

Transdermal Methylphenidate, Behavioral, and Combined Treatment for Children With ADHD

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Stimulant medication and behavioral treatments are evidence-based for children with attention-deficit/hyperactivity disorder, but the combination of the 2 treatments has been understudied. In this investigation, methylphenidate (MPH) was crossed with 2 levels of behavior modification (BMOD) in a summer treatment program. Twenty-seven children with attention-deficit/hyperactivity disorder, aged 6–12, participated. Children received placebo and 3 doses of transdermal MPH (12.5 cm², 25.0 cm², and 37.5 cm²). BMOD was implemented on alternating weeks. Both treatments produced large and significant effects. Combined treatment was superior to either treatment alone. The effects of transdermal MPH were comparable to those found in this setting in previous studies with multiple stimulant medications and formulations. Consistent with other research, low doses of MPH—even lower than in previous studies—yielded enhanced effects in combination with behavior modification.

Keywords: attention deficit hyperactivity disorder, methylphenidate, behavioral treatment, combined treatment

Only two interventions for attention-deficit/hyperactivity disorder (ADHD) have an evidence base: medication, primarily with a central nervous system stimulant (Spencer et al., 1996; Swanson, McBurnett, Christian, & Wigal, 1995), and behavior modification (Pelham, Wheeler, & Chronis, 1998). The combination of the two is also widely recommended (American Academy of Pediatrics, 2001).

Central nervous system stimulants are the most widely used pharmacological treatments for ADHD, and numerous studies have demonstrated the short-term efficacy of these medications, especially methylphenidate (MPH), in the treatment of ADHD (American Academy of Child and Adolescent Psychiatry, 2002; Swanson et al., 1995). Immediate release (IR) MPH has a narrow window of effect

(60–240 min after ingestion) and peaks at 2 hr following ingestion (Swanson, Kinsbourne, Roberts, & Zucker, 1978). Therefore, it must be administered b.i.d. to ensure coverage over the school day, and a late-afternoon dose must be given to cover after-school hours and evenings.

A number of preparations have been developed to increase the duration of action associated with typical stimulant medication and have been in use for some time (Pelham et al., 1990; Pelham, Swanson, Furman, & Schwindt, 1995). More recently, amphetamine mixed salts have been found to have a span of action that covers the school day with a single dose for many children (Pelham, Aronoff, et al., 1999; Pelham, Gnagy, et al., 1999; Swanson et al., 1998). Several newer long-acting stimulant formulations have also been developed. Some exert coverage for a school day (Lopez, Pistreich, Lee, & Muniz, 2003; Swanson et al., 2002), whereas others are designed to last up to 12 hr (Biederman, Lopez, Boellner, & Chandler, 2002; Pelham, Gnagy, et al., 2001). All of these preparations are oral formulations.

Recently, an MPH transdermal system (MTS) was developed (Noven Pharmaceuticals, Miami, FL) containing MPH in a multipolymeric adhesive platform. A series of studies has shown the efficacy and tolerability of the MTS formulation in laboratory and naturalistic settings. In a small, laboratory classroom study, an MTS formulation was found to produce blood levels and behavioral effects comparable to those of a matched dose of mg IR MPH given t.i.d. (Pelham, Schentang, et al., 2005). In a dose-ranging study in a summer treatment program (STP) context, doses ranging from 6.25 cm² to 25.00 cm² (nominal doses of 5–20 mg, approximating a t.i.d. schedule) were found to produce effects comparable to those obtained in other studies with

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both short- and long-acting stimulants (Pelham, Manos, et al., in press). Parent ratings indicated that the effects of the MTS continued into the evening. Side effect profiles were similar to those previously reported in our stimulant trials with children with ADHD in laboratory analog and STP settings.

Since the 1970s, a number of studies have shown that behavioral interventions cause short-term amelioration of ADHD symptoms, and that these acute effects are comparable in some domains to those obtained with low doses of stimulant medication (Pelham & Murphy, 1986; Pelham & Waschbusch, 1999; Pelham et al., 1998). Despite the fact that behavioral interventions for ADHD have been established as effective and are recommended in current practice guidelines (American Academy of Child and Adolescent Psychiatry, 2002; American Academy of Pediatrics, 2001; Goldman, Genel, Bezman, & Slanetz, 1998), there is considerable disagreement among ADHD experts regarding the effectiveness of behavioral treatments. Prominent ADHD researchers have written that behavioral treatments either do not work or are only minimally effective compared with pharmacological treatments (Greenhill, Halperin, & Abikoff, 1999; Hinshaw, Klein, & Abikoff, 1998; Jensen & Payne, 1998; Klein & Abikoff, 1997; MTA Cooperative Group, 1999; Wigal et al., 1999). A major source of this disagreement derives from the fact that most comparative studies have involved nonintensive clinical levels of outpatient behavior therapy such as parent training (Horn et al., 1991; Klein & Abikoff, 1997; Pelham et al., 1988) or faded behavior therapy (MTA Cooperative Group, 1999; Pelham, 1999). Pelham and Murphy (1986) argued many years ago that contingency management-based behavioral interventions were clearly more potent than clinical behavior therapy, and that "dose" of behavior therapy was an important consideration in comparative studies (Fabiano & Pelham, 2002). The STP uses a number of contingency-management techniques in a behavioral treatment that is intensive and has been shown to produce large effects on children's behavior (Carlson, Pelham, Milich, & Dixon, 1992; Chronis et al., 2004; Fabiano et al., 2004; Pelham, Fabiano, et al. 2005; Pelham & Hoza, 1996).

During the past two decades there have been a number of studies suggesting that the most effective short-term treatment for the majority of children with ADHD appears to be an intervention that combines pharmacologic and behavioral treatment (Pelham & Murphy, 1986; Pelham & Waschbusch, 1999). However, as with the effects of behavior therapy alone, prominent ADHD researchers have written that combined treatments have not been demonstrated to have an advantage over medication alone (Greenhill et al., 1999; Hinshaw et al., 1998; Jensen & Payne, 1998; Klein & Abikoff, 1997; MTA Cooperative Group, 1999; Wigal et al., 1999). As with the effects of behavioral treatments, the source of this disagreement likely rests with the relative "dosing" of behavioral treatments and medication (MTA Cooperative Group, 1999; Pelham, 1999).

Several studies of combined treatments have been carried out in the context of the intensive STP (Pelham, Fabiano, et al., 2005; Pelham & Hoza, 1996). Carlson and colleagues (1992) found that the effects of a behavioral intervention

and a 0.3 mg/kg dose of MPH were equivalent and additive on several measures of behavior, such that the combination of the two resulted in behavioral improvement equal to the 0.6 mg/kg dose of MPH alone. There was no incremental benefit from the combined intervention at the high dose of medication. In a second, similar study (Pelham et al., 1993), both treatments were effective, but MPH was superior to behavioral treatment on most measures, particularly when individual effect sizes and normalization of functioning was examined. One limitation of these studies is that both occurred only in a classroom setting, and carryover from other parts of the day (in which intensive behavioral treatment was in place) may have occurred, minimizing the apparent effect of behavioral treatment.

In a comparison of children during the STP portion of the MTA study, very few differences were found between the group receiving combined treatment (average MPH dose of 31 mg/day throughout the STP) and the group receiving the behavioral treatment alone (Pelham et al., 2000). The authors speculated that the reason for the lack of difference (and thus the apparent ineffectiveness of an obviously effective drug) may have been that when behavioral treatment is very intensive, few incremental effects of medication are obtained—a finding analogous to those showing little incremental benefit of behavioral treatment beyond robust stimulant dosing. However, the behavioral treatment was not manipulated in this study.

In the current study we sought to extend the findings of previous studies in several ways. First, three doses of the MTS were used, including a 50% higher dose than had previously been studied, to extend the dose-ranging information. Second, the MTS was used for 6 weeks versus the 8 days of Pelham et al.'s (in press) study to investigate tolerability over an extended time period. Third, all behavioral treatment components were withdrawn for 2 full weeks in the STP, alternating with behavior modification, so that behavior modification could be fully crossed with medication. This enabled a comparison of the dose-response of medication both in the presence and absence of intensive behavioral treatment, addressing issues raised above regarding dose of MPH in combined treatment studies. On the basis of previous work, we hypothesized that both treatments would produce significant change and that medication dose effects would be smaller in the presence of behavioral treatment than in its absence.

Method

Participants

Twenty-five boys and 2 girls between the ages of 6 and 12 entered the investigation. All participants were enrolled in the 2001 STP for children with ADHD, conducted in the Center for Children and Families at the University at Buffalo, and were recruited from the 52 children enrolled in the program. Of the children who participated in the STP, 10 of their parents declined participation in the study because they chose not to medicate their children for the summer. Four children were excluded because they did not meet age or diagnostic criteria, 2 were participating in other clinical trials, and 3 were taking nonstimulant medications

and thus ineligible for the study. The remaining parents of non-participating children preferred their children receive medication steadily throughout the STP rather than enroll in a clinical trial.

Participants were required to meet *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; American Psychiatric Association, 1994) criteria for ADHD on the basis of the National Institute of Mental Health Diagnostic Interview Schedule for Children Version IV (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000) and the Disruptive Behavior Disorders Rating Scales (Pelham, Gnagy, Greenslade, & Milich, 1992), as completed by parents and teachers. Twenty-five participants were combined type and 2 were primarily hyperactive/impulsive. Ten of the children also met diagnostic criteria for oppositional/defiant disorder, and 15 met criteria for a diagnosis of conduct disorder. Participants were also required to have an estimated full-scale IQ of at least 80 and to have no documented adverse response or nonresponse to MPH. Children with sensitive skin or allergies to ingredients in the skin patch were also excluded. Parents and children provided informed consent, and the University at Buffalo Health Sciences Institutional Review Board approved the protocol. The sample was 93% Caucasian; 1 child was Native American and 1 was of mixed Asian and Caucasian race. Table 1 presents descriptive and diagnostic information on the sample.

Table 1
Means and Standard Deviations for Participant Characteristics

Item	M	SD
Age in years	9.76	2.11
Full scale IQ ^a	112.38	17.83
Reading achievement ^b	102.67	14.78
Arithmetic achievement ^b	106.78	17.39
Spelling achievement ^b	98.93	13.76
<i>DSM-IV</i> items endorsed by parents or teachers		
Inattention	8.60	0.94
Hyperactivity/impulsivity	8.35	0.81
Oppositional/defiant	6.50	1.64
Conduct disorder	3.00	3.32
Abbreviated Conners Rating Scale—Parent ^c	18.35	3.50
IOWA Conners Parent Rating Scale ^d		
Inattention/overactivity	10.15	2.41
Oppositional/defiant	9.90	2.53
Abbreviated Conners Rating Scale—Teacher	17.40	5.43
IOWA Conners Teacher Rating Scale ^d		
Inattention/overactivity	10.85	3.28
Oppositional/defiant ^d	7.00	4.47
Disruptive Behavior Disorders Parent Rating Scale ^e		
ADHD	2.01	0.40
Oppositional/defiant	1.74	0.43
Conduct disorder	0.25	0.16
Disruptive Behavior Disorders Teacher Rating Scale ^e		
ADHD	1.75	0.63
Oppositional/defiant	1.37	0.69

Note. IOWA = Inattention/Overactivity With Aggression. ADHD = attention-deficit/hyperactivity disorder.
^aWechsler Intelligence Scale for Children—3rd ed. (Wechsler, 1991). ^bWechsler Individual Achievement Test (Psychological Corporation, 2002). ^cGoyette, Conners and Ulrich (1978). ^dLoney and Milich (1982). ^ePelham, Gnagy, Greenslade, and Milich (1992).

Six children withdrew from the study prior to completion. Two withdrew after the first day of the study, during which they experienced severe side effects (including tics, buccal-lingual movements, and insomnia) on the highest dose of the medication. These boys had been previously medicated with low doses of stimulants, and their side effects were thought to be dose-related rather than formulation-related. A 3rd boy withdrew following 1 week of treatment because of parent-reported side effects of increased emotionality; this boy had not been previously medicated with a stimulant. A 4th boy withdrew following 2 weeks of treatment after self-report of stomachache from the medication (his reports were thought to be a function of his oppositional behavior and not medication-related). The 5th boy withdrew after 4 weeks of treatment because his parents found his negative behavior on placebo days to be unmanageable, and they chose to medicate him steadily. The 6th boy withdrew after 4 weeks of treatment because of a skin reaction to the patches. These 6 boys were not included in the analyses presented herein. Except for the boy noted above, the 5 participants who left had all been previously medicated with a stimulant, and all returned to their previous medications in the STP. Only one of these cases (skin irritation) was thought to be uniquely related to the MTS. The children who discontinued the study did not differ from those who completed the study on any of the variables in Table 1.

In addition, 3 of the youngest children experienced moderate to severe side effects (mainly buccal-lingual movements) on the highest dose of medication, presumably because they were small in stature and weight (dosing was not weight adjusted); the highest dose was discontinued for these children and was replaced with the 25.0 cm² dose. Two of these children were excluded from the analyses that included the highest dose of the medication because they did not have a sufficient number of data points for analysis.

Design

The current study consisted of two within-subject factors: medication (placebo, 12.5 cm² MTS, 25.0 cm² MTS, 37.5 cm² MTS) and behavior modification (no behavior modification, behavior modification). Medication was randomly assigned and varied daily on Mondays–Thursdays for 24 days (the final 6 weeks of the 8-week STP). Behavioral treatment was varied on a weekly basis for 4 weeks. Thus, each participant had 2 days in each medication condition without behavioral treatment, and 4 days in each medication condition with behavioral treatment.

Setting

The study took place in the context of the STP (Pelham, Fabiano, et al., 2005; Pelham, Greiner, & Gnagy, 1997). Children were grouped by 12 and supervised by five counselors (undergraduate and graduate students) trained and supervised by senior staff members. The STP lasted 9 hr Monday through Friday and ran for 8 weeks. A comprehensive behavioral treatment package was implemented, consisting of a point system with reward and cost components, time out, social reinforcement, daily report cards (DRCs), parent training, and the other interventions described below. Children spent 2 hr in academic settings and the remainder of the day in recreational activities and an art class. A large portion of each day was spent teaching children how to play sports, practicing sports skills, and developing physical skills and abilities.

Behavior Modification (BM)

In the BM condition, all STP behavioral treatments were implemented (Pelham, Greiner, & Gnagy, 1997). The primary stan-

standard behavioral intervention consisted of a comprehensive point system with both reward and cost components, which was in place throughout the day. Children earned daily social rewards for high point totals, and earned daily and weekly rewards (i.e., recess, field trips) for meeting point goals. In the classroom setting, behavior was managed through a modified version of the point system that is typical of a special education setting. In the recreational settings, children earned points for appropriate behaviors (e.g., following rules, good sportsmanship, complying with commands) and lost points for inappropriate behavior (e.g., teasing peers, noncompliance, interrupting). In the classroom setting, each child received a fixed sum of points at the beginning of each class period and lost points for any rule violations; children earned points for completion and accuracy of academic assignments. Time-out procedures were used when children exhibited aggressive, destructive, or defiant behavior. Each day, children received report cards evaluating their performance on individualized target behaviors. DRCs were reviewed with parents at the end of the day, and parents provided positive consequences at home when children reached their daily goals. Staff members provided frequent praise and social reinforcement to children who behaved appropriately. In addition, any time the standard procedures were not sufficient to produce the desired behavioral changes, individualized behavioral programs were developed. Parents also attended weekly evening sessions in which they learned behavior management skills to apply with their children in the home setting (Cunningham, Bremner, & Secord-Gilbert, 1998).

No Behavior Modification (NBM)

Following the procedures developed in our previous studies (Carlson et al., 1992; Chronis et al., 2004; Pelham et al., 1993), in the NBM condition the behavior modification system was suspended to emulate a typical classroom or camp setting. The structure and content of the activities remained the same. Staff members recorded all point system behaviors and rule violations that children exhibited, but did not award or take away points. Children did not receive DRCs in the NBM condition, and social skills training, problem-solving discussions, and time-out procedures were not used. Counselors and teachers did not provide systematic social reinforcement. Children earned daily and weekly STP reinforcers noncontingently, as in a regular camp or school environment. If a child's behavior was seriously disruptive to the rest of the group or was dangerous, he or she was immediately placed on a behavioral treatment program (DRC, time out, and individualized behavioral programs) for the remainder of the day; the behavioral interventions were removed again the following morning. This happened on 1 day for 3 children, on 2 days for 4 children, on 3 days for 2 children, on 4 days for 2 children, and on 5 days for 2 children. Data from these days were included in the NBM condition.

Because all parents were participating in parent training, we did not attempt to manipulate behavioral contingencies in the home setting because of possible carryover from the BM weeks. Staff members provided less specific feedback to parents about children's days, and DRCs were not sent home, but the home setting was not included in the behavior modification (BMOD) manipulation. Data from the home setting was thus only used for the medication evaluation and represents medication effects in the context of behavioral parent training.

Medication Assessment

The medication assessment procedure was a double-blind, within-subject evaluation of placebo and three doses of the MTS: 12.5

cm², 25.0 cm², and 37.5 cm². The drug conditions varied on a daily basis, and were randomized so that each child received each drug condition once each week. All MTS doses were applied at 7:00 a.m. by parents and were removed at 3:30 p.m. by staff members. The MTS could be removed earlier than 3:30 p.m. if a child displayed any moderate or severe side effects. This was done for 6 children, for a total of 10 times during the summer. The children, their parents, and all staff members were blind to medication condition. This procedure, including daily manipulations of dose and the dependent measures described below, has been used in many previous studies on stimulant effects in this setting, and the dependent measures have been shown to be reliable and sensitive to treatment effects (e.g., Pelham et al., 1987, 1989, 1990, 1993, 2002).

Dependent Measures

Point system. Indices of peer- and staff-directed social behavior were derived from a subset of point system categories: (a) following activity rules and rule violations, (b) noncompliance, (c) interrupting, (d) complaining, (e) conduct problems (lying, stealing, intentional destruction of property, and intentional aggression), and (f) negative verbalizations (verbal abuse to staff, teasing peers, and swearing). These behaviors were recorded by use of identical procedures in both BMOD conditions, although points were not used in NBM.

Independent observers collected reliability data by watching 25% of the children in a group for an entire day, sampled across groups and days, independently classifying and recording point system behaviors for those children. Kappa statistics were calculated for the following activity rules category, which was recorded in fixed intervals. Reliabilities for the other behavioral categories were determined by computing correlations and mean differences between the counselors and the observer. Correlations averaged .79 across measures (range = .44–.96; range of mean differences was 0.3–16.8 across categories), and kappa averaged .48 across groups and days.

Classroom measures. In the STP academic classroom setting, the children were assigned individual seatwork (e.g., reading, language arts, and arithmetic) at the appropriate academic level, on which they worked independently for 30 min. Productivity (percentage of assigned seatwork completed) and accuracy (percentage of completed work that was accurate) in seatwork tasks were recorded daily. Frequency of rule violations served as a behavioral measure.

Independent observers collected reliability data for rule violations by watching 25% of the children in a group for a class period. Correlations between teachers and observers averaged .84 across rule categories (range = .64–.94; range of mean differences was 0.4–3.7 across categories).

DRC. All children received DRCs as part of the treatment package in the BM condition (O'Leary, Pelham, Rosenbaum, & Price, 1976; Pelham et al., 2002). Behavioral goals and criteria were individualized for each child on the basis of his or her areas of impairment in the STP (Jacob & Pelham, 1999). In their parent training groups, parents learned how to establish consequences at home for positive DRCs; parents only implemented these procedures in BM weeks. In NBM weeks, counselors tracked all DRC target behaviors, but children did not receive report cards. Percentages of target criteria met each day served as a dependent measure. Odds ratios (Pelham et al., 2002) were computed for the additive value of combined treatment beyond either treatment alone.

Ratings. Each day, counselors, teachers, and parents completed the Pittsburgh Modified Conners Rating Scale, which incorporates items from several standardized behavior rating scales,

including the Swanson, Nolan, and Pelham Rating Scale (Atkins, Pelham, & Licht, 1985), the Abbreviated Conners Rating Scale (Goyette, Conners, & Ulrich, 1978), and the Inattention/Overactivity With Aggression (IOWA) Conners Rating Scale (Loney & Milich, 1982; Pelham, Gnagy, et al., 2001). The two subscales of the IOWA Conners Rating Scale, Inattention/Overactivity and Oppositional/Defiant, and the Abbreviated Conners Rating Scale were used as dependent measures.

Effectiveness and stress ratings. Each day, staff members completed ratings of the pleasantness and stress of interacting with the children, how well the children got along with peers, and their overall effectiveness in the treatment role. These ratings ranged from 0 (*not at all*) to 3 (*very much*). To reduce the number of measures subject to analysis, we aggregated the pleasantness, stress, and overall effectiveness ratings into an overall effectiveness factor. Parents completed a series of questions referring to the pleasantness and stress of interacting with their child; success in getting the child to behave during mealtime, complete homework, and complete bedtime routine activities; and overall effectiveness in the parenting role. These ratings consisted of a series of Likert ratings ranging from 0 (*not at all*) to 6 (*very much*). To reduce the number of measures subject to analysis, the pleasantness, stress, and overall effectiveness ratings were aggregated into an overall effectiveness factor, and mealtime, homework, and bedtime ratings were aggregated into an evening routine factor. These and similar questions have been shown to discriminate between parental interactions with children who have disruptive behavior problems and those with children who do not (Pelham, Lang, et al., 1997) and to detect medication effects (Chronis, Pelham, Gnagy, Roberts, & Aronoff, 2003) and behavior modification effects (Chronis et al., 2004).

Child ratings. Children also completed ratings at the end of each day during the investigation. These Likert ratings included items regarding how much the children liked the STP, how well they thought they behaved, and how well they thought other children in their groups behaved. These ratings ranged from 0 (*not at all*) to 6 (*very much*).

Side effects. Counselors, teachers, and parents completed the Pittsburgh Side Effects Rating Scale (Pelham, 1993) daily, and study staff monitored the ratings for clinically significant adverse events. The number of reports of moderate or severe side effects served as a dependent measure.

Results

Overview

For dependent measures taken during the day, 4 (drug: placebo, 12.5 cm², 25.0 cm², 37.5 cm²) × 2 (BMOD: NBM, BM) repeated-measures, multivariate analysis of variance (SPSS GLM, Chicago) were conducted. Significant effects of drug were followed up by examination of pairwise tests among all doses. Significant two-way interactions were followed up by examining the simple effects of BMOD for each dose of medication. For parent ratings, BMOD was not included in analyses because the behavioral conditions were not manipulated in the home setting. Effects of each unimodal treatment are presented first, followed by the combined effects in cases of significant Drug × BMOD interactions.

Main Effects of Medication

Point system. The analysis of point system measures indicated a multivariate effect of drug, $F(24, 147) = 2.48$, $p < .01$ (see Table 2). Results of the pairwise tests are presented in Table 2 and show in general that all three doses were different from placebo; fewer significant differences were found among the higher doses of medication. No significant differences were found between the 25.0 cm² and 37.5 cm² conditions.

Classroom measures. The analysis of classroom measures showed a multivariate effect of drug, $F(9, 135) = 4.59$, $p < .01$ (see Table 2). Pairwise tests showed that all three active doses were different from placebo, but none of the active doses were different from each other.

DRC. On the percentage of daily target criteria each child met, a significant main effect was found for drug only, $F(3, 54) = 51.28$, $p < .01$. Means and standard deviations are presented in Table 2.

Counselor and teacher ratings. This analysis showed significant effects of multivariate main effects of drug, $F(18, 153) = 3.24$, $p < .01$ (see Table 3). The analysis of effectiveness and stress ratings also produced a significant effect of drug, $F(12, 149) = 26.23$, $p < .01$. Results of the pairwise tests between doses again showed that all three active doses were different from placebo, with fewer significant differences between the higher doses.

Parent ratings. The analysis of parent ratings, using drug condition only, produced a significant multivariate main effect of drug for both behavior ratings, $F(9, 152) = 5.61$, $p < .01$, and stress and effectiveness ratings, $F(6, 104) = 3.68$, $p < .01$ (see Table 4). Pairwise tests between each combination of doses show that all three active doses were different from placebo and that the two highest doses did not differ from each other. Ratings were generally quite positive (e.g., mean placebo ratings of 4 on both IOWA subscales), presumably reduced to normative levels as a result of the behavioral parent training in which the parents were participating.

Child self-ratings. The analysis of child self-ratings produced a significant main effect of drug, $F(9, 162) = 3.47$, $p < .01$. Follow-up pairwise tests showed significant differences between all three conditions and placebo for participants liking camp and behaving well (see Table 5).

Main Effects of Behavior Modification

Point system. The analysis of point system measures indicated a multivariate effect of BMOD, $F(8, 11) = 5.19$, $p < .01$, with significant effects at the univariate level for all measures except conduct problems (see Table 2).

Classroom measures. The classroom measures also showed a multivariate effect of BMOD, $F(3, 13) = 11.81$, $p = .01$. As shown in Table 2, BMOD produced significant effects on classroom rule following and seatwork productivity, but not on accuracy of seatwork.

DRC. The DRC measure showed significant effect of BMOD, $F(1, 18) = 59.83$, $p < .01$. Means and standard deviations are presented in Table 2.

Table 2
Mean (Standard Deviation) Behavioral Measures as a Function of Behavior Modification and Medication Dose

Measure	No behavior modification				Behavior modification				Effects
	Placebo	12.5 cm ²	25.0 cm ²	37.5 cm ²	Placebo	12.5 cm ²	25.0 cm ²	37.5 cm ²	
Point system									
Following activity rules	37.0 (20.8)	55.5 (21.0) ^b	66.2 (16.8) ^{bc}	70.0 (13.1) ^b	53.5 (20.9)	70.9 (14.2) ^b	79.8 (11.3) ^{bc}	81.1 (9.2) ^b	B, D
Rule violations	152.7 (182.7)	77.8 (145.0) ^b	26.9 (24.1) ^b	20.4 (17.0) ^b	106.9 (135.6)	17.8 (18.8) ^b	16.6 (29.9) ^b	8.4 (8.3) ^b	B, D
Noncompliance	52.0 (87.3)	18.3 (24.2) ^b	10.5 (13.8) ^{bc}	10.0 (18.8) ^b	12.3 (14.2)	3.1 (3.5) ^b	2.1 (3.4) ^{bc}	1.6 (2.2) ^b	B, D
Interruption	40.5 (33.9)	32.3 (41.1)	15.2 (20.3) ^b	14.8 (15.9) ^b	31.8 (36.3)	9.4 (9.8) ^b	6.1 (6.8) ^{bc}	5.8 (5.9) ^b	B, D
Complaining	32.4 (39.5)	18.7 (19.5) ^b	8.5 (7.6) ^{bc}	8.5 (8.2) ^b	14.5 (15.6)	7.7 (10.0) ^b	5.1 (7.4) ^b	2.7 (2.5) ^b	B, D, B × D
Conduct problems	24.3 (51.1)	7.0 (15.4)	2.8 (4.8)	1.3 (1.7)	13.3 (24.6)	1.3 (2.0)	0.7 (1.4)	0.2 (0.4)	B
Negative verbalizations	109.5 (150.8)	67.7 (100.1) ^b	28.9 (40.9) ^{bc}	25.6 (47.0) ^b	41.1 (64.5)	11.7 (19.7) ^b	6.8 (12.1) ^b	4.5 (6.2) ^b	B, D, B × D
Classroom									
Seatwork rule violations ^a	97.8 (94.7)	34.5 (57.5) ^b	10.5 (25.7) ^b	8.3 (16.9) ^b	16.1 (13.6)	3.5 (7.5) ^b	1.5 (3.3) ^b	0.8 (1.1) ^b	B, D, B × D
Seatwork completion ^a	41.7 (25.8)	59.6 (31.3)	74.5 (22.8) ^b	75.7 (21.8) ^b	50.5 (24.0)	82.0 (14.8) ^b	80.3 (14.6) ^b	78.6 (15.9) ^b	B, D
Seatwork accuracy ^a	85.7 (11.5)	92.3 (5.8) ^b	93.4 (3.7) ^b	92.8 (3.6) ^b	85.1 (10.8)	90.7 (4.4) ^b	91.4 (3.8) ^b	90.7 (5.0) ^b	D
Daily report card % positive	20.8 (20.0)	41.9 (27.7) ^b	63.1 (22.1) ^{bc}	66.2 (22.1) ^b	54.7 (17.4)	73.7 (15.0) ^b	87.5 (8.5) ^{bc}	86.2 (13.5) ^b	B, D

Note. B = behavior modification; D = drug; B × D = interaction.
^a N = 18. ^b Significantly different ($p < .05$) from placebo in pairwise tests. ^c Significantly different ($p < .05$) from the next-lower dose in pairwise tests.

Counselor and teacher ratings. For the behavior ratings, the analysis showed a significant effect of BMOD, $F(6, 13) = 9.62, p < .01$ (see Table 6). No effects of BMOD were found at the multivariate level for staff ratings of stress and their effectiveness. Significant effects were shown at the univariate level for teachers' ratings on these items; however, these analyses were not followed up because multivariate tests were not significant.

Child self-ratings. The Drug × BMOD analysis on the child self-ratings produced a significant multivariate main effect of BMOD, $F(3, 16) = 5.75, p < .01$. Table 5 presents the main effect means and standard deviations for these ratings. Only the item asking how well other children in the group behaved was significant at the univariate level; children rated others (but not themselves) as behaving better in the BM condition than in the NBM condition.

Effects of Combined Treatment

Point system. The analysis on the point system measures indicated a multivariate effect of the interaction, $F(24, 147) = 1.75, p < .05$ (see Table 2). Figure 1 illustrates the interaction for several sample measures. To follow up the significant interaction, we computed simple effects of BMOD for each medication dose. The multivariate effect of BMOD was significant ($p < .05$) for placebo, 12.5 cm², and 25.0 cm² doses of medication.

Classroom measures. The interaction was significant for the classroom measures, $F(9, 135) = 2.88, p < .01$. Figure 1 illustrates the interaction for rule violations. The simple effects of BMOD were significant ($p < .05$) for only the placebo and 12.5 cm² doses of medication.

DRCs. The Drug × BMOD interaction was not significant in the multivariate analysis of variance conducted on the DRC percentages. As a second method of examining children's attainment of their daily goals, odds ratios were used to analyze the results of children's DRCs (Pelham et al., 2002). The likelihood of a child's reaching the target goal of 75% positive marks on his or her DRC was computed for this analysis and crossed with treatment conditions. A goal of 75% is standard within the STP for earning daily and weekly rewards on the DRC, and target criteria are set to be attainable at that level when the child tries hard during the day (Pelham, Greiner, & Gnagy, 1997). Common odds ratios were computed (Maentel-Haenszel statistic in SPSS crosstabs) for the following conditions: first, for each active dose of medication + BMOD compared with a baseline of placebo + BMOD, and second, for BMOD + each dose of medication compared with a baseline of NBM + the same dose of medication (odds ratios could not be completed for medication vs. placebo in the absence of BMOD because of the small number of days in the NBM/placebo condition). The common odds ratios are listed in Table 5. As the table shows, the children were significantly more likely to reach their target goals with combined treatment relative to either treatment alone and with BMOD relative to no treatment.

Counselor and teacher ratings. IOWA/Connors ratings showed a significant interaction, $F(18, 153) = 1.96, p <$

Table 3
Mean (Standard Deviation) Behavior Ratings as a Function of Behavior Modification and Medication Dose

Rating	No behavior modification				Behavior modification				Effects
	Placebo	12.5 cm ²	25.0 cm ²	37.5 cm ²	Placebo	12.5 cm ²	25.0 cm ²	37.5 cm ²	
Counselor									
I/O	8.3 (2.9)	6.1 (2.6) ^b	5.2 (2.4) ^{bc}	4.5 (2.1) ^b	6.6 (2.5)	4.2 (1.8) ^b	3.6 (1.8) ^{bc}	3.5 (1.7) ^b	B, D
O/D	8.1 (4.2)	6.1 (4.0) ^b	4.0 (2.6) ^{bc}	3.2 (2.7) ^b	5.9 (3.5)	3.0 (2.2) ^b	2.3 (1.7) ^{bc}	2.0 (1.4) ^b	B, D, B × D
Abbrev.	15.5 (6.2)	11.7 (6.2) ^b	9.1 (4.3) ^{bc}	7.4 (3.8) ^{bc}	11.7 (5.3)	7.2 (3.6) ^b	5.9 (3.2) ^{bc}	5.9 (3.2) ^b	B, D, B × D
Effective ^a	1.2 (0.7)	2.3 (0.6) ^b	2.2 (0.4) ^b	2.6 (0.4) ^b	1.9 (0.6)	1.7 (0.6)	2.4 (0.3) ^b	2.5 (0.3) ^b	D, B × D
Peer ^a	1.5 (0.6)	2.1 (0.6) ^b	2.1 (0.5) ^b	2.3 (0.5) ^b	1.9 (0.5)	1.7 (0.4) ^b	2.2 (0.4) ^{bc}	2.3 (0.4) ^b	D, B × D
Teacher									
I/O	11.9 (3.2)	7.3 (4.8) ^b	4.1 (3.5) ^{bc}	3.0 (2.2) ^b	7.1 (4.2)	2.5 (2.0) ^b	1.4 (1.7) ^{bc}	0.6 (0.8) ^b	B, D, B × D
O/D	8.7 (3.9)	4.6 (3.7) ^b	1.9 (2.3) ^{bc}	1.2 (1.5) ^{bc}	4.9 (3.7)	1.2 (1.4) ^b	0.5 (0.9) ^{bc}	0.4 (0.7) ^b	B, D, B × D
Abbrev.	22.9 (6.8)	12.9 (8.8) ^b	6.5 (5.8) ^{bc}	4.6 (3.9) ^b	13.0 (8.3)	4.0 (3.5) ^b	2.3 (2.8) ^{bc}	1.1 (1.2) ^b	B, D, B × D
Effective ^a	0.4 (0.4)	2.5 (0.5) ^b	2.6 (0.6) ^b	2.9 (0.2) ^{bc}	1.8 (0.9)	1.7 (0.9)	2.8 (0.4) ^{bc}	3.0 (0.9) ^{bc}	B, D, B × D
Peer ^a	0.3 (0.4)	2.3 (0.6) ^b	2.1 (0.9) ^b	3.0 (0.1) ^{bc}	1.7 (1.0)	1.6 (0.9)	2.5 (0.5) ^{bc}	2.5 (0.7) ^b	D, B × D

Note. B = behavior modification, D = drug, B × D = interaction of behavior modification and drug, I/O = inattention/overactivity; O/D = oppositional/defiant; Abbrev. = Abbreviated Conners Rating Scale (Goyette, Connors, & Ulrich, 1978) score; Effective = aggregate of effectiveness in counselor role, stressfulness of interactions, and pleasantness of interactions. Peer = how well child got along with peers.

^a Scale of 0 (not at all) to 3 (very much). ^b Significantly different from placebo ($p < .05$) in pairwise tests. ^c Significantly different from next lower dose ($p < .05$) in pairwise tests.

.02. Simple effects of BMOD were significant ($p < .02$) for all four doses of medication. On the analysis of staff ratings, the interaction was significant at the multivariate level, $F(24, 147) = 3.31, p < .01$. Simple effects of BMOD were significant ($p < .01$) for the placebo, 12.5 cm², and 37.5 cm² doses of medication.

Child self-ratings. The Drug × BMOD interaction was not significant for these ratings.

Effect Size

By use of procedures that we have previously used to evaluate magnitude of effects in within-subject designs in this setting (Evans et al., 2001; Pelham et al., 1993; Smith et al., 1998), for each participant, the effect size of each unimodal treatment and combination treatment was computed for each measure. This was done by taking the difference between the treatment score and the NBM/placebo (i.e., no-treatment condition) score, and dividing by the

standard deviation of the NBM/placebo condition. Averages and standard deviations of these individual effect sizes are shown in Table 6.

Side Effects

Table 7 lists the numbers of participants for whom counselors, teachers, or parents reported side effects as occurring on the average to a degree greater than mild (thus at a level of concern). As noted in the *Participants* section, 4 children withdrew from the study because of parental concerns regarding side effects, and a 5th withdrew because of irritation from the patch. Data for these children are included in the side effects tables, with the exception of the 2 boys who withdrew after only 1 day of treatment. In addition, as noted above, 3 children's high dose was reduced as a result of their small size and concerns regarding side effects; their data are included for the days they received each condition. Beyond these children, reports of side effects were minimal.

Table 4
Mean (Standard Deviation) Parent Behavior Ratings as a Function of Medication Dose

Rating	Placebo	12.5 cm ²	25.0 cm ²	37.5 cm ²
I/O	3.91 (3.18)	2.06 (1.72) ^b	1.49 (1.30) ^b	1.45 (1.63) ^b
O/D	4.10 (2.89)	2.64 (2.08) ^b	1.56 (0.36) ^b	1.83 (1.29) ^b
Abbrev.	6.53 (5.29)	3.24 (2.73) ^b	2.07 (1.90) ^b	2.55 (2.45) ^b
Effective ^a	3.88 (0.93)	4.23 (0.85) ^b	4.43 (0.78) ^b	4.61 (0.82) ^b
Evening routine ^a	4.38 (1.09)	4.46 (1.12)	4.78 (0.99)	4.86 (1.12) ^b

Note. N = 19. I/O = inattention/overactivity; O/D = oppositional/defiant; Abbrev. = Abbreviated Conners Rating Scale (Goyette, Connors, & Ulrich, 1978) score. Effective = aggregate of effectiveness in parenting role, stressfulness of interactions, and pleasantness of interactions. Evening routine = aggregate of success in getting child to behave at mealtime, while doing homework, and at bedtime.

^a Scale of 0 (not at all) to 6 (very much). ^b Significantly different from placebo ($p < .05$) in pairwise tests.

Table 5
Child Ratings as a Function of Behavior Modification and Medication Dose

Item	No behavior modification			Behavior modification			Effects
	Placebo	12.5 cm ²	25.0 cm ²	Placebo	12.5 cm ²	25.0 cm ²	
How much did you like camp?	4.05 (2.4)	4.88 (1.9)	5.12 (1.5) ^a	4.42 (1.5)	5.02 (1.5)	5.31 (1.4) ^a	5.37 (1.4) ^a
How well did you behave?	3.79 (2.1)	4.76 (1.8) ^a	5.02 (1.4) ^a	4.14 (1.8)	5.19 (1.2) ^a	5.55 (0.7) ^{ab}	5.37 (1.0) ^a
How well did the other kids in your group behave?	3.43 (2.1)	3.86 (1.9)	3.55 (1.6)	3.96 (1.7)	4.60 (1.3) ^a	4.77 (1.3) ^a	4.62 (1.3) ^a

Note. Ratings were completed on a scale of 0 (*not at all*) to 6 (*very much*). D = drug; B = behavior modification.

^a Significantly different from placebo ($p < .05$) in pairwise tests.

^b Significantly different from next lower dose ($p < .05$) in pairwise tests.

As shown in Table 7, counselor reports of appetite loss increased as dose increased; this was the only side effect consistently reported for the majority of participants. The MTSs were removed at 3:30 p.m., and parents did not report large numbers of side effects, including appetite loss or trouble sleeping, although their behavior ratings indicated appropriate behavior into the evening for the children.

Discussion

This investigation examined the independent and interactive effects of a once-daily MPH formulation and intensive behavioral treatment. Both single treatments provided significant improvement across a variety of domains, raters, and settings. Thus, the study provides additional validation for the efficacy of the MTS as an acute treatment for ADHD. The study also expands upon previous studies documenting the effects of the STP package of behavioral interventions for ADHD children. Finally, the two modalities interacted such that the effects of the low doses of MTS were dramatically enhanced in the presence of behavior modification.

Effects of the Transdermal MPH Preparation

This is the second study of the MTS conducted in an STP setting (Pelham, Manos, et al., in press), with a larger number of days per medication condition (6 compared with 2) and a dose range that included a higher dose than previously studied. The findings show clear efficacy of the preparation, with significant drug effects being found on every behavioral measure taken during the day, as well as on parent ratings completed in the evening. As might be expected, the effects of the MTS on various domains of behavior were comparable to those obtained in other recent studies in the same setting with IR MPH given two or three times per day and amphetamine mixed salts given once or twice daily (Pelham, Aronoff, et al., 1999; Pelham, Gnagy, et al., 1999; Pelham et al., 2002). Thus, consistent with the earlier study, the MTS improved daily academic productivity and rule following in the classroom, as well as rule following, negative interactions with peers and adults, and compliance in both classroom and recreational settings. As in our previous studies, these analyses were based on daily totals of behavior, indicating that the effects were obtained between the hours of 8 a.m. and 5 p.m. This study did not include a head-to-head comparison with other stimulant formulations, so direct dose comparisons cannot be made. However, results in the BM condition (equivalent to our previous studies) are comparable to those of recent studies (Pelham, Aronoff, et al., 1999; Pelham, Gnagy, et al., 1999) that used similar samples, similar doses, and the same setting and dependent measures.

The dose-response results are consistent with previous studies conducted in this context showing that increases in dosage of stimulants often produce diminishing returns beyond a relatively low dose (Evans et al., 2001; Smith et al., 1998). Depending on the behavioral condition (see discussion below), optimal effects were obtained at doses of

Table 6
Individual Effect Sizes for Single and Combined Treatments

Measure	BMOD alone		Low dose alone		Medium dose alone		High dose alone		BMOD + Low dose		BMOD + Medium dose		BMOD + High Dose	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Point system														
Following activity rules	2.4	3.0	2.0	2.4	3.3	2.5	3.4	2.6	3.8	2.8	5.0	3.4	4.2	3.9
Rule violations	4.5	9.8	4.3	8.5	3.8	6.6	3.7	7.0	5.7	10.1	6.0	9.6	4.2	12.0
Noncompliance	3.7	9.8	2.4	4.0	4.5	10.2	4.2	8.9	4.7	9.9	5.0	10.5	4.7	10.5
Interruption	1.0	5.2	-0.7	11.9	3.9	5.9	3.2	6.7	3.9	4.9	5.0	6.1	4.3	6.6
Complaining	2.9	3.8	1.4	9.8	2.2	3.9	0.5	6.8	3.3	5.4	5.3	5.9	3.3	7.2
Conduct problems	1.5	2.2	1.8	2.3	1.9	2.0	1.8	2.0	2.2	2.2	2.3	2.3	1.7	3.2
Negative verbalizations	5.8	15.7	3.6	7.7	6.5	14.3	5.5	10.6	7.4	14.8	7.8	15.8	6.9	16.3
Classroom														
Seatwork rule violations	8.3	33.5	0.7	47.2	9.8	32.9	9.8	33.0	8.8	33.4	10.9	34.2	9.6	34.0
Seatwork completed	1.2	2.0	2.0	4.5	2.9	5.7	2.3	3.7	3.3	6.0	3.9	5.7	3.2	4.7
Seatwork accuracy	0.0	0.8	0.4	1.0	0.5	0.9	0.5	0.7	0.4	0.8	0.4	0.9	0.4	0.9
Ratings														
Counselor I/O	2.3	3.7	3.0	4.7	4.2	7.2	4.4	6.5	5.1	7.4	6.1	9.1	6.2	10.5
Counselor O/D	1.5	2.8	1.7	3.2	3.2	6.3	4.0	8.1	3.7	6.1	4.8	8.1	4.5	8.0
Counselor Abbrev. Conners	1.2	1.8	1.5	1.9	2.3	2.2	2.6	2.4	2.7	1.7	3.3	2.4	2.7	3.1
Teacher I/O rating	2.2	2.1	1.9	2.6	3.5	2.8	3.4	2.9	4.2	2.9	5.0	3.5	4.5	4.4
Teacher O/D rating	1.6	1.5	1.5	1.6	2.3	1.8	2.5	2.0	2.7	2.0	3.1	2.8	2.7	3.5
Teacher Abbrev. Conners	3.1	2.9	2.2	2.5	4.2	2.6	4.6	3.5	5.4	3.5	6.0	3.6	5.5	4.3

Note. Effect sizes were computed for each participant by taking the mean difference between each treatment and the NBM/placebo (no treatment) condition, divided by the NBM/placebo standard deviation. Abbrev. Conners = Abbreviated Conners Rating Scale (Goyette, Conners, & Ulrich, 1978).

medication that were relatively low—similar to 5 mg or 10 mg of oral MPH per dose. The dose beyond these levels rarely added incremental benefit, a pattern that we have shown with oral preparations in previous studies (Pelham, Aronoff, et al., 1999) and that was obtained with similar methods in one study in regular classrooms (Greenhill et al., 1996). These results suggest that dose may be optimized in the context of behavior modification for many if not most children at lower levels than might otherwise be expected. On the majority (70%) of objective measures, maximal effect was obtained at the lowest dose—particularly in the BM condition—as reported in other studies with adolescents (Evans et al., 2001; Smith et al., 1998). On counselor and teacher ratings, significant incremental medication effects were obtained at the middle dose, but the ratings are within the normative levels even without the increased dose.

Older research has suggested that a 0.15 mg/kg dose of MPH would be pharmacologically effective (Pelham, Bender, Caddell, Booth, & Moorner, 1985; Werry & Sprague, 1974), and the present results confirm this. We have subsequently replicated this result with 0.15 mg/kg IR MPH (Fabiano et al., 2003; Pelham et al., 2003); thus, these results are not specific to the MTS.

Results of the child self-ratings indicate that the children rated themselves as behaving better on days they were medicated. We have found this same pattern of ratings in previous studies, with regard to daily behavior (Pelham, Murphy, et al., 1992), classroom performance (Carlson et al., 1992), and task performance (Pelham, Hoza, Kipp, Gnagy, & Trane, 1997; Pelham, Waschbusch, Hoza, Pillow, & Gnagy, 2001). This finding indicates that children are

generally aware of daily changes in their behavior, as they did behave better when medicated and received more positive feedback about their behavior—although they do not attribute these improvements directly to the medication (Pelham et al., 2002; Pelham, Murphy, et al., 1992).

The results of the parent ratings indicate that behavioral effects were apparent into the evening even though the MTS was usually removed at 3:30 p.m. (earlier on a few days with a few children to reduce side effects). The evening ratings from parents were comparable to those reported with oral long-acting stimulant preparations (Biederman et al., 2002; Pelham, Gnagy, et al., 2001; Wolraich et al., 2001) or with IR stimulants given in the late afternoon (Pelham, Gnagy, et al., 2001; Pelham, Gnagy, et al., 1999).

The results also demonstrate several aspects of the MTS. First, there might be concern that patches would be inappropriate for children with the activity levels and impulse control difficulties that characterize ADHD children. In this sample (as well as our previous ones), very few children took off their patches. The children who did remove patches were those with comorbid conduct problems. It is notable that upon instatement of behavioral contingencies for keeping their patches on, these children did not remove patches for the remainder of the study. Furthermore, the wear characteristics of the MTS have been good, with few patches falling off during the day. This is despite the heat of the summer and the active sports-oriented schedule of the STP, including daily swimming.

A final aspect of the MTS preparation is that the length of dosing would appear to be controllable by parents removing the patch at different times. This flexibility would appear to

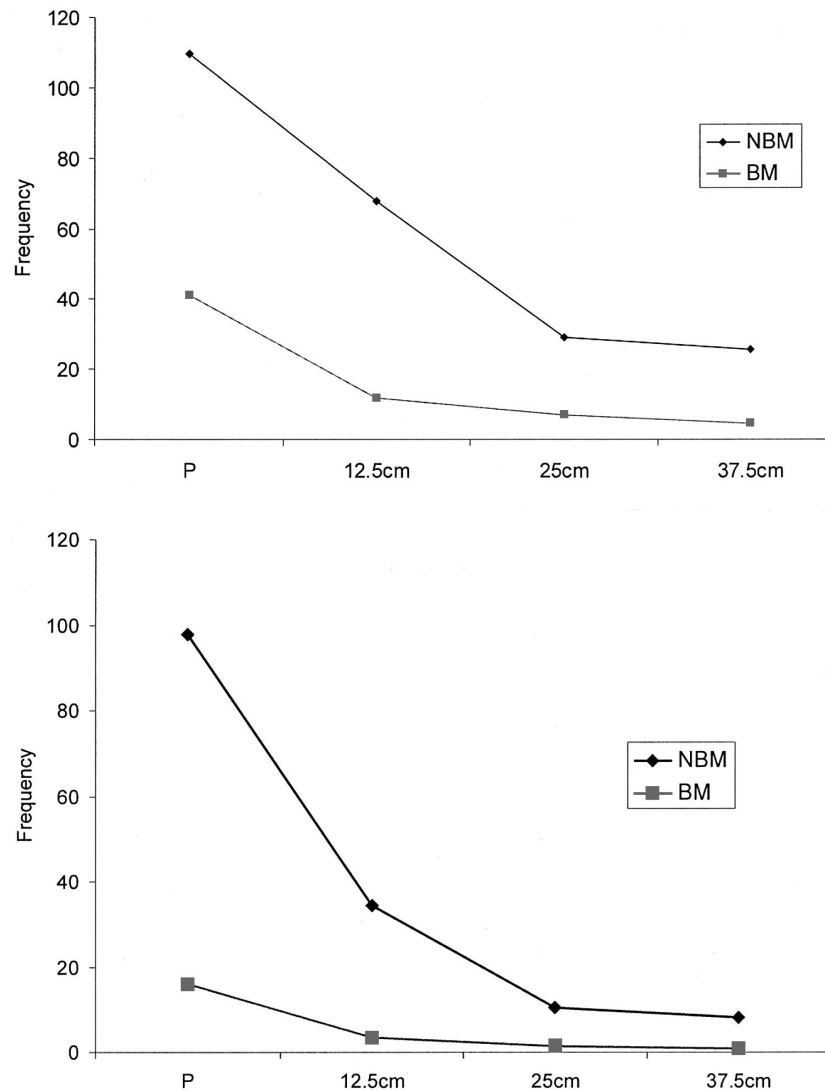


Figure 1. Drug \times BMOD interaction for the measure of negative verbal behaviors (top panel; teasing peers, verbal abuse to staff, swearing) and classroom rule violations (bottom panel). BMOD = behavior modification; NBM = no behavior modification; BM = behavior modification; P = placebo.

be an advantage over long-acting oral formulations in situations when dosing is desired only for a shorter period of time—for a weekend soccer game or for school hours only, for example. Large-scale studies using manipulations of application and removal time will be necessary to test the onset and offset rates of the MTS. Because of the well-documented individual differences in children's response to MPH, physicians and parents should work together to determine the optimal dosing schedule for individual children.

Effects of Behavioral Treatment

The behavioral treatment package used in the STP produced large and significant main effects on nearly all measures in multiple domains across classroom and recreational

settings. These findings replicate our previous crossover studies carried out in the classroom setting (Carlson et al., 1992; Pelham et al., 1993) on academic productivity and rule following. By removing the behavioral treatment from all settings throughout the day, we removed possible BMOD carryover effects from recreational settings occurring on either side of the classroom time that may have minimized BMOD effects in our previous classroom studies. In addition, these findings add to data from our previous treatment withdrawal study (Chronis et al., 2004) that showed very large effects of the STP treatment. As in that study, the present manipulation documented substantial effects of behavior modification on multiple measures of social functioning—the same domains that were improved with medication. The effects of the behavioral treatment

Table 7
Number of Children With Average Side Effects Reported as Moderate or Severe by Parents, Counselors, and Teachers

Side effect	Placebo			12.5 cm ²			25.0 cm ²			37.5 cm ²		
	C	T	P	C	T	P	C	T	P	C	T	P
Tics	0	0	0	0	0	0	0	0	0	1	0	0
Buccal-lingual	0	0	0	0	1	0	0	1	0	2	0	0
Picking	0	0	0	0	0	0	1	0	0	0	0	0
Worry/anxious	0	0	0	0	0	0	0	0	0	1	2	0
Dull, listless	0	0	0	0	0	0	0	0	0	2	3	0
Headache	0	0	0	0	0	0	0	0	0	1	2	0
Stomachache	0	0	0	0	0	0	0	0	0	2	2	0
Crabby	2	5	0	0	0	0	0	1	0	0	2	0
Tearful/sad	1	0	0	0	0	0	0	0	0	1	2	0
Withdrawn	0	0	0	0	0	0	0	0	0	2	3	0
Hallucinations	0	0	0	0	0	0	0	0	0	1	0	0
Appetite loss	3	—	0	9	—	0	14	—	0	22	—	1
Insomnia	—	—	0	—	—	0	0	—	1	—	—	0

Note. N = 25. C = counselor; T = teacher; P = parent. For counselor ratings of appetite loss, ratings were counted moderate or severe if the child was reported as eating less than half of his or her lunch.

package were approximately equivalent to the moderate dose of MTS, depending on the dependent measure. For example, noncompliance, classroom rule violations, and the DRC all showed this pattern. The DRC is arguably the keystone measure in this study, as it is individualized for each child, incorporating only domains of functioning that were identified as critical for that child’s adaptive functioning. The odds ratios (see Table 8) for the probability that children reached their daily goals on placebo BM days versus placebo NBM days show that children were nearly 19 times more likely to succeed on days when BM was in effect.

As shown in Table 6, the magnitude of these behavioral treatment effects supports our post hoc hypothesis regarding the absence of medication effects during the STP component of the MTA—specifically that the behavioral treatment package was so potent that no incremental benefit could be obtained with medication (Pelham et al., 2000). The effects

are also similar in magnitude to those that others have reported in single case studies with behavioral treatments and children with ADHD (Abramowitz, Eckstrand, O’Leary, & Dulcan, 1992; Atkins, Pelham, & White, 1989; Hoza, Pelham, Sams, & Carlson, 1992; Northup et al., 1999; Waschbusch, Kipp, & Pelham, 1998). These studies and others document substantial effects of behavioral interventions on children with ADHD (DuPaul & Eckert, 1997; Pelham et al., 1998). They dramatically contradict recent reviews that have concluded that behavioral treatments are relatively ineffective for ADHD (Jadad, Boyle, Cunningham, Kim, & Schachar, 1999; Miller et al., 1998).

Although children rated themselves as behaving better in the BM condition than the NBM condition, the difference was small and missed significance, although they indicated that the overall behavior of the group was better in the BM condition than in the NBM condition. Notably, many of the children rated themselves as a 5–6 on the 6-point scale

Table 8
Common Odds Ratios for Combined Treatments Relative to Medication or Behavior Modification

Treatment	Common odds ratio	95% confidence interval	p	Homog. test χ^2 (N = 20)	p
Medication added to BMOD					
12.5 cm ² MTS ^a	4.14	2.12–8.06	.000	23.93	.199
25.0 cm ² MTS ^b	10.26	4.94–21.31	.000	23.76	.253
37.5 cm ² MTS ^b	13.26	5.29–32.02	.000	35.87	.016
BMOD added to medication					
Placebo ^c	18.90	2.35–151.79	.006	8.24	.876
12.5 cm ² MTS ^d	10.40	2.90–37.34	.000	12.71	.694
25.0 cm ² MTS ^d	6.04	2.39–15.25	.000	22.21	.137
37.5 cm ² MTS ^e	6.13	2.13–17.61	.001	21.06	.072

Note. The odds ratio indicates the likelihood that the child would earn 75% positive marks on the daily report card if he or she received the specified treatment. Homog. = homogeneity. MTS = methylphenidate transdermal system. BMOD = behavior modification.

^a Common odds ratio and Homog. test χ^2 degree of freedom is 19. ^b Common odds ratio and Homog. test χ^2 degree of freedom is 20. ^c Common odds ratio and Homog. test χ^2 degree of freedom is 14. ^d Common odds ratio and Homog. test χ^2 degree of freedom is 16. ^e Common odds ratio and Homog. test χ^2 degree of freedom is 13.

(with 6 indicating *very well*), and children rated themselves as behaving better than the other children in the group by about 1 point on the scale. These findings appear to support the general self-serving bias and inaccurate self-perceptions that we have found in children with ADHD across a number of studies (Hoza, Pelham, Dobbs, Owens, & Pillow, 2002; Hoza, Waschbusch, Owens, Pelham, & Kipp, 2001; Hoza, Waschbusch, Pelham, Molina, & Milich, 2000; Pelham et al., 2002; Pelham, Murphy, et al., 1992).

There were several individual patterns of behavior that warrant further investigation. As evidenced in Table 2, on some variables, BMOD was less effective than on others, with large standard deviations; Table 6 illustrates that individual effect sizes for the different treatments had wide variability. In the NBM condition, some children showed such dramatic deterioration of functioning that BM had to be reinstated for them to preserve the functioning of the rest of the children's groups. The varying medication conditions in this study make it difficult to draw firm conclusions regarding the reasons behind this deterioration, but analysis of single-subject data from other children in the same summer who were not participants in this study (Coles et al., in press) raises the possibility that peer reinforcement of negative behavior may have played a role, particularly in the children with comorbid conduct problems. Peer reinforcement of negative behavior, also labeled *deviancy training*, (Dishion, McCord, & Poulin, 1999; Onyango et al., 2003) is a group process thought to occur in the absence of effective treatment for children with conduct problems or oppositional/aggressive behavior (93% of children in this study). Such persistence would have minimized the BM effect. For many of these same children, the second NBM week resulted in more negative behavior than did the first week, suggesting that repeated treatment withdrawals might result in inconsistent and therefore nonoptimal BM.

Another, opposite pattern of individual response may have also contributed to lessened effects of BM. When the behavioral treatment was first withdrawn, some children—primarily those without conduct problems/aggression—maintained appropriate behavior for a period of several days before their behavior deteriorated. Finally, some children were maintained in the NBM condition with little behavioral deterioration. We have previously shown in a classroom setting that there is a range of response to BM, as is the case with MPH (Pelham et al., 1993). Because of the small *N* in this study and the limited number of days per condition, we were unable to analyze formally whether baseline individual difference factors predicted these different patterns of response to the behavioral treatment, but future research on this issue is clearly needed.

Effects of Combined Treatments

The final set of findings—and among the most interesting—relate to our combined treatment conditions. This is the first study that has manipulated the entire STP behavioral treatment package, including a no treatment condition, and crossed that condition with varied doses of stimulant medication. The results show more clearly than any previ-

ous study that (a) much lower doses of medication are needed to optimize functioning in the presence versus the absence of BMOD and (b) combined treatment is superior to either treatment alone on the average. As Table 2 and Figure 1 illustrate, either intervention alone produced substantial improvements over no treatment, but the combined treatment brought about the largest change. The results were obtained across virtually all dependent measures in multiple domains and settings, and across both teacher and counselor ratings. As the figure illustrates, one effect of BMOD was to flatten the dose-response curve for medication, such that the impact of the lower doses were dramatically enhanced. The odds ratios depicted in Table 8 illustrate the magnitude of the combined treatment effect for the addition of each condition to the other. Children were 4–13 times more likely to reach their daily individual treatment goals when medicated (vs. placebo) on BM days, and they were 6–10 times more likely to reach their daily goals on BM (vs. NBM) days when medicated. Given that the DRC is an idiographic index of a child's impairments in daily life functioning (Pelham, Fabiano, & Massetti, in press; Pelham et al., 2002), it is arguably the most important measure of treatment response for each child. These odds ratios therefore demonstrate the exceptionally strong benefits that individuals obtain from combined versus unimodal treatment.

The dose-response curves, effect sizes, and odds ratios also illustrate a crucial issue in the discussion of combined psychosocial and pharmacological treatments: The incremental value of a combined treatment depends on the doses of the treatments being examined (Pelham et al., 2000). Adding a low dose of medication to the intensive behavioral treatment resulted in smaller odds ratio than did adding the intensive behavioral treatment to the low dose of medication. This relationship then reverses when higher doses of medication are used. We have previously discussed the importance of considering dose and intensity of separate treatments in combined treatment studies. For example, we have argued that the MTA (MTA Cooperative Group, 1999) confounded dose with modality in concluding that (a) an escalating and therefore high dose of medication was superior to a faded and therefore nonintensive behavioral treatment and (b) the incremental benefits of combined treatments were minimal relative to medication alone (Pelham, 1999). An active behavioral treatment and a low to moderate dose of medication in the MTA may well have yielded equivalence of the behavioral treatment and medication as well as advantages of combined over unimodal treatments.

A further point regarding the dose response curves in each behavioral condition is, as Carlson et al. (1992) found, the low dose of medication produced as much change in the BM condition as the higher doses of medication produced in the NBM condition. On some variables, the effect of even the highest dose of medication in the NBM condition did not surpass the effect of the lowest dose in the BM condition. We have long argued that one of the benefits of combining treatment modalities is that one can produce equivalent improvement in functioning using substantially lower doses of medication. The current results replicate Carlson et al.'s findings and extend them to (a) a recre-

ational setting and (b) a lower dose of medication. The present results show that if a physician or parent desires to keep the dose of medication low for a child, they can obtain that result—a 67% reduction in daily dosage—by instating an in-school behavioral program that is analogous to the one used in this study. Although the STP in its entirety is not widely available, the procedures used in the STP classroom are comparable to those utilized widely in both special education and regular education settings (Fabiano et al., 2001, 2002; Walker, Ramsey, & Gresham, 2003–2004) and can be feasibly implemented as part of Individualized Educational Plans or 504 Plans required for children with ADHD under federal special education law. The STP has been replicated in numerous clinical settings, and its procedures can easily be incorporated into any summer camp setting (Pelham, Fabiano, et al., 2005) so the intervention manipulated in this study can be provided in the community.

There is a lack of information on long-term side effects of stimulant drugs (National Institutes of Health Consensus Statement, 1998). New analyses have shown that the efficacy of the high-dose medication condition in the MTA came with a substantial cost with respect to growth in height and weight (MTA Cooperative Group, 2004). It would therefore appear prudent to take steps to minimize daily and therefore lifetime dose levels if effectiveness can be maintained—an argument for using combined behavioral and stimulant treatments. Because the MTS can be removed when medication effects are no longer needed, it may lend itself well to the goal of minimizing dose levels.

The inclusion of the NBM condition produced results that have implications regarding interpretation of our previous medication studies in the STP context. Although we have always noted that our medication studies reflect the effect of medication in the presence of BM and therefore reflect combined interventions, the studies have rarely been interpreted that way because we have not manipulated BM. The present results show clearly that absolute levels of functioning reached with medication in our previous studies reflected the impact of combined treatment, producing greater response to medication than would have been seen otherwise. We have briefly discussed this possibility in previous studies (Pelham, Gnagy, et al., 2001), but the results of this study clearly demonstrate that this is happening. To the extent that many medication studies are conducted in settings in which programs to manage behavior are in place in the background, this phenomenon may be widespread. For example, behavioral interventions are often used in laboratory settings to place limits on children's behavior on placebo days (Pelham et al., 1995; Swanson et al., 1998). In school settings, classroom behavior management is ubiquitously present as a background (Fabiano et al., 2001, 2002; Walker et al., 2003–2004). Therefore, when clinical trials are conducted in school settings, behavior management is clearly being utilized along with the medication (e.g., Wolraich et al., 2001).

This study has several limitations. A major one is that only one dose of behavioral treatment—an intensive dose—was used, compared with three doses of MTS. As we have

discussed above, the dose of each unimodal treatment influences the effects of a combined treatment. We thus do not know what effects a lower-intensity behavioral intervention—more typical of a clinical behavior therapy intervention carried out by parents and teachers—would have in combination with different doses of medication. The MTA results suggest that such an intervention would also lower the medication dose needed substantially (Vitiello et al., 2001), but it was not manipulated in that study. Pelham, Schnedler, Bologna, and Contreras (1980) also suggested the same with a clinical behavioral intervention, but BM was not manipulated. Studies of combined low-dose medication and low dose BMOD are needed because of the high cost of intensive BMOD (approximately \$3,000 for an STP, including parent training, in Buffalo) and the side effects associated with high doses of medication (MTA Cooperative Group, 2004).

In addition, although significant effects of medication were found on parent ratings, behavioral treatments were not manipulated in the home setting in the present investigation, and we were unable to investigate separate and combined effects of treatments in that setting. There were not enough girls in the sample to analyze them separately, so further study will be necessary to determine whether these results will generalize to girls and beyond the age range studied herein. Finally, participants and staff members could not be blinded to BMOD conditions. This should not make a difference for most of our counselor- and teacher-recorded behavioral frequency counts, as we have documented in this and other studies reliability with independent observers. Furthermore, the classroom measures were product records, which are not liable to be biased.

Summary

In summary, the transdermal MPH preparation showed efficacy in all doses tested, with few reports of side effects and good wear characteristics. The behavioral manipulation in this study allowed for the examination of medication effects in the presence and absence of behavioral treatments. Results showed that behavioral treatment alone was efficacious, and that the effects of behavioral treatment and medication were similar. Finally, optimal treatment effects were observed at very low doses of medication when both treatment modalities were combined.

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