was a ceiling effect, between 78% and 91% of the adolescents showed clearly beneficial effects on at least one dose of MPH. Similarly high rates of improvement in social behavior were found with this group of adolescents (Smith, Pelham, Evans, et al., 1998). Finally, these results extended our analysis of the social behavior of these adolescents by replicating the finding of diminishing gains with increasing dose reported in Smith, Pelham, Evans, et al. We discuss each of these main results in turn.

This is the first large study to demonstrate beneficial effects of stimulant drugs on ecologically valid measures of classroom performance for adolescents with ADHD. These findings extend the vast literature regarding stimulant effects on academic tasks in children with ADHD to a population of adolescents. We devised the classroom in this study to reflect the sort of academic tasks in which adolescents engage. In doing so we have demonstrated beneficial stimulant effects on note-taking, quiz performance, written language, and study hall assignments that are comparable in magnitude (highest ES was .91) to medication effects on academic tasks in children. The argument has been made in many studies that these daily beneficial stimulant effects are likely to translate into long-term gains in academic achievement for elementary-aged children who are steadily medicated. Our results suggest that such a hypothesis could be extended into the adolescent years. Because it is very difficult, if not impossible, to conduct long-term, randomized studies of stimulant medication on achievement, examination of effects in daily classroom measures provides the best window into potential drug effects on academic achievement.

The nature of the academic tasks we used and the implications of the drug effects merit comment. With respect to grades, the improvements obtained on quiz scores and study hall assignments corresponded to grade changes from "F" to "C," a clearly meaningful change for an adolescent. The medication effects on quality of notes taken indicate that medicated adolescents will have a better quality of notes for future studying, hopefully translating into continued future gains. Finally, the changes on written language are noteworthy. Adolescents with ADHD have dramatic academic deficits in written language (Evans, Pelham, Gnagy, Smith, & Molina, 1999). Most studies of stimulant effects in children have focused on gains in arithmetic and reading worksheets, and occasionally in handwriting. Our results extend those studies to the quantity and quality of the adolescents' written expression. Because our measures are standard measures of the quality of written expression (Jentzsch & Tindal, 1991; Parker et al., 1991) these results document beneficial effects for medicated adolescents in this important domain.

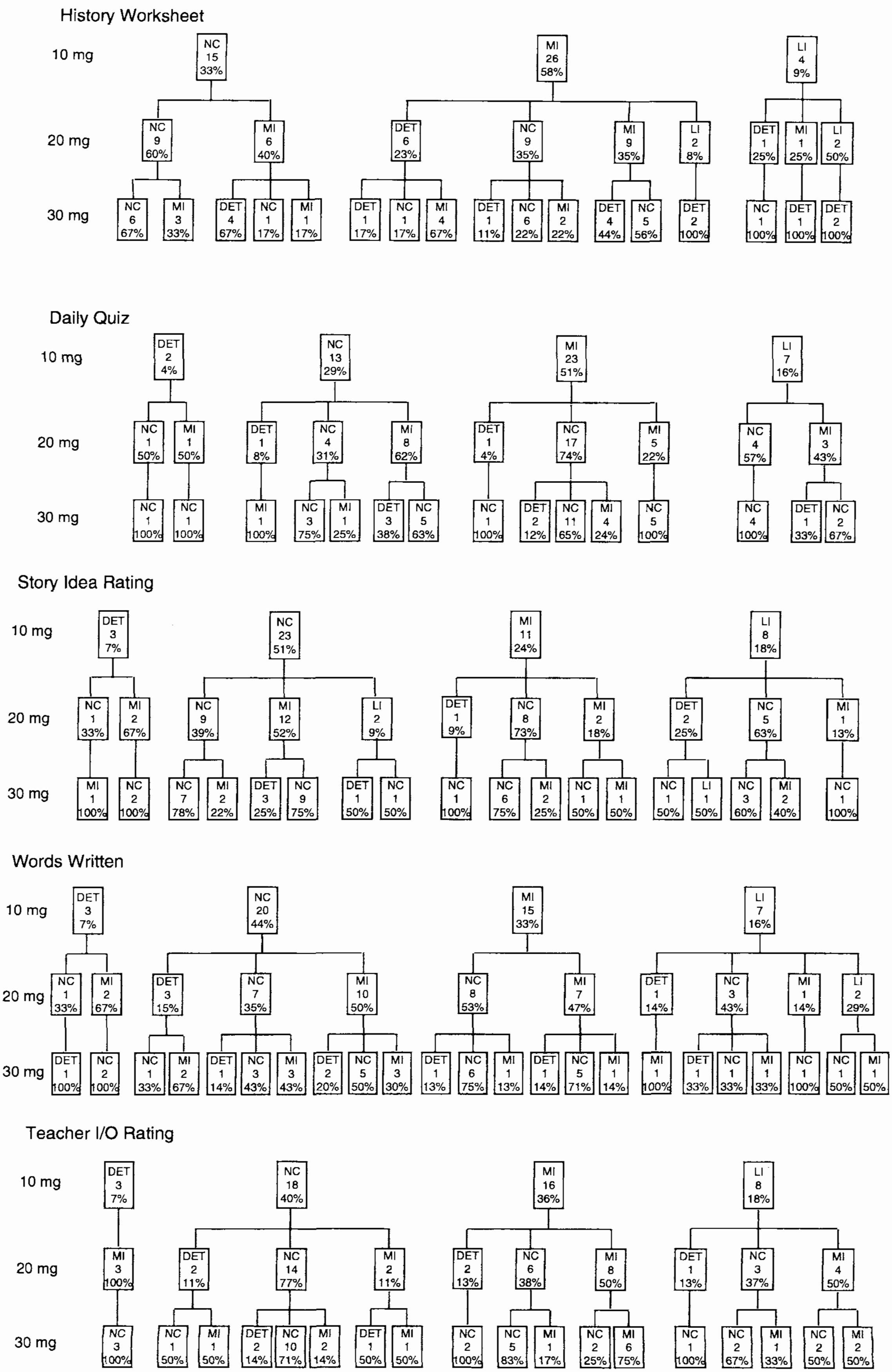
History Worksheet
10 mg
20 mg
30 mg
NC 15 33%
MI 26 58%
LI 4 9%
NC 9 60%
MI 6 40%
DET 6 23%
NC 9 35%
MI 9 35%
LI 2 8%
DET 1 25%
MI 1 25%
LI 2 50%
NC 6 67%
MI 3 33%
DET 4 67%
NC 1 17%
MI 1 17%
DET 1 17%
NC 1 17%
MI 4 67%
DET 1 11%
NC 6 22%
MI 2 22%
DET 4 44%
NC 5 56%
DET 2 100%
NC 1 100%
DET 1 100%
DET 2 100%
Daily Quiz
10 mg
20 mg
30 mg
DET 2 4%
NC 13 29%
MI 23 51%
LI 7 16%
NC 1 50%
MI 1 50%
DET 1 8%
NC 4 31%
MI 8 62%
DET 1 4%
NC 17 74%
MI 5 22%
NC 4 57%
MI 3 43%
NC 1 100%
NC 1 100%
MI 1 100%
NC 3 75%
MI 1 25%
DET 3 38%
NC 5 63%
NC 1 100%
DET 2 12%
NC 11 65%
MI 4 24%
NC 5 100%
NC 4 100%
DET 1 33%
NC 2 67%
Story Idea Rating
10 mg
20 mg
30 mg
DET 3 7%
NC 23 51%
MI 11 24%
LI 8 18%
NC 1 33%
MI 2 67%
NC 9 39%
MI 12 52%
LI 2 9%
DET 1 9%
NC 8 73%
MI 2 18%
DET 2 25%
NC 5 63%
MI 1 13%
MI 1 100%
NC 2 100%
NC 7 78%
MI 2 22%
DET 3 25%
NC 9 75%
DET 1 50%
NC 1 50%
NC 1 100%
NC 6 75%
MI 2 25%
NC 1 50%
MI 1 50%
NC 1 50%
LI 1 50%
NC 3 60%
MI 2 40%
NC 1 100%
Words Written
10 mg
20 mg
30 mg
DET 3 7%
NC 20 44%
MI 15 33%
LI 7 16%
NC 1 33%
MI 2 67%
DET 3 15%
NC 7 35%
MI 10 50%
NC 8 53%
MI 7 47%
DET 1 14%
NC 3 43%
MI 1 14%
LI 2 29%
DET 1 100%
NC 2 100%
NC 1 33%
MI 2 67%
DET 1 14%
NC 3 43%
MI 3 43%
DET 2 20%
NC 5 50%
MI 3 30%
DET 1 13%
NC 6 75%
MI 1 13%
DET 1 14%
NC 5 71%
MI 1 14%
MI 1 100%
DET 1 33%
NC 1 33%
MI 1 33%
NC 1 100%
NC 1 50%
MI 1 50%
Teacher I/O Rating
10 mg
20 mg
30 mg
DET 3 7%
NC 18 40%
MI 16 36%
LI 8 18%
MI 3 100%
DET 2 11%
NC 14 77%
MI 2 11%
DET 2 13%
NC 6 38%
MI 8 50%
DET 1 13%
NC 3 37%
MI 4 50%
NC 3 100%
NC 1 50%
MI 1 50%
DET 2 14%
NC 10 71%
MI 2 14%
DET 1 50%
MI 1 50%
NC 2 100%
NC 5 83%
MI 1 17%
NC 2 25%
MI 6 75%
NC 1 100%
NC 2 67%
MI 1 33%
NC 2 50%
MI 2 50%

Table 4
Summary of Continuing Gains Analysis

Dose and category[a]	Worksheet	Quiz	Story idea	Words written	IOWA I/O rating	Overall[b] (%)
10 mg						
Deterioration	0	2	3	3	3	5
No change	15	13	23	20	18	40
Moderate improvement	26	23	11	15	16	40
Large improvement	4	7	8	7	8	15
20 mg						
Deterioration	7	2	3	4	5	9
No change	18	26	23	19	23	48
Moderate improvement	16	17	17	20	17	39
Large improvement	4	0	2	2	0	4
30 mg						
Deterioration	15	6	4	7	3	16
No change	20	33	32	25	28	61
Moderate improvement	10	6	8	13	14	23
Large improvement	0	0	1	0	0	0

Note. I/O = Inattention/Overactivity factor.
[a] The continuing returns categories were defined as follows: Deterioration = effect size less than −0.5, no change = effect size between −0.5 and 0.5, moderate improvement = effect size greater than 0.5 and less than 1.5, and large improvement = effect size greater than or equal to 1.5. Calculation of effect sizes is described in the Method section. [b] The overall percentage is the sum of the individuals in each category across all five dependent variables divided by (45 × 5) then multiplied by 100%.

We should emphasize that during the first several weeks of the STP, the adolescents took an intensive course in note-taking, using the same classroom teacher, topics, and schedule as in the current study (Evans et al., 1995; Spires & Stone, 1989). We did not manipulate the note-taking program in this study, so we cannot conclude that it interacted with our MPH effects, but we strongly believe that to be the case. Without training in note-taking, the adolescents would not have known what a main idea was, and MPH would not likely have caused improvement in the percentage of main ideas evident in the adolescents' notes. Because note-taking influences subsequent studying and test performance (Evans et al., 1995), the medication effects obtained in these measures may also depend on the note-taking course.

It is important to comment on the high response rate in this study compared with previous studies of adolescents with ADHD (see Smith, Pelham, Evans, et al., 1998). Seventy-eight percent of the adolescents reached an ES of 0.5 or greater on some dose of MPH (range across all variables except disruptive behavior = 65–91%). The explanation for this high response rate may arise from the separate or combined effects of the measures used in this study and the context in which data were collected. Most of the previous studies in this area have relied almost exclusively on teacher ratings. Although teacher ratings were a part of the dependent measures in this study, direct observations and achievement variables were also carefully assessed, allowing for a greater range of domains in which medication-related improvement could be detected. Moreover, the teacher in this study had only 11 to 21 adolescents in her class and was trained to focus on the behaviors being assessed.

Using teacher ratings exclusively as dependent measures may result in a weakening of putative medication ESs. This is particularly true for adolescents in junior and senior high schools, whose teachers see them for only a brief period of time each day and may have as many as 25 or more students in their classes. Although it would be ideal to have direct observation of behavior in the natural environment for every adolescent evaluated for medication response, it is not practical in most clinical applications. Nevertheless, it is usually possible to obtain some direct measures of academic performance. Using a daily report card to measure the adolescents' performance on selected behaviors is a relatively simple way to obtain valid estimations of their behavior and performance in the classroom (Pelham et al., 2001). Addi-

Figure 3 (opposite). Incremental effects of increasing doses on individual adolescents. DET = deterioration (i.e., an effect size less than −0.5); NC = no change (i.e., an effect size between −0.5 and 0.5); MI = moderate improvement (i.e., an effect size greater than 0.5 and less than 1.5); LI = large improvements (i.e., an effect size greater than or equal to 1.5); I/O = Inattention/Overactivity factor. The numbers in the boxes report the number of participants who were in the category indicated by the letters. For example, 26 participants (58% of the sample) demonstrated moderate improvement on the history worksheet with 10 mg of medication over placebo. Of those 26 participants, 6 participants' (23%) performance on the history worksheet deteriorated from the level of performance with 10 mg of medication when they were given 20 mg. On the other hand, 2 participants' (8%) performance on the history worksheet revealed large improvement from the level of performance with 10 mg of medication when they were given 20 mg.

Table 5
Percentage of Teacher-Reported Side Effects Reported as Moderate or Severe

Side effect	Placebo		10 mg		20 mg		30 mg	
	Ever	Average	Ever	Average	Ever	Average	Ever	Average
Tics	17	2	15	2	9	4	7	2
Buccal/lingual movements	17	2	13	0	11	0	2	0
Picking	17	2	15	0	26	0	15	0
Worried or anxious	37	7	15	0	17	2	13	0
Dull or tired	37	2	20	0	13	0	13	0
Headache	13	0	2	0	11	0	7	0
Stomachache	7	0	4	0	17	0	11	0
Crabby	63	4	26	0	22	0	17	0
Tearful	9	0	7	0	7	0	7	0
Withdrawn	4	0	0	0	2	0	0	0
Hallucinations	0	0	0	0	0	0	0	0

Note. Ever = side effect reported as moderate or severe on at least 1 day for each drug condition. Average = side effect reported at an average of moderate or severe for that drug condition.

tionally, teacher grade records, which are typically kept on a weekly basis, may be used in a manner analogous to the way we used quiz scores. Although current laboratory analogue measures (e.g., continuous performance tasks) are not sufficiently ecologically valid to be clinically useful, development of computerized simulations of real-life tasks appropriate for junior- or senior-high school students is a potentially promising area of development. Multiple repetitions of assessments in each drug condition are necessary to produce stable data in studies such as this, and the use of Internet-based simulation protocols may afford the opportunity to gather such data without repeated visits to the doctor's office or repeated data collection in schools.

In addition to the putative impact of the note-taking instruction discussed above, it is possible that other aspects of the context in which the data were collected contributed to the high response rate and low rate of disruptive behavior. The classroom in this study was highly structured, as were the activities outside of the classroom. There was intensive supervision by staff in classroom, study hall, and recreational settings; consistent and immediate feedback about behavior; immediate consequences for seriously inappropriate behavior; and concrete incentives for appropriate participation in the program, including classroom behavior and performance. Moreover, the adolescents' parents were given training on developmentally appropriate behavior management procedures, and many parents chose to target academic performance in contingency contracts. It is possible there was an interaction between medication effects and effects of the behavioral interventions. We have previously argued that such behavioral interventions facilitate medication effects in children (e.g., Carlson, Pelham, Milich, & Dixon, 1992; Pelham, Schnedler, Bologna, & Contreras, 1980); they may have had similar synergistic effects in the current study with adolescents. Few schools, if any, maintain similar high levels of behavioral and academic structure. If such behavioral programs and prompts are important antecedent conditions for stimulant effects, then the effects we obtained would not generalize to school settings without similar psychoeducational structures and programs, and therefore would not translate into long-term gains in academic achievement. No studies of combined behavioral and pharmacological interventions in adolescents with ADHD have been conducted; therefore this topic is an important one for future investigations.

Our study replicated findings with children regarding the dose–response effects of MPH. The orthogonal decompositions and the graphs in Figures 1 and 2 showed that for both social and academic measures, the effects were not simply linear—that is, equal improvement at each increase in dose—but were generally curvilinear, with significant quadratic components in three of four behavioral measures and six of seven academic measures. Furthermore, the improvements obtained occurred for the most part at low to moderate doses of MPH—0.18 mg/kg/dose and 0.356 mg/kg/dose. Although some investigators have recommended considerably higher doses of MPH for children, adolescents, and adults with ADHD (Spencer et al., 1996), our data suggest that low doses suffice for the great majority of adolescents.

With regard to behavioral measures (i.e., time-out, teacher ratings, and observed disruptive behavior), the pattern of means in Table 2 reveals that for all measures the greatest amount of change occurred between placebo and the 10-mg MPH dose. The change from 10 mg to 20 mg produced an equivalent difference to that of placebo versus 10 mg for the measure of disruptive behavior, but much smaller changes for the other three measures (between one fourth and one third as great). In contrast, the change from 20 mg to 30 mg was minimal for all measures. With regard to the academic measures, the same patterns emerged. The pattern of means in Table 2 generally show marked improvement on all measures at 10 mg relative to placebo and varying rates of change across the dependent measures at higher doses. On five of seven measures, the 20-mg dose produced half as much incremental improvement from 10 mg as 10 mg produced compared with placebo; for two measures (main ideas recorded and story idea) the incremental value of 20 mg was comparable with that of 10 mg. Across all measures, there was minimal or no further improvement with an increase to 30 mg. However, as the individual results illustrate, the patterns of response varied across children and across variables.

The variability of response to stimulant treatment reported in many other studies is also evident in these results (e.g., Pelham & Smith, 2000). The data presented in Figure 1 indicate to clinicians the likelihood of improved performance on various measures given certain doses. For example, story idea ratings and words written were measures of the quality and quantity of adolescents' written language, respectively. Slightly more than half (52%) of the participants did not experience any change in story idea rating with 10 mg of MPH. However, 58% of those who experienced no change showed improvement at the 20-mg dose. Increasing the dosage to 30 mg resulted in no further improvement in those who benefited from an increase to 20 mg and helped only 20% of those who experienced no change at 10 or 20 mg. In other words, if the quality of a student's writing is a presenting problem and the student is not showing much improvement at 20 mg, then raising the dose to 30 mg is unlikely to produce improvement. However, if the main problem for the adolescent is quantity of work produced, then there is a good chance for improvement by increasing the dosage to 30 mg (see Words Written in Figure 3).

An important consideration when selecting a dose is the potential for a reversal of incremental benefit at progressively higher doses. In this study, there does not appear to be an adverse effect of MPH on academic performance at the group level within the range of doses studied (see means in Table 2). To the contrary, the continuing returns analysis revealed an escalating rate of deterioration as the doses were raised. The increased risk of potential negative impact on academic performance as the dose is increased is illustrated by computing ratios between rates of large improvement and rates of deterioration (see Table 4). At the 10-mg dose, the adolescents were 11 times more likely to show overall improvement (55%) than overall deterioration (5%). At the 20-mg dose, that ratio decreased to 4.8, whereas at the 30-mg dose the ratio of improvement to deterioration was only 1.4. Overall, looking at Table 4, it is evident that the large majority of beneficial MPH effects comes with either 10 or 20 mg. At the 10-mg dose, 45% showed no change or deterioration from placebo, with 55% showing improvement. When the dose was increased to 20 mg, 57% showed no change or deterioration from the previous dose, whereas only 43% improved, and at 30 mg, 77% deteriorated or did not change compared with only 23% of participants showing moderate improvement and none showing a large improvement.

We should emphasize the fact that the majority of the stimulant effects were positive. As long as doses were at or below 20 mg, the benefits of medication clearly outweighed the risks. Even though the risk to benefit ratio was less favorable at the 30-mg dose, there were a few adolescents for whom the 30-mg dose was clearly appropriate. In almost all of these cases, the adolescent exhibited severely inappropriate social behavior (Smith, Pelham, Evans, et al., 1998) in addition to poor academic performance. However, there was one case where the 30-mg dose was recommended primarily because of improved academic performance.

It is noteworthy that these response rates are higher than those found in previous studies of MPH treatment for adolescents with ADHD (see Smith, Pelham, Gnagy, & Yudell, 1998). Potential reasons for the higher response rate are discussed in detail in Smith, Pelham, Evans, et al. (1998). Briefly, the higher response rate in this study may be due to greater statistical and methodological power to detect medication effects compared with previous studies, including (a) a larger sample, (b) a broader range of doses, (c) measurement in a well-controlled, naturalistic setting, (d) repeated replications of medication conditions, and (e) using a statistical cutoff of 0.5 to define a positive response to medication. These various explanations warrant systematic investigation.

Notably, the side effects reported by these adolescents and their parents were minimal and tended not to increase as dosage became larger (Smith, Pelham, Evans, et al., 1998). Table 5 presents the classroom teacher's ratings of side effects for this sample; very few side effects were reported in the classroom setting (particularly after repeated dosing), and the reports did not increase with increasing doses. Thus, side effects did not influence medication decisions for any of these adolescents.

Taken together, the results of this study and those of Smith, Pelham, Evans, et al. (1998) indicate that medication with a central nervous system stimulant is an effective acute treatment for adolescents with ADHD in both social and academic domains. Furthermore, efficacy can be achieved with doses of 10 mg (0.8 mg/kg/dose) to 20 mg (0.36 mg/kg/dose) of MPH, provided the medication is in conjunction with psychosocial treatment. Future research should focus on whether the acute changes we observed mediate changes in academic achievement and whether these effects are in part a function of the concurrent behavioral interventions.

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