9-9-2021

Tolerance to Psychostimulant Medication Among Children with ADHD

Fiona Macphee
fiona.macphee@seattlechildrens.org

FLORIDA INTERNATIONAL UNIVERSITY

Miami, Florida

TOLERANCE TO PSYCHOSTIMULANT MEDICATION AMONG CHILDREN WITH ADHD

A dissertation submitted in partial fulfillment of the

requirements for the degree of

DOCTOR OF PHILOSOPHY

in

PSYCHOLOGY

by

Fiona Lesley Macphee

2021

To: Dean Michael R. Heithaus
College of Arts, Sciences and Education

This dissertation, written by Fiona Lesley Macphee, and entitled Tolerance to Psychostimulant Medication Among Children with ADHD, having been approved in respect to style and intellectual content, is referred to you for judgment.

We have read this dissertation and recommend that it be approved.

Joseph Raiker

Nicole Schatz

Andy Pham

William Pelham, Major Professor

Date of Defense: September 9, 2021

The dissertation of Fiona Lesley Macphee is approved.

Dean Michael R. Heithaus
College of Arts, Sciences and Education

Andrés G. Gil
Vice President for Research and Economic Development
and Dean of the University Graduate School

Florida International University, 2021

ABSTRACT OF THE DISSERTATION

TOLERANCE TO PSYCHOSTIMULANT MEDICATION AMONG CHILDREN WITH ADHD

by

Fiona Lesley Macphee

Florida International University, 2021

Miami, Florida

Professor William Pelham Jr., Major Professor

Medication is the most commonly received treatment for childhood Attention-Deficit/Hyperactivity Disorder (ADHD). In one U.S. sample, 90% of children with ADHD received medication at some point in their lives (Danielson et al., 2018). Central Nervous System (CNS) stimulant medication is a well-established short-term treatment for childhood ADHD (Pliszka, 2007). However, there is little support in the literature for long-term benefit of psychostimulants. One possible explanation for this lack of sustained effect is the development of tolerance to the drug. The current study aimed to examine possible evidence of short-term tolerance to stimulant medication, methylphenidate (MPH). Additionally, we investigated previous stimulant medication treatment as a potential predictor of developing indicators of tolerance during the study. Overall, results demonstrate that therapeutic effects of stimulant medication on academic productivity and rule following behavior do not significantly dissipate over three weeks among most children with ADHD. There was one exception in that children who had received a high dose of psychostimulant treatment from their community provider prior to the initiation

of the current study showed weakened effects of medication over time as measured by academic productivity but not by rule following behavior.

TABLE OF CONTENTS

I. PORTFOLIO OF RESEARCH PERTAINING TO THE DISSERTATION

My program of research focuses on the evaluation and refinement of interventions for children and adolescents with disruptive behavior. One area I have particularly focused on is multimodal treatment of elementary-aged children with ADHD. That is, the effects of stimulant medication and other therapies as standalone *and* combined treatments for child behavior. My first study in this area examined the effect of combining stimulant medication with common occupational therapy interventions (Macphee et al., 2019) using data collected during the Summer Treatment Program (STP) at FIU. This study used the same methodology as my dissertation study. The resulting manuscript is included in this portfolio alongside another article I wrote summarizing the occupational therapy study and other relevant multimodal treatment evaluations for children with ADHD (Macphee et al., 2016). This research, alongside my clinical research experiences monitoring medication treatment adherence and effects, led me to focus my dissertation on evaluating possible of indicators of tolerance to psychostimulants among children with ADHD. I chose to examine possible tolerance to stimulant medication in my dissertation as a potential explanation for why there are no long-term effects of stimulants documented in the literature, despite their large, acute effects.

II. CHAPTER 1.

THE EFFECT OF WEIGHTED VESTS AND STABILITY BALLS IN COMBINATION WITH AND WITHOUT PSYCHOSTIMULANT MEDICATION ON CLASSROOM OUTCOMES IN CHILDREN WITH ADHD

This manuscript has been published in School Psychology Review, Volume 48, Issue 3, pages 276-289.

Macphee, F. L., Merrill, B. M., Altszuler, A. R., Ramos, M. C., Gnagy, E. M., Greiner, A. R., … & Pelham, W. E. (2019). The effect of weighted vests and stability balls in combination with and without psychostimulant medication on classroom outcomes in children with ADHD. *School Psychology Review,* 48(3), 276-289. doi: 10.17105/SPR-2017-0151.V48-3

Abstract

Current evidence-based, school-based interventions for children with attention deficit hyperactivity disorder (ADHD) include academic intervention, behavioral classroom management, and psychopharmacological intervention. However, some approaches that are commonly used have not been studied in controlled evaluations. The current study is the first rigorous evaluation of the effect of occupational therapy (OT) weighted vests and stability balls on classroom behavior and academic productivity in elementary-age children with ADHD ($N = 64$). The effect of psychostimulant medication and its combination with each of the OT interventions on classroom outcomes was also examined. The study consisted of a 2 (medication: methylphenidate, placebo) × 3 (OT intervention: stability ball, weighted vest, control) within-subjects design and was conducted over a 6-week period in a weekday, 60-min summer classroom. OT intervention was randomized daily within a medication crossover design. Overall, results indicated that medication but not weighted vest nor stability ball interventions resulted in improvement in two key areas of functioning in school settings: following classroom rules and academic productivity.

Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is among the most common mental health disorders during childhood and adolescence with an estimated prevalence rate of 8 to 12% (Visser et al., 2016). Given the high prevalence rate, it is likely that at least two children in each elementary classroom in the U.S. are affected. Children with ADHD experience significant impairment in school settings including behavioral difficulties surrounding the developmentally inappropriate levels of inattention and/or

hyperactivity/impulsivity that characterize the disorder (American Psychiatric Association, 2013).

Elementary age children with ADHD exhibit an array of academic problems in comparison to their peers including lower schoolwork completion, schoolwork accuracy, on-task behavior, and homework performance. Further, children with ADHD perform significantly below their peers across academic subjects (DuPaul & Stoner, 2014; Loe & Feldman, 2007). These children also experience difficulty staying on task, which reduces opportunities to respond to teacher instruction and time to practice academic skills during independent seatwork time (Abikoff, Gittelman-Klein & Klein, 1977; Pfiffner & DuPaul, 2014). In addition to problems associated with inattention, many children with ADHD exhibit impulsive and disruptive behavior in the classroom including high rates of noncompliance with teacher commands and classroom rules (DuPaul & Jimerson, 2014). Serious problems in school functioning and academic achievement persist throughout their academic career due to the chronic nature of the disorder (Raggi & Chronis, 2006). Problems during middle and high school include lower grades, poorer organizational skills, and higher rates of retention (Barkley, Fischer, Smallish & Fletcher, 2006; Kent et al., 2011; Molina et al., 2009; Robb et al., 2011).

School-Based Intervention for Children with ADHD

Decades of school-based intervention research have targeted the behavioral and academic problems associated with ADHD. Currently, the well-established evidence-based treatments for ADHD across settings include academic intervention, behavioral intervention, stimulant medication, and the combination of behavioral and psychopharmacological intervention (Altszuler et al., 2017; DuPaul, Eckert, & Villardo,

2012; Evans, Owens, & Bunford, 2014; Evans, Owens, Wymbs, & Ray, 2018; Fabiano et al., 2009; Jensen et al., 2001; Macphee, Altszuler, Merrill & Pelham, 2017; Pelham & Fabiano, 2008; Pelham, Wheeler & Chronis, 1998). Stimulant medications are the most widely used treatment for children with ADHD. About 75% of children diagnosed with ADHD are prescribed psychostimulants at some point in time (Center for Disease Control and Prevention, 2010). Stimulant medications produce large acute effects on classroom behavior and daily academic productivity (Faraone & Buitelaar, 2010). Studies have also shown empirical support for applications of variations of behavioral classroom management on behavioral and academic productivity outcomes (BCM; DuPaul et al., 2012: DuPaul & Stoner, 2014), which are classroom-wide contingencies based on clearly set rules (e.g., the Good Behavior Game [Barrish, Saunders, & Wolf, 1969]) and more individualized approaches (e.g., Fabiano et al., 2010; Iznardo, Rogers, Volpe, Labelle & Robaey, 2017).

Occupational Therapy Interventions for ADHD in the Classroom: Weighted Vests and Stability Balls

Approximately 10.8% of children with ADHD in special education settings receive occupational therapy (OT) interventions in school settings (Schnoes, Reid, Wagner, & Marder, 2006). Utilization of OT interventions is increasing — New York City public schools spent an estimated $58 million in 2014 on OT, a $20 million increase from just five years prior (Harris, 2015). Similarly, Chicago experienced a 30% increase in OT referrals over five years and Los Angeles a 20% increase over three years (Harris, 2015).

Two OT classroom accommodations, stability balls and weighted vests, have been used for children with ADHD. In a large survey sample ($N = 350$) of school-based OT practitioners, 76.4% reported that they recommend OT weighted vests for children with ADHD (Olson & Moulton, 2004). In a smaller sample ($N = 62$) of general education teachers, 47% reported that they were either currently using or had used stability balls in the past (Kafka & Limberg, 2013). Weighted vests are fitted vests usually weighing 5 – 10% of the child's total body weight. Stability balls are large, inflated rubber balls, on which children sit rather than chairs in the classroom. These interventions are categorized as sensory integration therapies and are theorized to decrease interfering hyperactivity and improve attention and focus (Bader & Adesman, 2014). OT sensory integration therapies include techniques that are proposed to help organize and strengthen sensory processing. Children with sensory processing difficulties are often classified as having Sensory Processing Disorder (SPD). Investigators of SPD have found that sensory processing problems are more common in children with ADHD than in typically developing children (Ghanizadeh, 2011). However, there is a disconnect in the literature as SPD is a common term in speech and OT fields but not in psychology. For example, SPD was not accepted into the most recent Diagnostic Statistical Manual of Mental Disorders (American Psychiatric Association, 2013) due to lack of consensus in the research for diagnosis (Barkley, 2014).

The theory guiding the use of both weighted vests and stability balls stems from the idea that children with ADHD experience sensory problems that conflict with the classroom environment. Weighted vests are proposed to improve the child's sensory modulation while stability balls may alter the environment to allow for increased

movement. Specifically, the theory guiding the use of weighted vests is that deep-pressure stimulation modifies levels of arousal in the central nervous system and thus ameliorates sensory modulation difficulties. This derives from sensory stimulation theory that proposes that the deep-touch pressure input influences the medulla, the thalamus, and finally the somatosensory cortex. Such stimulation is theorized to result in decreased arousal and excitability via down-regulation of the reticular formation (Vandenberg, 2001).

Initial utilization of stability balls in classrooms emerged from sensory modulation authors who proposed that adapting the environment to meet children's needs (e.g., excess movement observed in children with ADHD) may improve classroom performance (Kimball, 1999; Mulligan, 1996) and informal observations that excitable children may be calmed by rocking that can be facilitated by a stability balls (Ayres, 1977). Emerging cognitive literature suggests that excess movement (i.e., hyperactivity) may serve a compensatory function during the use of higher-order cognitive abilities (e.g., working memory) in children with ADHD during task execution (e.g., academic seatwork). Experimental (Rapport et al., 2009) and meta-analytic (Kofler, Raiker, Sarver, Wells, & Soto, 2016) investigations have found that working memory tasks — particularly those with high central executive demands — are associated with increased minor motor activity in individuals with ADHD. These results suggest that movement (that does not reflect avoidance or escape behavior [e.g., leaving the room, crawling under the desk]) may augment cortical under arousal and ultimately facilitate task performance. Follow-up studies offered additional support for this possibility by demonstrating that greater minor motor activity is associated with better cognitive task

performance (e.g., working memory, flanker task) in children with ADHD but not typically developing children (Hartanto, Krafft, Iosif, & Schweitzer, 2015; Sarver, Rapport, Kofler, Raiker, & Friedman, 2015). Collectively, these studies highlight the need for evaluating the utility and effectiveness of interventions such as stability balls, which may allow for minor motor movement (e.g., bouncing) and potentially lead to improvements in task performance and classroom functioning.

Despite the emerging research demonstrating a relationship between cognitive performance and excess activity in children with ADHD, limited applied research is available that examines the effect of weighted vests or stability balls on classroom behavior and productivity among children with ADHD. Moreover, existing studies suffer substantial limitations such as small and/or under-representative samples, subjective measures, and mixed findings. A handful of studies have cited improved on task behavior as associated with wearing weighted vests or sitting on stability balls (Fedewa, Davis & Ahn, 2015; Fedewa & Erwin, 2011; Kercood & Banda, 2010; Lin, Lee, Wen-Dient, & Fu-Yuan, 2014; Olson & Moulton, 2004; Schilling, Washington, Billingsley & Deitz, 2003; Vandenberg, 2001). However, these studies were based on informal therapist observations (Olson & Moulton, 2004) or small sample size (range: 3 to 16 [Collins & Dworkin, 2011; Fedewa et al., 2015; Fedewa & Erwin, 2011; Kercood & Banda, 2010; Schilling, Washington, Billingsley & Deitz, 2003; Vandenberg, 2001]).

An investigation of "Disc 'O' Sit" (an inflatable cushion that is placed on the child's chair) showed significant pre-post improvements on teacher-ratings of executive function, but the sample was comprised of children without a formal ADHD diagnosis (Pfeiffer, Henry, Miller, & Witherell, 2008). One small pilot study (n = 10) of weighted

vests utilized randomization, blinded observations, and an objectively defined measure of on-task behavior, and failed to find improvement when children wore the weighted vests compared to a control condition of vests without any weights (Collins & Dworkin, 2011). A final study indicated a beneficial effect of wearing weighted vests on sustained attention and speed of processing and responding on the Conners Continuous Performance Test (CPT; Conners, 2000) and on-task behavior (Lin, Lee, Wen-Dient, & Fu-Yuan, 2014). However, the study was conducted in a clinic setting rather than classrooms where weighted vests are typically used. Lastly, none of the existing studies manipulated commonly used stimulant medication for ADHD. Some studies did not report children's stimulant medication status (Fedewa et al., 2015; Olson & Moulton, 2004), while others suspended (Fedewa & Erwin, 2011; Kercood & Banda, 2010; Lin et al., 2014) or kept medication constant for the duration of the study (Schilling et al., 2003). Given that over 80% of youth with ADHD are prescribed psychostimulants in a given year (Visser et al., 2016), systematically investigating concurrent use of these medications with other commonly used ADHD interventions is important for the generalizability of the findings (Macphee et al., 2017).

Current Study. To our knowledge, the current study will be the first to examine the contribution of weighted-vest and stability-ball interventions to already well-established interventions for ADHD (i.e., medication) in a controlled classroom setting with a relatively large sample of children diagnosed with ADHD. Weighted vests and stability balls were chosen due to the burgeoning but inconclusive literature surrounding the implementations of these interventions in school settings for children with ADHD. We conducted the current study within a Summer Treatment Program (STP), which is the

optimal setting for studying interventions for children with ADHD in classroom and recreational settings (e.g., Altszuler et al., 2017; Pelham et al., 1990). Two classroom outcomes were examined: classroom rule following and accuracy of academic worksheet completion. The outcome measures capture the most common impairments that youth with ADHD experience in the classroom. Specifically, children with ADHD complete fewer problems and fewer problems correctly when compared to same-aged peers (e.g., Atkins, Pelham & Licht, 1985). Children with ADHD also display high rates of disruptive behavior in the classroom (DuPaul & Jimerson, 2014). These outcomes have been used in numerous previous studies of classroom interventions conducted in the STP setting evaluating the impact of behavior modification and medication (e.g., Carlson, Pelham, Milich & Dixon, 1992; Fabiano et al., 2007; Pelham et al., 1993; Pelham et al., 2005), classroom accommodations (Hart, Massetti, Fabiano, Pariseau & Pelham, 2011; Pariseau, Fabiano, Massetti, Hart, Pelham, 2010), and distractions (Pelham et al., 2011).

We hypothesized that the weighted vests and the stability balls would significantly improve children's rule following behavior and seatwork productivity in the classroom. The stability ball hypothesis was driven by prior experimental research demonstrating a positive relationship between cognitive performance and excess minor motor activity in children with ADHD (e.g., non-task interfering fidgeting [Kofler et al., 2016; Rapport et al., 2009]). Further, the only rigorous study to examine the impact of weighted vests on the behavior of children with ADHD showed improvements in sustained attention when the children wore the vests (Lin et al., 2014). We also hypothesized that implementation of psychostimulant medication would be associated with larger improvements in children's classroom rule following behavior and accurate

classroom work completion than when either of the OT interventions were employed. This was based on the longstanding literature supporting that psychostimulants consistently produce acute and large ameliorative effects on ADHD symptoms and related disruptive behavior for most children with ADHD (Faraone & Buitelaar, 2010; Pelham et al., 2001; Pliszka, 2007).

Method

Participants included 64 children between the ages of 5 and 12 (M = 8.14 years, SD = 1.69) diagnosed with ADHD. Participants were predominantly male (82.8%) and of Hispanic origin (85.7%). Best practice recommendations for assessment and diagnosis were followed (Pelham, Fabiano, & Massetti, 2005). Diagnostic procedures included parent and teacher ratings of DSM-IV symptoms (Disruptive Behavior Disorders Scale [DBD; Pelham, Gnagy, Greenslade & Milich, 1992]), structured parent interview (Diagnostic Interview Schedule for Children IV, computerized version [Shaffer, Fisher, & Lucas, 1998]), and impairment across settings (Impairment Rating Scale [Fabiano et al., 2006]). Two Ph.D. /M.D. level clinicians independently reviewed the files to make a diagnosis for each child who participated in the study. If disagreements related to diagnosis between clinician's arose (e.g., disagreements related to ADHD subtype, presence of co-occurring oppositional defiant disorder [ODD]) a third clinician was consulted, and majority decisions were used as final diagnostic assignment. This occurred in fewer than 5% of the participants included in the current sample. To estimate IQ, children were administered the subtests of Wechsler Preschool and Primary Scale of Intelligence, Fourth Edition (Wechsler, 2012) or the Wechsler Abbreviated Scale of Intelligence, Second Edition (Wechsler, 2011) dependent on the child's age.

Achievement testing included the Word Reading, Numerical Operations, and Spelling subtests of the Wechsler Individual Achievement Test, Third Edition (Wechsler, 2009). See Table 1 for a summary of participant characteristics.

Table 1
Participant Characteristics (N = 64)

Gender (% Male)	82.8
Age *M* (*SD*)	8.1 (1.7)
Ethnicity (%)	
Hispanic or Latino	85.7
Non-Hispanic or Latino	14.3
Race (%)	
Black or African American	6.3
White	90.6
Did not respond	3.1
ADHD Diagnosis (%)	
Combined	67.2
Inattentive	15.6
Hyperactive/Impulsive	17.2
Comorbidities (%)	
ODD	64.1
CD	9.4
WIAT II Word Reading Score *M* (*SD*)	97.1 (19.7)
WIAT II Numerical Operations Score *M* (*SD*)	104.2 (14.6)
WIAT II Spelling Score *M* (*SD*)	98.4 (15.2)
Estimated Full-Scale IQ *M* (*SD*)	98.2 (14.3)

All children were enrolled in a single cohort of a larger, NIMH-funded study examining tolerance to stimulant medication in children with ADHD (MH099030). The parents of 15 of the 79 of the children enrolled in this cohort of the larger study declined participation in the current study. The Western Institutional Review Board approved the larger study. Exclusion criteria for the main study included a Full-Scale IQ below 80, a diagnosis of autism spectrum disorder, currently receiving psychotropic medication for any condition other than ADHD, and a documented intolerability or lack of response to psychostimulant medication. The host institution's Institutional Review Board (IRB)

approved the present study. Participants consented/assented to the main study as well as the current sub-study prior to implementation of study procedures.

Study Design and Intervention Conditions

The study took place in a one-hour classroom that occurred daily over an 8-week STP. OT conditions, stability balls and weighted vests, were randomized daily by classroom across the last 6 weeks of the STP. Medication or placebo was administered for three weeks each, with order counterbalanced across children. The first two weeks of the STP were used to allow the children to become adjusted to the STP. Additionally, the teachers used the first two weeks of the STP to ensure that each child received an appropriate difficulty level of academic work. Finally, medication doses were carefully titrated during the first two weeks of the STP such that each child received an effective dose of medication with minimal side effects during the current study. We investigated if weighted vests and stability balls were effective on 1) academic functioning and 2) behavior in a classroom setting using well-validated measurement tools that were developed to study intervention effects on children with ADHD.

The 64 children in the study were rank ordered according to age and then placed into groups of 12-14 children of similar age. Therefore, each analogue classroom contained comparably aged children similar to a typical elementary school classroom. The sample was split into three sets of these groups to make the age variable used in the current analysis. One teacher and one teacher's aide taught each age group.

Stability Balls

Ball sizes were determined based on children's height. The majority of children sat on 21.6" balls; smaller children sat on 17.7" balls. Additionally, desk height was

adjusted so that children could easily perform his or her seatwork while seated on the ball. In order to control for potential novelty effects, children were given the opportunity to sit on the stability balls during the assent process. Teaching staff also demonstrated for the children how to safely sit on the stability balls. Further, appropriate use of the stability balls was defined as putting forth necessary effort to sit on the ball as a chair and face forward prior to the initiation of the study. Children sat on the stability balls for the entire 60-minute classroom period during the stability ball condition.

Weighted Vests

Children wore vests that comfortably fit their bodies and weighed 5% of their body weight as recommended by previous OT work (Olson & Moulson, 2004; Vandenberg, 2001). Vests included buttons on the front and pockets to hold the customized weights along the inside bottom lining. As with the stability balls, children were given the opportunity to wear the vest during the assent process. Additionally, appropriate use of the weighted vests was defined as keeping the vest buttoned and the weights in the pockets. Identical to the stability ball condition, children wore the weighted vests for the entire 60-minute classroom period during the weighted vest condition. In the control condition, children sat on standard plastic classroom chairs for elementary-aged children and did not wear weighted vests.

Medication

In the first two weeks of the STP, children underwent a brief 9-day trial of 2-3 doses of extended-release methylphenidate (MPH; typically OROS methylphenidate 18 mg, 27 mg, and 36 mg/day) to determine the best dose for each individual child. After investigators reviewed data from the brief trial, the lowest dose that produced substantive

efficacy with minimal side effects was then prescribed for each child for three weeks during the six-week, placebo-controlled, crossover phase of the study. Parents and teaching staff completed side effect ratings to ensure that medication was well tolerated by the children. Order of medication and placebo was randomized on an individual basis (e.g., approximately half of the children in each classroom were in the medication-first or placebo-first condition). Parents were directed to give the medication to each child at home before 7:30 am and to write down on a provided medication card the time their children received the medication. Medication cards were collected from each parent every morning, and if a parent did not provide a medication card, the study nursing staff contacted them. If a parent did not administer the medication, study nursing staff administered the medication at the STP. Therefore, every child who was randomly assigned to medication received medication on assigned days. Classrooms were held from 60 to 225 minutes after the child was administered the medication. The average daily dose was 19.0 mg (*SD* = 4.1), 0.66 mg/kg/day (*SD* = 0.23). Thus, during the classroom hour, the average active medication dose was 0.22 mg/kg (*SD* = .08).

The Background Behavioral Classroom Management

A behavioral management system was consistently in place across study conditions that was comprised of response-cost and reward components. Classroom rules were displayed publicly (e.g., obey adults, stay in assigned seat), and children lost points if they violated any rule. Children earned points for seatwork completion and accuracy. Additionally, children had individualized goals on their Daily Report Card (DRC) related to classroom rule following and academic productivity. Educational staff provided in-vivo feedback to the children on their behavior and seatwork productivity. Points earned

during the classroom period were added to points children earned during recreational periods, and children exchanged points for age-appropriate toys and games on a weekly basis at a "point store." Children who met daily goals on the DRC also earned special weekly activities such as movies, water slides, and video games. Caregivers were also instructed to provide daily and weekly home rewards for children who met their DRC goals.

Dependent measures

Classroom rule violations. Behavioral response was measured as teacher-recorded frequencies of classroom rule violations. Classroom rule violations were typical of those employed in elementary-aged classrooms in the U.S. and included: (1) be respectful of others, (2) obey adults, (3) work quietly, (4) use materials appropriately, (5) remain in assigned seat or area, (6) raise hand to speak or ask for help, and (7) stay on task. The classroom rules were derived from the Classroom Observations of Conduct and Attention Deficit Disorder (Atkins et al., 1985). This approach has been shown in many studies to be reliable and sensitive to effects of medication and classroom interventions within the STP (e.g., Carlson et al., 1992; Fabiano et al., 2007; Pelham, Bender, Caddell, Booth, & Moorer, 1985; Pelham et al., 1990; 1993; 1999ab; 2002; 2005).

Educational staff recorded rule violations specific to inappropriate use of the weighted vests or stability balls in order to evaluate whether the children could utilize the equipment as intended. Appropriate use of stability balls and weighted vests were defined for children prior to implementation of the interventions and were reviewed throughout the study. Appropriate use of the stability balls was defined as putting forth necessary effort to sit on the ball as a chair and face forward. If a child did not put forth effort to sit

on the ball and intentionally rolled away from his or her desk, he or she would receive a rule violation for not remaining in assigned seat or area. If a child used the stability ball for any other purpose (e.g., jumping on the ball or picking up and bouncing the ball), he or she would receive a rule violation for not using materials appropriately. Appropriate use of the weighted vests was defined as keeping the vest buttoned and the weights in the pockets. If a child did not follow these guidelines, he or she would receive a rule violation for not using materials appropriately.

Seatwork productivity. Children completed seatwork in the areas of math, reading, and language arts during a 30-minute period within each classroom and the order of assignment type was randomized by day. All three types of assignments were titrated during the 2 weeks of STP prior to the initiation of the current study such that the difficulty level was appropriate for each child. Specifically, each child's initial assigned work was based on his or her WIAT scores. During those 2 weeks, each child's seatwork accuracy indicated that the initial level was too high or too low, it was adjusted by the teacher to select a level for the rest of the summer that was sensitive to the effects of the manipulations on seatwork productivity. Difficulty levels then remained consistent for the current 6-week study for each child. Additionally, educational staff assigned enough problems to fill the 30-minute seatwork period to prevent ceiling effects of work completion, and this assignment was held constant over the 6 weeks of the study. The resulting seatwork productivity variable was the number of items the child completed correctly across content areas within the 30-minute period.

Treatment integrity and fidelity. Staff attended a weeklong training that included didactic instruction and role-plays with feedback. Weekly quizzes were administered

throughout the STP to monitor staff knowledge of treatment procedures. Specifically, the quizzes presented scenarios of child classroom behavior and the educational staff wrote which parts of the classroom behavioral management system would be employed in response. A master's level educational classroom supervisor scored the quizzes and reviewed them with each educational staff member in order to ensure an understanding of procedures.

The classroom behavioral management system was monitored using an observational treatment integrity checklist form that was completed by one independent observer and that included all treatment components (e.g., each rule violation was marked on a public point board; behavioral feedback was given to children). Each teacher was observed at least four times during the STP, and fidelity checklists indicated that on average 99.6% of the classroom procedures were implemented. Additionally, the teachers implemented the OT interventions on their intended randomized study day 100% of the time.

Missing data. Missingness was low across measures with 4% of main predictor and outcome values missing. All missingness of outcome variables was due to child absences. *t*-tests comparing individuals with missing or non-missing values did not reveal meaningful significant group differences (all *p*s > .05) on all variables including baseline and main outcome measures such that data could be considered missing at random. Baseline variables included IQ, age, gender, ethnicity, race, grade, and ADHD, ODD, CD diagnoses. Item level multiple imputation (Rubin, 1987) was conducted in SPSS 20 using the preferable inclusive approach that included auxiliary variables from baseline (Collins, Schafer, & Chi-Ming, 2001). Ten imputations were performed in order to yield sufficient

statistical power (Schafer, 1999). Results were pooled in PROC MI ANALYZE in SAS 9.4.

Analyses. All outcomes were analyzed using a Poisson regression version of a generalized mixed model to accommodate the non-normal, Poisson distribution of the data and the repeated measures study design (Coxe, West, & Aiken, 2009; Stroup, 2012). Data were analyzed in PROC GLIMMIX in SAS 9.4. Models included the natural log of time spent in the classroom as an offset variable to account for differences in time spent in the classroom (M = 28.87, SD = 3.60) — initial results therefore reflected classroom rule violations and academic items correct per minute. Initial academic productivity estimates were subsequently multiplied by 30 such that model results show estimated effects for the entire 30-minute academic work period. Initial classroom rule violation estimates were multiplied by 60 such that results reflect estimated effects for the entire 60-minute classroom period.

Each model included the following predictors: age group, medication condition, and OT condition. Conduct problems as measured by ODD and CD symptoms from the baseline parent rated DBD were included as a covariate. The two-way interactions between age group and medication, age group and OT condition, and medication condition and OT condition were included. Three-way interactions between age group and OT condition and medication condition were also included. The three age groups were included as categorical predictors (i.e., dummy coded) with the oldest age group as the reference group. There was one teacher for each age group, thus, including age group in the three-way interaction analyses controlled for any teacher effects on the primary

outcome. The OT and control intervention conditions were also analyzed as categorical predictors (i.e., dummy coded) with control condition as the reference group.

Results

Raw means and standard deviations of the outcome variables are presented in Table 2 for ease of interpretation. However, the statistical models utilized estimated means and standard errors, which are presented and discussed below.

Classroom Rule Violations

Neither the stability ball nor weighted vest condition led to statistically significant differences in classroom rule violations when compared to the no OT control condition. The model analyzing classroom rule violations revealed a statistically significant main effect of medication, $b = .78$, $SE = .35$, $t(1446) = 2.24$, $p = .032$ and being in the youngest age group, $b = 1.59$, $SE = .69$, $t(1446) = 2.30$, $p = .024$. Overall, when children received a placebo pill they violated classroom rules twice as often as when they received medication. Additionally, the youngest children violated rules nearly twice as often as the oldest children, regardless of medication or OT condition. No other predictor variables were statistically significant.

Seatwork Productivity

Neither weighted vests nor stability balls were statistically significant predictors of seatwork productivity, but, as with rule violations, there was a general trend of lower productivity when stability balls were used. In contrast, the effect of medication on seatwork productivity was statistically significant, $b = .24$, $SE = .07$, $t(1457) = 3.37$, $p < .001$. Children completed 1.2 times more academic problems accurately when they

received medication compared to placebo. No other predictor variables were statistically significant.

Table 2

Raw Means and Standard Deviations for Outcome Variables

			Placebo			MPH	
Outcome	Age Group	No OT	Stability Ball	Weighted Vest	No OT	Stability Ball	Weighted Vest
Total Rule Violations[a]	All ages[d]	5.37 (9.56)	6.42 (10.52)	5.92 (10.50)	2.64 (5.13)	3.95 (8.25)	2.99 (6.05)
	Youngest[e]	12.65 (13.89)	15.25 (15.11)	14.40 (15.79)	5.89 (7.41)	9.44 (12.83)	6.92 (9.34)
	Middle[f]	3.11 (5.35)	3.63 (6.01)	3.00 (5.05)	1.71 (4.05)	1.93 (4.70)	1.75 (3.56)
	Oldest[g]	1.93 (4.04)	2.32 (2.77)	2.20 (2.80)	1.03 (1.46)	1.68 (2.41)	1.14 (2.00)
Academic Productivity[c]	All ages[d]	52.13 (33.93)	50.19 (33.67)	52.01 (36.33)	59.06 (37.76)	55.95 (37.24)	59.15 (37.68)
	Youngest[e]	34.76 (21.99)	33.77 (18.84)	37.07 (20.64)	37.30 (19.65)	35.43 (22.86)	41.99 (21.14)
	Middle[f]	63.65 (24.57)	59.57 (24.71)	57.50 (25.43)	73.87 (22.43)	69.80 (27.59)	64.63 (24.13)
	Oldest[g]	54.21 (43.00)	53.66 (44.23)	58.22 (49.51)	61.26 (50.70)	58.16 (46.53)	67.10 (51.94)

Discussion

We examined the effects of OT interventions stability balls and weighted vests in a sample of 64 children with ADHD. To the authors' knowledge, this is the first controlled evaluation of the use of stability balls and weighted vests in a controlled classroom setting for children with ADHD. In addition, it is the first study to compare the effects of stability balls and weighted vests to psychostimulant medication and to evaluate the potential interaction of the two modalities. The outcomes examined were the performance of children with ADHD in two key areas of functioning in the school setting widely and traditionally used in this literature — following classroom rules and academic productivity. Four findings are apparent: a) sitting on stability balls did not improve nor adversely affect children's behavioral or academic performance, b) wearing weighted vests also had no effect on these outcomes, c) receiving psychostimulant medication significantly improved both behavior and productivity in the classroom, (d) there were no interactions between medication and the OT interventions, and (e) although younger age in our sample was associated with higher rates of classroom rule violations, this finding did not interact with any of the other findings. Each finding is discussed in turn below.

Results clearly indicate that OT stability balls do not improve classroom rule-following or academic productivity among children with ADHD. Past studies suggested that stability balls for children with ADHD-related behavior led to improved attention. However, the existing literature suffers from small sample sizes, absence of formal ADHD diagnoses, and lack of controlled evaluation (Fedewa & Erwin, 2011; Kercood & Banda, 2010; Pfeiffer et al., 2008; Schilling et al., 2003). Both of the outcome measures utilized in the current study – academic productivity and following classroom rules – are

consistent with the on-task behavior measurements reported by previous studies. For example, a child must complete his or her academic work to stay on task. Our findings add to the previous literature by robustly demonstrating that neither OT intervention improved academic functioning in with ADHD beyond that of the existing classroom management program.

Although previous literature has demonstrated that increased motor activity during tasks is associated with better cognitive task performance among children with ADHD (Hartanto, Krafft, Iosif, & Schweitzer, 2015; Sarver, Rapport, Kofler, Raiker, & Friedman, 2015), the current results indicated that utilizing stability balls as a potential mechanism to encourage more movement in a classroom setting did not extend benefits to classroom productivity. One potential explanation of the lack of improved academic (i.e., cognitive) performance when children with ADHD sat on stability balls may be that the stability balls may have placed excess demands on children who already experience difficulty with self-control. Another explanation may be that the stability balls allowed for so much excess movement that motor activity was no longer task facilitative. However, data on the children's motor activity levels are not available. These possibilities may have overshadowed the potential benefits of the increased motor activity facilitated by the stability balls. Notably, there were many classroom rule violations surrounding using the balls appropriately, which was consistently above 19% and as high as 38% of the total rule violations. Indeed, 14 out of the 35 stability balls utilized for the study were purposefully destroyed by the children (e.g., puncturing the balls with pencils) over the six weeks of the study. Cost of stability balls vary per distributer, but a sample of 10 vendors indicated an average cost of $20 per ball.

Therefore, the high level of stability ball destruction observed in the current study surmounted to an estimated $280 loss. Our findings demonstrate clearly that stability balls should not be routinely recommended as classroom interventions for children with ADHD.

Similarly, the results showed that wearing weighted vests did not lead to a change in classroom rule violations or academic productivity. Thus, there is no added benefit of wearing a weighted vest in a well-managed classroom for a child with ADHD. The results of the current study clarify the mixed findings of the limited literature on weighted vests for children with ADHD. The majority of the extant literature is limited by lack of experimental control, subjective measures (Olson & Moulton, 2004), or small sample size (Collins & Dworkin, 2011; Vandenberg, 2001). One study (Lin et al., 2014) that included a larger sample size and was conducted in a laboratory setting suggested improvement in sustained attention as measured by the CPT-II task (Conners, 2000). However, cognitive laboratory tasks do not translate to tasks placed on children with ADHD in the "real world" settings in which they experience difficulties in daily life functioning in home and school (Rapport, Orban, Kofler & Friedman, 2013). As with the stability balls, the current study results indicate that weighted vests are not an effective intervention for children with ADHD in an ecologically valid classroom setting.

In contrast to our failure to find an effect of the two OT interventions, low doses of psychostimulant medication consistently improved children's rate of following classroom rules and academic productivity across OT and the control conditions. This result is not surprising as the acute effects of psychostimulants on such measures (in the very setting we used) have been documented for decades and shown repeatedly (Carlson

et al., 1992; Fabiano et al., 2007; Pelham et al., 1985; Pelham et al., 1987; Pelham et al., Pelham et al. 1999a; Pelham et al., 1999b; Pelham et al. 2001; Pelham et al., 2005). It is important to note that there was no effect of stability balls or weighted vests regardless of medication condition and no interactions. Thus, findings show that the effect of medication did not mask any potential benefits of the stability balls or the weighted vests. Further, a number of studies in this same setting have shown clear relationships between low doses of medication and behavioral classroom management interventions in the summer classrooms, such that the combination of the low doses of treatments was substantially better than either modality separately (Fabiano et al 2007; Pelham et al, 2005). No similar effect was apparent with the OT interventions and medication in this study.

Finally, the youngest group exhibited significantly more classroom rule violations across conditions than the older age groups. This result is not surprising because younger children with ADHD commonly show higher rates of negative behavior than older children (e.g., Applegate et al., 1997; Dupaul & Stoner, 2014). However, this result did not interact with medication or with the OT interventions. Thus, regardless of the implementation of stability balls or weighted vests in the classroom, young children with ADHD are nonetheless likely to display higher rates of negative behavior than older children with ADHD in the elementary age range.

Limitations

All teachers were blind to medication condition but were necessarily aware of OT condition. It is conceivable that this might have influenced the results. However, there were no differences in teacher implementation of the interventions across OT

conditions, as indicated by the independently observed treatment implementation. It should be noted that interobserver data on reports of fidelity was not available as there was only one observer, which is a limitation of the study.

It is possible that the well-implemented behavioral classroom intervention masked potential beneficial effects of the OT interventions on classroom behavior and work completion. However, even though behavioral classroom management (BCM) was consistently in place, the placebo condition columns in Table 2 show a relatively high rate of negative behavior. Thus, it is unlikely that BCM used throughout the study produced a ceiling effect. Additionally, many previous STP classroom studies have shown significant effects of manipulations (e.g., medication) when BCM was kept consistent (e.g., Pariseau et al. 2010; Pelham et al. 1985; 1990; 1999ab; 2001; 2002).

It is important to note that the analogue classroom in which the study was conducted does not replicate a traditional general education classroom. Data was only collected during independent seatwork completion; therefore, results cannot necessarily be generalized to instructional or active learning classroom settings. At the same time, the vast majority of studies of classroom interventions for ADHD (educational, behavioral, and pharmacological) focus on the setting and tasks we employed. Further and as mentioned above, implementation of DRCs and token economies is not common practice. Therefore, generalizability of the findings may be limited. Our treatment fidelity measurements indicated that the behavioral classroom intervention was consistently implemented. However, we did not collect fidelity data on whether caregivers were providing the daily and weekly home rewards for children who met their DRC goals as instructed. Variability in parents' implementation of this component of the program may

have influenced the child's behavior. However, the within-subject nature of the analysis and the children's random assignment to the various conditions likely attenuated any differential impact of this potential confound on the OT interventions.

No empirical guidelines are available for the length of implementation of weighted vest or stability balls. In this investigation, OT interventions were implemented for 30-minute periods per day for 6 weeks. Some may argue that a longer period of exposure to the OT intervention is necessary. Future controlled evaluations should consider and or manipulate length of exposure and how much weight is used in the weighted vests.

Lastly, the sample was comprised of mostly Hispanic boys with a high rate of co-occurring ODD who were referred to a specialty clinic for children with ADHD, which may limit the generalizability of the findings. The high rate of ADHD and ODD comorbidity makes it difficult to determine whether similar effects would be observed in an ADHD sample without such comorbidity. However, the comorbidity rate in our sample was 64%, which is consistent with the rate observed in the population of children with ADHD (i.e., 40 to 60%; Jensen et al., 2001). The study was conducted in Miami, Florida where 71% of school-aged children are Hispanic (Miami-Dade County Public Schools, 2018). Therefore, although recruitment was not intentionally focused on Hispanic youth, the study sample reflected the demographics of the study location. This can be considered a strength of the study as investigations relating to treatment response for specific ethnic groups are limited within the ADHD treatment literature (Evans et al., 2014) despite academic and social problems being documented among these youth (Bauermeister et al., 2005).

Clinical Implications

The results of the current study clearly demonstrate that OT interventions weighted vests and stability balls do not lead to increased classroom rule following or academic productivity in elementary-aged children with ADHD, and their use in school settings does not appear to be justifiable. Many children with ADHD meet criteria for 504 plans or individualized educational plans and special educational services through Section 504 of the Rehabilitation Act of 1973 and the American with Disabilities Act of 1990 and the Individuals with Disabilities Education Act of 2004, respectively. Thus, all school districts should have established guidelines for implementing evidence-based interventions in classroom settings for children with ADHD. School psychologists are particularly poised to facilitate the implementation of evidence-based practices in school settings (Shernoff, Bearman & Kratochwill, 2017). School psychologists are important members of the interdisciplinary team that designs a child's 504 plan or Individualized Education Plan and can uniquely contribute evidence-based strategies —specifically behavioral classroom management — to the plan. Certainly, occupational therapists are an integral member of the school staff who may facilitate empirically supported intervention alongside individuals such as school psychologists. *Although additional research is of course possible, there is currently no evidence that stability balls and weighted vests lead to improved functioning for children with ADHD in classroom settings*.

The current research supports the cautionary statement released by the American Academy of Pediatrics on the inconclusive research surrounding sensory integration therapy and that such approaches should not be the primary treatment for children with

behavioral disorders such as ADHD (American Academy of Pediatrics, 2012). Rather, efforts should focus on training school staff in the implementation of evidence-based behavioral and academic approaches (Evans, Owens, & Bunford, 2014; Evans et al., 2018; Fabiano et al., 2009; Pelham & Fabiano, 2008).

References

Abikoff, H., Gittelman-Klein, R., & Klein, D. F. (1977). Validation of a classroom observation code for hyperactive children. *Journal of Consulting and Clinical Psychology*, *45*(5), 772–783. http://doi.org/10.1037/0022-006X.48.5.555

Altszuler, A. R., Macphee, F. L., Merrill, B. M., Morrow, A. S., Schatz, N. K., & Pelham, W. E. (2017). Attention-deficit hyperactivity disorder. In J. Piacentini & C. Flessner (Eds.), *Clinical handbook of psychological disorders in children and adolescents: A step-by-step treatment manual*.

American Academy of Pediatrics. (2012). Sensory integration theories for children with development and behavioral disorders. *Pediatrics, 129,* 1186-1189. http://doi.org/10.1542/peds.2012-0876

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders, 5th Edition: DSM-5* (5th ed.). Arlington, VA: American Psychiatric Publishing.

Applegate, B., Lahey, B. B., Hart, E. L., Biederman, J., Hynd, G. W., Barkley, R. A., … Shaffer, D. (1997). Validity of the age of onset criterion for attention-deficit/hyperactivity disorder: A report from the DSM-IV field trials. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*, 1211-1221.

Bader, A. & Adesman (2014). Complementary and alternative medicine for ADHD. In R. A. Barkley (Ed.), *Attention Deficit/Hyperactivity Disorder: A handbook for diagnosis and treatment* (4th ed., pp. 728 - 738). New York, NY: Guilford Press.

Barkley, R. A. (2014). Psychological assessment of children with ADHD. In R. A. Barkley (Ed.), *Attention Deficit/Hyperactivity Disorder: A handbook for diagnosis and treatment* (4th ed., pp. 455–474). New York, NY: Guilford Press.

Barkley, R. A., DuPaul, G. J., & McMurray, M. B. (1990). Comprehensive evaluation of attention deficit disorder with and without hyperactivity as defined by research criteria. *Journal of Consulting and Clinical Psychology*, *58*(6), 775-789. http://doi.org/10.1037/0022-006X.58.6.775

Barkley, R. A., Fischer, M., Smallish, L., & Fletcher, K. (2006). Young adult outcome of hyperactive children: Adaptive functioning in major life activities. *Journal of the American Academy of Child & Adolescent Psychiatry*, 45, 192–202. https://doi.org/10.1097/01.chi.0000189134.97436.e2

Barrish, H. H., Saunders, M., & Wolf, M. M. (1969). Good behavior game: Effects of individual contingencies for group consequences on disruptive behavior in a classroom. *Journal of Applied Behavior Analysis*, 2(2), 119-124. https://doi.org/10.1901/jaba.1969.2-119

Barnard-Brak, L., & Brak, V. (2011). Pharmacotherapy and academic achievement among children with attention-deficit/hyperactivity disorder. *Journal of Child and Adolescent Psychopharmacology*, *21*(6), 597–603. http://doi.org/10.1089/cap.2010.0127

Bauermeister, J. J., Matos, M., Reina, G., Salas, C. C., Martínez, J. V., & Barkley, R. A. (2005). Comparison of the DSM-IV combined and inattentive types of ADHD in a school-based sample of Latino/Hispanic children. *Journal of Child Psychology and Psychiatry, 46*, 166–179. http://doi.org/10.1111/j.1469-7610.2007.01750.x

Cantwell, D. P., & Satterfield, J. H. (1978). The prevalence of academic underachievement in hyperactive children. *Journal of Pediatric Psychology*, *3*(4), 168-171. https://doi.org/10.1093/jpepsy/3.4.168

Carlson, C.L., Pelham, W.E., Milich, R., & Dixon, M.J. (1992). Single and combined effects of methylphenidate and behavior therapy on the classroom performance of children with attention-deficit hyperactivity disorder. *Journal of Abnormal Child Psychology, 20,* 213-232. https://doi.org/10.1007/BF00916549

Center for Disease Control and Prevention (CDC). (2016). *ADHD in young children: Use recommended treatment first*. *Vital Signs*. Retrieved from https://www.cdc.gov/vitalsigns/pdf/2016-05-vitalsigns.pdf

Collins, A., & Dworkin, R. J. (2011). Pilot study of the effectiveness of weighted vests. *American Journal of Occupational Therapy*, *65*(6), 688–694. http://doi.org/10.5014/ajot.2011.000596

Collins, L., Schafer, J. L., & Chi-Ming, K. (2001). A comparison of restrictive strategies in modern missing data procedures. *Psychological Methods*, *6*(4), 330–351. http://doi.org/10.1037/1082-989X.6.4.330

Conners, C. K. (2000). *Conners' Continuous Performance Test (CPT-2) computer program for windows, technical guide, and software manual*. Toronto, ON: Multi Health Systems Inc.

Coxe, S., West, S. G., & Aiken, L. S. (2009). The analysis of count data: A gentle introduction to poisson regression and its alternatives. *Journal of Personality Assessment*, *91*(2), 121–136. http://doi.org/10.1080/00223890802634175

DuPaul, G. J., Eckert, T.L., & Villardo, B. (2012). The effects of school-based interventions for attention deficit hyperactivity disorder: A meta-analysis 1996-2010. *School Psychology Review, 41(4)*, 387-412.

DuPaul, G. J., & Jimerson, S. R. (2014). Assessing, understanding, and supporting students with ADHD at school: Contemporary science, practice, and policy. *School Psychology Quarterly*, *29*(4), 379–384. http://dx.doi.org/10.1037/spq0000104

DuPaul, G. J., & Stoner, G. (2014). *ADHD in the schools: Assessment and intervention strategies* (3rd ed.). New York, NY: Guilford Publications.

Evans, S. W., Owens, J. S., & Bunford, N. (2014). Evidence-based psychosocial treatments for children and adolescents with attention-deficit/hyperactivity disorder. *Journal of Clinical Child and Adolescent Psychology*, *43*(4), 527–551. http://doi.org/10.1080/15374410701820117

Evans, S. W., Owens, J. S., Wymbs, B. T., & Ray, A. R. (2018). Evidence-based psychosocial treatments for children and adolescents with attention-deficit/hyperactivity disorder. *Journal of Clinical Child and Adolescent Psychology*, *47(2),* 157-198. http://doi.org/10.1080/15374416.2017.1390757

Fabiano, G. A., Pelham, W. E., Coles, E. K., Gnagy, E. M., Chronis-Tuscano, A., O'Connor, B. C., … O'Connor, B. C. (2009). A meta-analysis of behavioral treatments for attention-deficit/hyperactivity disorder. *Clinical Psychology Review*, *29*(2), 129–40. http://doi.org/10.1016/j.cpr.2008.11.001

Fabiano, G. A., Pelham, W. E., Gnagy, E. M., Burrows-Maclean, L., Coles, E. K., Chacko, A., … Robb, J. A. (2007). The Single and Combined Effects of Multiple Intensities of Behavior Modification and Methylphenidate for Children with Attention Deficit Hyperactivity Disorder in a Classroom Setting. *School Psychology Review*, *36*(2), 195–216.

Fabiano, G. A., Pelham, W. E., Waschbusch, D. A., Gnagy, E. M., Lahey, B. B., Chronis, A. M., … Burrows-MacLean, L. (2006). A practical measure of impairment: psychometric properties of the impairment rating scale in samples of children with attention deficit hyperactivity disorder and two school-based samples. *Journal of Clinical Child and Adolescent Psychology*, *35*(3), 369–385. https://doi.org/10.1207/s15374424jccp3503_3

Fabiano, G., Vujnovic, R. K., Pelham, W. E., Waschbusch, D. A., Massetti, G. M., Pariseau, M. E., … Volker, M. (2010). Enhancing the effectiveness of special education programming for children with attention deficit hyperactivity disorder using a daily report card. *School Psychology Review*, *39*(2), 219–239.

Faraone, S. V, & Buitelaar, J. (2010). Comparing the efficacy of stimulants for ADHD in children and adolescents using meta-analysis. *European Child & Adolescent Psychiatry*, *19*(4), 353–64. http://doi.org/10.1007/s00787-009-0054-3

Fedewa, A., Davis, M. A. C., & Ahn, S. (2015). Effects of stability balls on children's on-task behavior, academic achievement, and discipline referrals : A randomized controlled trial. *American Journal of Occupational Therapy, 69*(2), 1–9. http://doi.org/10.5014/ajot.2015.014829

Fedewa, A. L., & Erwin, H. E. (2011). Stability balls and students with attention and hyperactivity concerns: Implications for on-task and in-seat behavior. *American Journal of Occupational Therapy*, *65*(4), 393-399. http://doi.org/10.5014/ajot.2011.000554

Fischer, M., Barkley, R. A., Fletcher, K. E., & Smallish, L. (1993). The adolescent outcome of hyperactive children: predictors of psychiatric, academic, social, and emotional adjustment. *Journal of the American Academy of Child & Adolescent Psychiatry*, *32*(2), 324-332. https://doi.org/10.1097/00004583-199303000-00013

Harris, E. A. (2015, February 17). Sharp rise in occupational therapy cases at New York's schools. *New York Times*. New York, NY. Retrieved from https://www.nytimes.com/2015/02/18/nyregion/new-york-city-schools-see-a-sharp-increase-in-occupational-therapy-cases.html?_r=0

Hart, K. C., Fabiano, G. A., Evans, S. W., Manos, M. J., Hannah, J. N., & Vujnovic, R. K. (2016). Elementary and middle school teachers' self-reported use of positive behavioral supports for children with ADHD : A national survey. *Journal of Emotional and Behavioral Disorders*, 1-11, http://doi.org/10.1177/1063426616681980

Hart, E. L., Lahey, B. B., Loeber, R., Applegate, B., & Frick, P. J. (1995). Developmental change in attention-deficit hyperactivity disorder in boys: a four-year longitudinal study. *Journal of Abnormal Child Psychology*, *23*(6), 729-749. https://doi.org/10.1007/BF01447474

Hart, K. C., Massetti, G. M., Fabiano, G. A., Pariseau, M. E., & Pelham, W. E. (2011). Impact of group size on classroom on-task behavior and work productivity in children with ADHD. *Journal of Emotional and Behavioral Disorders, 19*(1)*,* 55-64. http://doi.org/10.1177/1063426609353762

Hartanto, T. A., Krafft, C. E., Iosif, A. M., & Schweitzer, J. B. (2016). A trial-by-trial analysis reveals more intense physical activity is associated with better cognitive control performance in attention-deficit/hyperactivity disorder. *Child Neuropsychology*, *22*(5), 618-626. https://doi.org/10.1080/09297049.2015.1044511

Hicks, T. B., Shahidullah, J. D., Carlson, J. S., & Palejwala, M. H. (2014). Nationally certified school psychologists' use and reported barriers to using evidence-based

interventions in schools: The influence of graduate program training and education. *School Psychology Quarterly*, *29*, 469– 487. https://doi.org/10.1037/spq0000059

Hoza, B., Mrug, S., Gerdes, A. C., Hinshaw, S. P., Bukowski, W. M., Gold, J. A., … Arnold, E. (2005). What aspects of peer relationships are impaired in children with attention-deficit/hyperactivity disorder? *Journal of Consulting and Clinical Psychology*, *73*(3), 411–423. http://doi.org/10.1037/0022-006X.73.3.411

Iznardo, M., Rogers, M. A., Volpe, R. J., Labelle, P. R., & Robaey, P. (2017). The effectiveness of daily behavior report cards for children with ADHD: A Meta-Analysis. *Journal of Attention Disorders*. https://doi.org/10.1177/1087054717734646

Jensen, P. S., Hinshaw, S. P., Swanson, J. M., Greenhill, L. L., Conners, C. K., Arnold, L. E., … Wigal, T. (2001). Findings from the NIMH multimodal treatment study of ADHD (MTA): Implications and applications for primary care providers. *Developmental and Behavioral Pediatrics*, *22*(1), 60–73. http://doi.org/10.1097/00004703-200102000-00008

Johnston, C. (1998, November). The impact of attention deficit hyperactivity disorder on social and vocational functioning in adults. In *NIH Consensus Development Conference on Diagnosis and Treatment of Attention Deficit Hyperactivity Disorder* (p. 81).

Kafta N. & Limberg R. (2013). Surveying teachers about the use of stability balls as an intervention. *Journal of Undergraduate Research at Minnesota State University, Mankato, 13*(3).

Kent, K. M., Pelham, W. E., Molina, B. S. G., Sibley, M. H., Waschbusch, D. A., Yu, J., … Karch, K. M. (2011). The academic experience of male high school students with ADHD. *Journal of Abnormal Child Psychology*, *39*(3), 451–462. http://doi.org/10.1007/s10802-010-9472-4

Kercood, S., & Banda, D. R. (2010). The effects of added physical activity on performance during a listening comprehension task for students with and without attention problems. *International Journal of Applied Educational Studies*, *13*(1), 19–32.

Kimball, J. (1999). Sensory integration frame of reference: postulates regarding change and application to practice. In P. Kramer & I. Hinosjosa (Eds.), *Frames of Reference for Pediatric Occupational Therapy* (2nd ed., pp. 169–204). Philadelphia: Lippincott Williams & Wilkins.

Kofler, M. J., Raiker, J. S., Sarver, D. E., Wells, E. L., & Soto, E. F. (2016). Is hyperactivity ubiquitous in ADHD or dependent on environmental demands?

Evidence from meta-analysis. *Clinical Psychology Review*, *46*, 12-24. http://dx.doi.org/10.1016/j.cpr.2016.04.004 0272-7358

Langberg, J. M., Molina, B. S. G., Arnold, L. E., Epstein, J. N., Altaye, M., Hinshaw, S. P., … Hechtman, L. (2011). Patterns and predictors of adolescent academic achievement and performance in a sample of children with attention-deficit/hyperactivity disorder. *Journal of Clinical Child and Adolescent Psychology 40*(4), 519–531. http://dx.doi.org/10.1080/15374416.2011.581620

Loe, I. M., & Feldman, H. M. (2007). Academic and educational outcomes of children with ADHD. *Journal of Pediatric Psychology 32*(6), 643-654. https://doi.org/10.1093/jpepsy/jsl054

Lin, H.-Y., Lee, P., Wen-Dient, C., & Fu-Yuan, H. (2014). Effects of weighted vests on attention, impulse control, and on-take behavior in children with attention deficit hyperactivity disorder. *The American Journal of Occupational Therapy*, *68*, 149–158. http://dx.doi.org/10.5014/ajot.2014.009365

Macphee, F. L., Altszuler, A. R., Merrill, B. M., & Pelham, W. E. (2017). Improving daily life functioning of children with ADHD: "Just say yes to drugs?" redux. *The Clinical Psychologist,* 70(1), 5-14.

Martinussen, R., Tannock, R., & Chaban, P. (2011). Teachers' reported use of instructional and behavior management practices for students with behavior problems: Relationship to role and level of training in ADHD. *Child & Youth Care Forum, 40*, 193-210. http://dx.doi.org/10.1007/s10566-010-9130-6

Miami-Dade County Public Schools. (2018). *Statistical Highlights 2017-2018.* Retrieved from http://drs.dadeschools.net/StatisticalHighlights/SH1718.pdf.

Molina, B. S. G., Hinshaw, S. P., Swanson, J. M., Arnold, L. E., Vitiello, B., Jensen, P. S.,...the MTA Cooperative Group. (2009). The MTA at 8 years: Prospective follow-up of children treated for combined-type ADHD in a multisite study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *48*, 484–500. http://dx.doi.org/10.1097/CHI.0b013e31819c23d0

Mulligan, S. (1996). An analysis of score patterns of children with attention disorders on the Sensory Integration and Praxis Tests. *American Journal of Occupational Therapy*, *50*, 647–654.

National Council for Accreditation of Teacher Education. (2008). Professional standards for the accreditation of teacher preparation institutions. Retrieved from http://www.ncate.org/Public/Publications/ProfessionalStandards/tabid/508/Default.aspx

Olson, L. J., & Moulton, H. J. (2004). Use of weighted vests in pediatric occupational therapy practice. *Physical & Occupational Therapy in Pediatrics*, *24*(3), 45–60. http://doi.org/10.1300/J006v24n03

Pariseau, M. E., Fabiano, G. A., Massetti, G. M., Hart, K. C., & Pelham, W. E. (2010). Extended time on academic assignments: Does increased time lead to improved performance for children with attention-deficit/hyperactivity disorder? *School Psychology Quarterly*, *25*(4), 236–248. http://doi.org/10.1037/a0022045

Pelham, W.E., Aronoff, H.R., Midlam, J.K., Shapiro, C.J., Gnagy, E.M., Chronis, A.M., … Waxmonsky, J. (1999a). A comparison of Ritalin and Adderall: Efficacy and time-course in children with attention-deficit/hyperactivity disorder. [14 pp.]. *Pediatrics* [On-line], *103.*

Pelham, W. E., & Bender, M. E. (1982). Peer relationships in hyperactive children: Description and treatment. In K. D. Gadow & J. Bialer (Eds.), *Advances in Learning & Behavioral Disabilities* (pp. 365–436). Greenwich, CT: JAI Press.

Pelham, W.E., Bender, M.E., Caddell, J., Booth, S., & Moorer, S. (1985). Methylphenidate and Children with Attention Deficit Disorder. Dose Effects on Classroom Academic and Social Behavior. *Archives of General Psychiatry, 42*, 948-952. http://doi.org/10.1001/archpsyc.1985.01790330028003

Pelham, W. E., Carlson, C., Sams, S. E., Vallano, G., Dixon, M. J., & Hoza, B. (1993). Separate and combined effects of methylphenidate and behavior modification on boys with attention deficit-hyperactivity disorder in the classroom. *Journal of Consulting and Clinical Psychology*, *61*(3), 506–515. http://dx.doi.org/10.1037/0022-006X.61.3.506

Pelham, W. E. & Fabiano, G. A. (2008). Evidence-based psychosocial treatments for attention-deficit/hyperactivity disorder. *Journal of Clinical Child & Adolescent Psychology*, *37*(1), 184–214. http://doi.org/10.1080/15374410701818681

Pelham, W. E., Fabiano, G. A, & Massetti, G. M. (2005). Evidence-based assessment of attention deficit hyperactivity disorder in children and adolescents. *Journal of Clinical Child and Adolescent Psychology, 34*(3), 449–476. http://doi.org/10.1207/s15374424jccp3403_5

Pelham, W.E., Greenslade, K.E., Vodde-Hamilton, M.A., Murphy, D.A., Greenstein, J.J., Gnagy, E.M., … Dahl, R.E. (1990). Relative efficacy of long-acting stimulants on children with attention deficit-hyperactivity disorder: A comparison of standard methylphenidate, sustained-release methylphenidate, sustained-release dextroamphetamine, and pemoline. *Pediatrics, 86*, 226-237.

Pelham, W. E., Gnagy, E. M., Burrows-Maclean, L., Williams, A., Fabiano, G. A., Morrisey, S. M., … Morse, G. D. (2001). Once-a-day Concerta methylphenidate

versus three-times-daily methylphenidate in laboratory and natural settings. *Pediatrics*, *107*(6), E105. https://doi.org/10.1542/peds.107.6.e105

Pelham, W.E., Gnagy, E.M., Chronis, A.M., Burrows-MacLean, L., Fabiano, G.A., Onyango, A.N., Meichenbaum, D.L., Williams, A., Aronoff, H.R., & Steiner R.L. (1999b). A comparison of morning-only and morning/late afternoon Adderall with morning-only, twice daily and three-times daily methylphenidate in children with attention-deficit/hyperactivity disorder. *Pediatrics, 104(6),* 1300-1311. https://doi.org/10.1542/peds.104.6.1300

Pelham, W. E., Gnagy, E. M., Greenslade, K. E., & Milich, R. (1992). Teacher ratings of DSM-III-R symptoms for the disruptive behavior disorders. *Journal of the American Academy of Child & Adolescent Psychiatry, 31(2),* 210-218. https://doi.org/10.1097/00004583-199203000-00006

Pelham, W. E., Gnagy, E. M., Greiner, A. R., Fabiano, G. A.,Waschbusch, D. A., & Coles, E. K. (2017). Summer treatment programs for attention-deficit/hyperactivity disorder. In J. R. Weisz & A. E. Kazdin (Eds.), *Evidence-Based Psychotherapies for Children and Adolescents* (3rd ed., pp. 215–232). New York, NY: Guilford Press.

Pelham, W.E., Hoza, B., Pillow, D.R., Gnagy, E.M., Kipp, H.L., Greiner, A.R., … Fitzpatrick, E. (2002). Effects of methylphenidate and expectancy on children with ADHD: Behavior, academic performance, and attributions in a summer treatment program and regular classroom settings. *Journal of Consulting and Clinical Psychology, 70(2),* 320-335. http://doi.org/10.1037/0022-006X.70.2.320

Pelham, W. E., Manos, M. J., Ezzell, C. E., Tresco, K. E., Gnagy, E. M., Hoffman, M. T., … Morse, G. (2005). A dose-ranging study of a methylphenidate transdermal system in children with ADHD. *Journal of the American Academy of Child and Adolescent Psychiatry*, *44*(6), 522–529. http://doi.org/10.1097/01.chi.0000157548.48960.95

Pelham, W.E., Sturges, J., Hoza, J., Schmidt, C., Bijlsma, J., Milich, R., & Moorer, S. (1987). Sustained release and standard methylphenidate effects on cognitive and social behavior in children with attention deficit disorder. *Pediatrics, 80*, 491-501.

Pelham, W. E., Waschbusch, D. A., Hoza, B., Gnagy, E. M., Greiner, A. R., Sams, S. E., … Carter, R. L. (2011). Music and video as distractors for boys with ADHD in the classroom: comparison with controls, individual differences, and medication effects. *Journal of Abnormal Child Psychology*, *39*(8), 1085–1098. http://doi.org/10.1007/s10802-011-9529-z

Pelham, W. E., Wheeler, T., & Chronis, A. (1998). Empirically supported psychosocial treatments for attention deficit hyperactivity disorder. *Journal of Clinical Child Psychology, 27*, 190–205. https://doi.org/10.1207/s15374424jccp2702_6

Pfeiffer, B., Henry, A., Miller, S., & Witherell, S. (2008). Effectiveness of disc "O" sit cushions on attention to task in second-grade students with attention difficulties. *American Journal of Occupational Therapy*, *62*(3), 274–281. http://doi.org/10.5014/ajot.62.3.274

Pfiffner, L. J. & DuPaul, G. J. (2014). Treatment of ADHD in school settings. In R. A. Barkley (Ed.), *Attention Deficit/Hyperactivity Disorder: A handbook for diagnosis and treatment* (4th ed., pp. 596-629). New York, NY: Guilford Press.

Pliszka, S. R. (2007). Pharmacologic treatment of attention-deficit/hyperactivity disorder: Efficacy, safety and mechanisms of action. *Neuropsychology Review, 17,* 61–72. https://doi.org/10.1007/s11065-006-9017-3

Raggi, V. L., & Chronis, A. M. (2006). Interventions to address the academic impairment of children and adolescents with ADHD. *Clinical Child and Family Psychology Review*, *9*(2), 85-111. https://doi.org/10.1007/s10567-006-0006-0

Rapport, M. D., Bolden, J., Kofler, M. J., Sarver, D. E., Raiker, J. S., & Alderson, R. M. (2009). Hyperactivity in boys with attention-deficit/hyperactivity disorder (ADHD): a ubiquitous core symptom or manifestation of working memory deficits? *Journal of Abnormal Child Psychology*, *37*(4), 521-534. https://doi.org/10.1007/s10802-008-9287-8

Rapport, M. D., Orban, S. A., Kofler, M. J., & Friedman, L. M. (2013). Do programs designed to train working memory, other executive functions, and attention benefit children with ADHD ? A meta-analytic review of cognitive, academic, and behavioral outcomes. *Clinical Psychology Review*, *33*(8), 1237–1252. http://doi.org/10.1016/j.cpr.2013.08.005

Robb, J. A., Sibley, M. H., Pelham, W. E., Foster, E. M., Molina, B. S. G., Gnagy, E. M., & Kuriyan, A. B. (2011). The estimated annual cost of ADHD to the U.S. education system. *School Mental Health*, *3*(3), 169–177. http://doi.org/10.1007/s12310-011-9057-6.

Rubin, D. B. (1987). *Multiple Imputation for Nonresponse in Surveys*. New York, NY: Wiley & Sons.

Sarver, D. E., Rapport, M. D., Kofler, M. J., Raiker, J. S., & Friedman, L. M. (2015). Hyperactivity in attention-deficit/hyperactivity disorder (ADHD): Impairing deficit or compensatory behavior? *Journal of Abnormal Child Psychology*, *43*(7), 1219-1232. https://doi.org/10.1007/s10802-015-0011-1

Schafer, J. L. (1999). Multiple imputation: a primer. *Statistical Methods in Medical Research*, *8*(1), 3–15. http://doi.org/10.1191/096228099671525676

Schilling, D. L., Washington, K., Billingsley, F. F., & Deitz, J. (2003). Classroom seating for children with attention deficit hyperactivity disorder: Therapy balls versus chairs. *American Journal of Occupational Therapy*, *57*(5), 534–541. http://doi.org/10.5014/ajot.57.5.534

Schnoes, C., Reid, R., Wagner, M., & Marder, C. (2006). ADHD among students receiving special education services: A national survey. *Exceptional Children*, *72*(4), 483–496. https://doi.org/10.1177%2F001440290607200406

Shaffer, D., Fisher, P., & Lucas, C. P. (1998). Computerized diagnostic interview schedule for children (CDISC 4.0). *New York: New York State Psychiatric Institute*.

Shernoff, E. S., Bearman, S. K., & Kratochwill, T. R. (2017). Training the next generation of school psychologists to deliver evidence-based mental health practices: current challenges and future directions. *School Psychology Review*, *46*(2), 219-232. https://doi.org/10.17105/SPR-2015-0118.V46.2

Stroup, W. W. (2012). *Generalized linear mixed models: Modern concepts, methods and applications.* Boca Raton, FL: CRC press.

Vandenberg, N. L. (2001). The use of a weighted vest to increase on-task behavior in children with attention difficulties. *The American Journal of Occupational Therapy*, *55*, 621–628.

Visser, S. N., Danielson, M. L., Wolraich, M. L., Fox, M. H., Grosse, S. D., Valle, L. A., … Peacock, G. (2016). Vital Signs : National and state-specific patterns of attention deficit / hyperactivity disorder treatment among insured children aged 2 – 5 Years — United States, 2008 – 2014. *Morbidity and Mortality Weekly Report* (Vol. 65). Retrieved from http://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6517e1.pdf

Wechsler, D. (2009). *Wechsler Individual Achievement Test* (3rd ed.). San Antonio, TX: Pearson.

Wechsler, D. (2011). *Wechsler Abbreviated Scale of Intelligence* (2nd ed.). San Antonio, TX: Pearson.

Wechsler, D. (2012). *Wechsler Preschool and Primary Scale of Intelligence* (4th ed.). San Antonio, TX: Pearson.

Willoughby, M. T. (2003). Developmental course of ADHD symptomatology during the

transition from childhood to adolescence: a review with recommendations. *Journal of Child Psychology and Psychiatry*, *44*(1), 88-106. https://doi.org/10.1111/1469-7610.t01-1-00104

III. CHAPTER 2.

IMPROVING DAILY LIFE FUNCTIONING OF CHILDREN WITH ADHD: MEDICATION, BEHAVIORAL INTERVENTION, OR THEIR COMBINATION – "JUST SAY YES TO DRUGS?' REDUX

This manuscript has been published in The Clinical Psychologist, Volume 70, Issue 1, pages 5-14.

Macphee, F. L., Altszuler, A. R., Merrill, B. M., & Pelham, W. E. (2017). Improving daily life functioning of children with ADHD: "Just say yes to drugs?" redux. *The Clinical Psychologist,* 70(1), 5-14.

Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is a chronic neurodevelopmental disorder with childhood onset characterized by core deficits in attention (e.g., distractibility, disorganization), hyperactivity/impulsivity (e.g., acting without thinking, restlessness) or both (American Psychiatric Association, 2013) that contribute to impairment across home, social, and academic settings (Pelham, Fabiano, & Massetti, 2005). ADHD is one of the most common mental health disorders among children and adolescents with an estimated prevalence rate of 8–12% (Visser et al., 2014), and the vast majority of children with ADHD continue to experience impairment in daily life functioning through adolescence and into adulthood (Barkley, Murphy, & Fischer, 2010). During childhood, children with ADHD experience a variety of impairments including, but not limited to, conflicts with parents, teachers, and other adults often leading to marked caregiver strain (Anastopoulos, Sommer, & Schatz, 2009; Johnston & Chronis, 2014), problems with peers including peer rejection (Hoza et al., 2005; Pelham & Bender, 1982), and low academic achievement and behavior problems in school (DuPaul & Jimerson, 2014; Loe & Feldman, 2007). These problems in daily life functioning mediate of current overall functioning and long-term outcomes in children with ADHD and are therefore the key targets of intervention (Pelham & Fabiano, 2008; Pelham et al., 2005).

Decades of research have identified three evidence-based treatments for ADHD: medication with central nervous system (CNS) psychostimulants (Conners, 2002; Greenhill et al., 2002), behavioral interventions (Evans, Owens, & Bunford, 2014; Fabiano et al., 2009; Pelham & Fabiano, 2008); and the combination of the two (Fabiano

et al., 2007, Pelham et al., 2014). Despite numerous controlled investigations of unimodal and multimodal treatment for ADHD, current treatment recommendations are inconsistent across professional groups and individual clinicians in large part due to disagreements among leading professionals. Current psychiatric recommendations include beginning treatment with medication and increasing dosage, switching medications, or adding a second medication in cases of low response (AACAP Work Group on Quality Issues, 2007). Other groups recommend initial psychosocial intervention with modifications if needed and subsequently adding medication only if response is insufficient (APA Working Group on Psychoactive Medications for Children and Adolescents, 2006). Initiating treatment with both medication and psychosocial supports is also endorsed by the largest advocacy organization for ADHD (http://ww.chadd.org). Most recently, the American Academy of Pediatrics guidelines recommended different treatment sequence strategies dependent on child age with combined treatment recommended across ages for most children (Subcommittee on Attention-Deficit/Hyperactivity Disorder, Steering Committee on Quality Improvement and Management, 2011). The puzzling differences in treatment recommendations may be in part due to mixed and limited research findings (see Fabiano, Schatz, Aloe, Chacko, & Chronis-Tuscano, 2015 for review). However, differences in professional orientation/training appear to play a major part, with psychiatric associations recommending medication first, psychologists recommending behavioral interventions first, and pediatric groups in between. In practice, more than 80% of ADHD youth nationwide are prescribed psychostimulant medication within a given year (Visser et al., 2016) with prescription rates having risen dramatically since 2000 and continuing to rise

(Dalsgaard, Nielsen, & Simonsen, 2013). Further, the vast majority of medicated children do not receive concurrent systematic behavioral interventions (Visser et al., 2016).

Psychopharmacological intervention as the first-line treatment for ADHD recommendations emerged from the widely cited *initial* results of the Collaborative Multimodal Treatment Study of Children with ADHD (MTA), in which behavioral, psychostimulant medication management, the combination of the two, and usual care treatment conditions were compared (MTA Cooperative Group, 1999). The MTA was a large, multisite Randomized Controlled Trial (RCT) implemented by NIMH following several decades of smaller studies showing that behavior therapy, stimulant medication, and the combination of the two produced short-term benefits for children with ADHD. The MTA trial demonstrated that directly following treatment, medication management and the combination of medication and behavioral treatment resulted in significantly fewer ADHD symptoms than behavioral treatment alone, which was equivalent to the community comparison group. Additionally, there was no difference between combined and medication-only treatment in ADHD symptom reduction. The results were widely interpreted as showing that medication, but not behavior therapy, was an effective treatment for ADHD, and that behavioral intervention did not produce incremental benefit when added to medication (MTA Cooperative Group, 1999). The widespread publicity associated with the first MTA publication, and the independent but simultaneous FDA approval of the two long-acting stimulant drugs—Concerta XR (e.g., Pelham et al., 2001) and Adderall XR (e.g., Biederman, Lopez, Boellner, & Chandler, 2002) along with their associated widespread marketing initiatives, drove the increase in the use of stimulants.

However, there were limitations in the design and methodology of the MTA study that limit interpretation of its results (Pelham, 1999). First, 70% of the community comparison group received routine ADHD medication from their own physicians and routine behavioral classroom management from their teachers, altering the interpretation of the equivalence of the behavioral and community comparison groups. Further, medication and behavioral treatment began simultaneously in the combined treatment arm, effectively making it impossible to determine which modality primarily contributed to outcomes. Moreover, both the medication and the behavioral components of the interventions in the MTA were provided at high doses/intensities, and it is not clear whether lower doses would have had similarly beneficial effects with lower risks (i.e., side effects) and lower costs for some or all children. It is plausible that the relatively high doses of medication in the MTA combined treatment group overpowered and therefore minimized the potential incremental benefits of the behavioral treatment. For example, medication decreased opportunities for parents and teachers to address problematic behaviors because they were largely eliminated by the acute effects of medication. Psychostimulant medication has immediate effects that wear off completely after 4 to 12 hours, depending on the formulation, while behavioral treatment (e.g., parent training, teacher consultation) takes time to establish and requires that both parents and children learn skills over time before impacts are apparent. A final but little-known MTA design limitation is that medication was continued through the posttreatment assessments whereas the behavioral interventions had been dramatically reduced 4-6 months before endpoint due to NIMH funding constraints.

Perhaps not surprising given the literature regarding stimulants, 1-year and 2-year follow-ups of the MTA participants showed that the benefits of medication in both the medication alone and in the combined condition dissipated partially (at 1-year) and then completely (at 2-years; Swanson et al., 2002). Further, the 8-year follow-up found no differences between children who had received medication during and continuing after the study versus those who did not (Molina et al., 2009). The authors of the 8-year follow-up noted that "data fail to provide support for long term advantage of medication treatment…for the majority of children…decisions about medication may have to be made on an individualized basis avoiding untested assumption about continuing benefit and using periodic trial discontinuation to check for need and benefit" (Molina et al., 2009, p. 497). Thus, the MTA results ultimately showed that medication had large acute effects but no sustained or residual benefits and is therefore not an effective treatment for ADHD when used as the sole intervention. Whether behavioral treatment or the combination of behavioral and pharmacological interventions would be more effective than medication alone in the long-term was not answered in the study because only ongoing medication treatment was tracked following the year of initial treatment. No information was gathered about whether long-term behavioral treatment or combined treatment was continued and therefore its long-term effect was not evaluated.

Dosing and Sequencing of Psychosocial and Psychostimulant Treatments

Our laboratory group has conducted a series of studies that addressed the questions raised by the results and limitations of the MTA study. These studies have investigated various aspects of sequencing, dosing, and combining behavioral and pharmacological treatment for ADHD to examine the parameters that yield the most

effective treatments for children with ADHD. Our investigations have addressed the effects of (1) combining varying acute doses of each treatment (behavioral and psychostimulant) on multiple outcomes in multiple settings, (2) beginning treatment with one modality (behavioral) and adding the other (medication) for insufficient responders, and (3) comparing the effects of initial treatment modality on outcomes, as well as on the need for and the results of subsequent treatment supplementation both within and across modalities.

The first study in the set involved an analogue summer camp setting, the Summer Treatment Program (STP; Pelham et al., 2010), to evaluate the acute comparative and combined effects of (1) high and low "doses" of behavior modification—that is intensities of behavioral intervention, (2) high and low doses of stimulant medication, and (3) their combination on measures of disruptive behavior and rule violations in classroom and peer-based recreational settings (e.g. sports games)—all compared to each other and to no treatment for elementary-aged children with ADHD (Fabiano et al., 2007; Pelham et al., 2014; Pelham et al., in preparation). That study showed that intensive behavior modification produced very large treatment effects as did high doses of medication, with minimal to no incremental value from adding the other modality. In contrast, low "doses" of one treatment modality produced small to moderate effects but left room for improvement by adding the other modality. As such, the combination of low doses/intensities across modalities resulted in positive outcomes comparable to high doses of either treatment alone with the added benefit of very low rates of medication side effects and a less complex and therefore less costly behavioral intervention. These outcomes were observed across multiple measures in both classroom and peer settings.

Further, children in this study were followed into the subsequent school year without medication and with either no additional psychosocial intervention or with a brief behavioral consultation with parents and teachers (several booster group parent training sessions and a school-home Daily Report Card; Pelham et al., in preparation). Medication was withheld during the school year until and unless a need was indicated on a predefined set of measures. Brief behavioral treatment was sufficient to eliminate or delay the need for concurrent medication for many children (only 53% needed adjunctive medication at school and 43% at home). Children who were receiving the behavioral intervention who needed medication also required substantially lower doses compared to the children who received no behavioral consultation (Pelham et al, in preparation). The beneficial impact of the brief behavioral consultation was especially large in children who had not previously been medicated at school or home. Children who had taken medication prior to the study were more than twice as likely to need it during the school year, despite not differing from previously medication naïve children on any demographic or diagnostic variables.

These studies showed that low dose treatments were sufficient for many children, and they suggested that behavioral treatment could eliminate or minimize the need for medication—especially if it was provided prior to medication. A subsequent study extended these findings in the first application of a Sequential Multiple-Assignment, Randomized Trial (SMART) in clinical psychology (Pelham et al. 2016). Children were randomly assigned to begin treatment with a low dose of medication (.15 mg/kg methylphenidate twice daily) or a low intensity behavioral intervention (a school-home Daily Report Card and 8 sessions of group behavioral parent training). Children who

responded insufficiently at monthly assessments were re-randomized to receive either a higher dose of the original modality or to have the other modality added to their treatment regimen. Thus, the study enabled us to ask which was the best initial treatment and what was the best additional treatment modality for initial poor responders. Regarding the question of sequencing the interventions, initiating treatment with behavioral supports resulted in significantly and substantially lower levels of direct observations of negative classroom behavior—the primary outcome measure—compared to initiating treatment with medication. That is, 33% of the children who began with the low dose behavioral intervention needed no further treatment at school for the rest of the school year. Moreover, adding medication when children were insufficiently responsive to initial behavioral treatment resulted in better outcomes across multiple domains than did adding behavioral treatment secondary to medication for insufficient responders (Pelham et al., 2016). Further, the parents of children who began treatment with medication but were insufficient responders and subsequently assigned to behavioral treatment attended only 20% of parent training sessions compared to those who began with behavioral treatment, who attended nearly 80% of the assigned sessions. Finally, this study included an analysis of the relative costs of the treatment strategies. In contrast to the widely held notion that medication is the most cost-effective treatment for ADHD, in our study beginning treatment with a low intensity behavior modification consisting of large-group parent training cost $700 less over the school year than did initiating treatment with medication (Page et al., 2016). The savings in medication costs for families beginning treatment with behavior therapy (i.e., the delay in starting or never initiating medication)

completely offset the additional costs of the masters-level therapists providing the behavioral intervention.

Extension to Understudied Domains and Interventions

Our most recent studies have examined efficacy of combined treatments versus medication and behavioral interventions alone in ameliorating peripheral, functional impairments in understudied domains—(1) evening homework time, (2) sports skills development, (3) Occupational Therapy (OT) interventions in the classroom, and (4) innovative academic curricula. Each of these studies were conducted in the STP setting with 5–12-year-olds with ADHD and the psychostimulant methylphenidate was used as the medication manipulation. We discuss each below.

The homework study evaluated the effect of unimodal and combined treatments on homework problems (n=75; Merrill et al., 2017). Specifically, the behavioral intervention, which was provided to half of the families (the other half received training after the summer), was a homework-focused behavioral group parent training, consisting of 2 hour-long evening sessions for 2 weeks, adapted from Power and colleagues' program (Power et al., 2012) with a Daily Report Card targeting homework completion and accuracy. Additionally, half of the children received psychostimulant medication for three weeks while the other half received placebo, and then these groups crossed over. This combination allowed for a between subjects examination of the effect of behavioral parent training, a within-subjects analysis of medication, and the ability to investigate the incremental benefit of combining psychosocial and medication treatments.

Children's objective homework performance (completion and accuracy) and parent-reported homework problems were evaluated. No effects were found on parent-

report measures. However, behavioral parent training and a Daily Report Card produced significant improvements on objective measures of homework completion and accuracy across subject areas (math and reading). The salutary effects of the behavioral treatment were, on average, the equivalent of improving homework grades from an F to a C—an enormous effect. Medication resulted in little to no benefit on homework performance, and the addition of medication to behavioral treatment provided no incremental improvement above behavioral treatment alone. These results are somewhat surprising, given that for the past 16 years the pharmaceutical companies that market Concerta and Adderall XR have advertised to parents (and pediatricians) the benefits of their long-acting medications at homework time. In contrast, our results demonstrate that teaching parents how to structure and oversee homework should be the primary recommendation for homework problems among children with ADHD. There is no evidence that medication improves homework performance in this population.

Another study aimed to investigate the unique and combined effects of stimulant medication and skills training on one critical area of daily life functioning in children with ADHD: peer relations in the context of youth sports (O'Connor et al, 2014). The STP has been developed over more than three decades to focus on the domain of peer relations—arguably the most deficient and most important to long term outcomes in children with ADHD (Pelham et al., 2010; Pelham & Bender, 1982). Three decades ago, our group published a study (Pelham et al, 1990) showing that medication facilitated on-task behavior in children with ADHD in the field during a baseball game. However, that study also showed that while it aided attention to task, medication did not benefit baseball skills. Nonetheless, that study was and remains widely cited among physicians as

justifying medicating children with ADHD for 12 hours daily and for 7 days per week to cover the times when they engage in sports with other children. The present study was designed to investigate whether sports skills training can improve children with ADHD's functioning and whether concurrent medication facilitates that training. The study (Altszuler et al., 2017) consisted of a 2 (medication, placebo) x 2 (sports training: instruction and practice: recreational play) between-groups design and lasted for a 3-week period. Sports training was conducted with a novel sport, badminton, to limit previous sport knowledge and to differentiate it from concurrent sports training that occurred within the STP. Results indicated that, overall, brief sports training produced the largest magnitude effects on the sports-related outcomes, including observed and counselor-rated sports skills, knowledge, game awareness, effort, frustration, and enjoyment. Combined intervention—that is the incremental benefit of medication beyond the direct skills training—only demonstrated benefits on observed rule following behavior and counselor-rated sportsmanship but not on sports skills or attention during the games. These results, combined with the fact that the majority of youth recreational activities take place in the evenings and on weekends, which may be important times for children to be unmedicated in order to minimize sleep and growth-related side effects, indicate that skills training, rather than medication alone, should be used in conjunction with behavioral intervention targeting negative behaviors to teach sports to youth with ADHD.

As further evidence for the effectiveness of behavioral intervention, in this study, consider the results for attention to task during the games. In the Pelham et al. (1990) baseball study, medication had a beneficial effect on children's attention to the ongoing

game. In order to measure attention during that study, we developed a procedure for asking children about their awareness of/attention to the game that we named "attention check questions." For example, the shortstop might be asked "where should you throw the ball if is hit to you?" In order to answer the question correctly, the child needs to know how many people are on base and where they are, how many outs there are, and where the best play is—that is, he or she needs to be paying attention to the game. In the 1990 Pelham study, we were impressed that the children's ability to answer such questions improved over the 4-day study over and above the effects of medication, indicating that asking the questions prompted the children to pay better attention during the games. Since that study, "attention checks" have been incorporated in the point system that is implemented across all aspects of the recreational activities in the STP, and children are rewarded with points for correctly answering attention check questions. In the 2017 Altszuler study, in contrast to the 1990 study, there was no effect of medication on the attention check measure presumably because the behavioral point system enhanced attention beyond what medication could improve—further indication of the potency of the behavioral intervention/skills training in the current study. It is important to note that children's behavior is an essential part of performance during sports activities. In the 2017 Altszuler study, an intensive behavioral intervention was present in both the training and recreational play condition. However, as our other studies suggest (e.g., Pelham et al., 2014), if behavioral intervention is less intensive than is present in the STP, medication may be a useful adjunct for children who display *very elevated* rates of negative behavior during recreational activities.

Another primary setting where children with ADHD experience impairment is in the school classroom, and our latest two studies have focused on this setting. As cited above, evidence strongly supports that psychostimulant medications produce acute benefits in classroom behavior (i.e., rule following, compliance, disruptive behavior) and academic productivity (amount of assigned seatwork completed) among children with ADHD. Additionally, behavioral classroom management (BCM) is well-established treatment for children with ADHD (DuPaul, Eckert, & Vilardo, 2012). Despite the widespread availability of these well-established classroom interventions, classroom supports that are far less studied are commonly implemented with children with ADHD in elementary schools. For example, 10.8% of children with ADHD in special education receive OT as part of their 504 or IEP plans (Schnoes, Reid, Wagner, & Marder, 2006). OT is likely employed with many other children with ADHD, but unless the children have an identified accommodation, statistics on the frequency of use are not available. A recent article in the New York Times revealed that New York City public schools spent up to $58 million per year on OT, a $20 million increase from just five years prior. Other major cities such as Chicago experienced a 30% increase in OT referrals over five years and Los Angeles a 20% increase over three years (Harris, 2015). Unfortunately, despite its widespread use in schools, OT lacks conclusive empirical support for improving behavior and academic functioning among children with ADHD (Bader & Adesman, 2015).

We conducted the first well-controlled evaluation of OT in a 6-week study in an STP analogue classroom (n=64) to address this question (Macphee et al., 2015). Children received either psychostimulant medication or placebo for three weeks with a crossover

for the following 3 weeks. The study layered two common OT accommodations used with elementary-aged children with ADHD—stability balls and weighted vests—with BCM components of the STP classroom that were consistent throughout the study. OT condition was randomized and counterbalanced across days using block randomization within each medication crossover period such that each child received each OT intervention for 4 separate classroom periods with placebo and 4 with medication. Children also spent 4 periods in the control condition (sitting on regular classroom chairs) with placebo and 4 periods with medication. Dependent measures were frequency counts of classroom rule violations and completed seatwork in the general areas of math, reading, and language arts. Seatwork periods lasted for 30 minutes and the order of assignment type was randomized by day. Thus, this design allowed for a within-subject analysis. This design and dependent measures have been utilized in many studies of behavioral and pharmacological interventions in ADHD and is well-validated (e.g., Fabiano et al., 2007). Results indicated that weighted vests did not impact classroom behavior (i.e., rule violations) regardless of whether the children received medication or placebo. Conversely, children completed significantly less seatwork when wearing the weighted vests, especially when receiving placebo. The stability ball intervention negatively impacted both the children's classroom behavior and their academic productivity. The adverse effect of the stability ball intervention on behavior was more pronounced when children received placebo. The results of this study document very clearly that two of the mostly commonly employed OT interventions for ADHD in school settings—stability balls and weighted vests—have either no benefits or adverse effects for children with ADHD in classroom settings when compared to sitting in regular desks

and chairs. Unfortunately, the vast majority of daily classroom 504 and Individualized Education Plans (IEP) accommodations that are implemented for children with ADHD have either not been studied or have been shown to lack evidence for classroom behavioral or academic improvements. The same state of affairs exists with respect to other non-evidence-based interventions in child mental health, e.g., homeopathic remedies (Bader & Adesman, 2015; Waschbusch & Hill, 2003) that warrant future systematic evaluations in order for the field to ensure children with ADHD are receiving the most effective treatments.

The last study we will discuss addressed the longstanding question of whether stimulant medication benefits academic achievement in children with ADHD (Morrow et al., 2014). Although stimulant medication improves classroom behavior and academic productivity, it has never been shown to have a salutary effect on academic achievement. Since achievement is one of the greatest deficits in ADHD and one of the most important mediators of outcome, it is critical to assess. The few studies that have examined achievement over the period of more than 1 school-year show that meaningful benefits of medication are not detected on such measures (Barnard-Brak & Brak, 2011; Loe & Feldman, 2007). However, there are many reasons why end-of-the-year standardized achievement scores may not be sensitive to interventions. An alternative approach that has not been attempted to date is to ask whether medication has a beneficial effect in a far more controlled setting over a shorter period of time but one in which meaningful gains in the acquisition of academic knowledge in a classroom setting can be ascertained. We set out to evaluate whether medication would facilitate the acquisition of academic content in three areas—social studies, science, and vocabulary building. Again in our

STP classroom context, we systematically evaluated the effect of psychostimulants on genuine indices of classroom learning over a 6-week period and the children were randomly assigned to receive medication or a placebo for 3 consecutive weeks, with crossover for the final 3 weeks.

Two evidence-based interventions using state-of-the-art instructional approaches and curriculum that were designed to be taught in 3-week segments were employed in the classroom by certified special education teachers: Content-Area Literacy Instruction (CALI; Connor, 2013) and vocabulary instruction. CALI consisted of lesson plans and worksheets that were developed to improve students' academic knowledge as well as their ability to learn from expository text. The vocabulary lessons included explicit, i.e., teaching word definitions, and implicit instruction, i.e., teaching words in context (National Reading Panel, 2000; Nash & Snowling, 2006, Clark et al., 2010). Children received 60 minutes of instruction per day, split into 30 minutes of CALI and 30 minutes of vocabulary instruction. Children received instruction at the grade level just above the level they finished (e.g., a child who just completed second grade before the summer program was taught third grade science) unless Weschler Individual Achievement Test scores were elevated, in which case children received instruction on the grade two levels above the level they just finished. Children received two different but grade-level-equivalent units of each learning intervention within the crossover medication design such that each child received science, social studies, and vocabulary instruction for 3 consecutive weeks with medication and for 3 consecutive weeks with placebo. The BCM component of the STP classroom was constant throughout the study.

Results indicated very large gains in achievement from the evidenced-based instructional modules, with very large effect sizes between pre- and post-curriculum-based tests. However, the improvements in knowledge occurred regardless of whether children received the academic instruction in conjunction with psychostimulant medication or placebo. In summary, the results strongly suggest that if teachers are implementing an evidence-based curriculum in which they have been trained, medication will not have any incremental benefits on academic achievement. The failure of medication to show gains in achievement over years may reflect these results or they could be present because teachers are not using evidence-based instructional practices, and medication also has no effect on poor instruction and curriculum. In either case, medication does not appear to be a useful intervention with children with ADHD with the often concurrent academic difficulties.

Conclusions

Our group has worked over the past three-plus decades to develop and evaluate evidence-based treatments for children with ADHD mostly in the elementary school ages. We have also completed investigations in younger and older ages of children, and the results have been similar to those reviewed. This review of our latest set of studies extends the basic work that we had previously done showing that behavioral treatments, stimulant medications, and their combination confer benefits for children with ADHD in classroom, home, and peer settings. The present results extend those studies to a new and refined set of dependent measures and show that dosing and sequencing of treatments and the nature of the psychosocial and psychoeducational interventions impact outcomes. To our knowledge, the studies presented above are the first controlled studies to examine a

number of questions previously unanswered in the field: First, do the order and dose of behavioral and pharmacological treatment for ADHD influence the effectiveness of and costs of the treatments and their combination? Yes—(a) low dose treatments can be combined to yield an intervention as effective as either treatment at a high dose and with fewer side effects and lower cost, but (b) but a third of children with ADHD can be adequately treated with behavioral intervention alone in school settings and as many as two-thirds at home, and (c) starting intervention with a behavioral treatment rather than medication is far more effective than beginning with medication. Second, does long-acting psychostimulant medication improve homework completion and accuracy for children with ADHD as so widely advertised by pharmaceutical companies and believed by pediatricians? (No, it does not). And does medication increase the clear benefit of established behavioral interventions in that domain? (No, it does not). Third, do medication and behavioral treatment improve the acquisition of knowledge and skill in learning a new sport in children with ADHD? (No, medication does not, but yes, behavioral interventions do) and are there benefits to a combined intervention in this context? (No, there are not). Fourt, is OT in the form of stability balls and weighted vests an effective intervention in schools for ADHD? (No, it is not). And fifth, does stimulant medication have a beneficial effect on the learning of academic skills/content in children with ADHD? (No, it does not).

Many questions remain regarding the effectiveness of treatments for children with ADHD, and the primary one is whether the existing interventions improve adult outcomes. We know from multiple long-term outcome studies that stimulants alone confer no long-term benefit. Unfortunately, there are not yet controlled studies of the

long-term benefit of behavioral interventions or combined interventions, and those are sorely needed. Another question is what are the mechanisms that underlie the effects of behavioral, pharmacological, and combined treatments and can an understanding of the mechanisms improve the effectiveness of the interventions?

Finally, we should like to make a point regarding the outcome measures in all of our studies. We do not measure DSM symptoms of ADHD as primary outcomes of treatment in our research or clinical practice and have not for several decades. The literature is quite clear that the important variables to treat in ADHD are the problems in daily life functioning—that is the impairments—that are associated with ADHD. As we have noted above, these constitute the major problems for which children with ADHD are referred for treatment and the major mediators of long-term outcomes (Pelham & Fabiano, 2008; Pelham, Massetti, & Fabiano, 2005), and they should be the focus of treatment. Our laboratory's use of the DSM symptoms of ADHD ends with the intake from which a diagnosis is currently required for a variety of administrative functions (e.g., eligibility for special education in school settings, reimbursement from insurance for treatment in community settings). We encourage others to adopt this approach in their work with children with ADHD.

We hope that this brief review of our recent research has been useful to the readers of The Clinical Psychologist, and we are grateful for the opportunity to have contributed to Division 12's efforts in evidence-based practice. If this article prompts others to change the way they are treating children with ADHD, training others to do so, or if it stimulates ideas for future research in ADHD or other areas of clinical psychology, we will be pleased to have contributed to those outcomes.

References

AACAP Work Group on Quality Issues (2007). Practice parameter for the assessment and treatment of children and adolescents with attention deficit/hyperactivity disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 46*, 7: 994-921. doi: 10.1097/chi.0b013e318054e724

APA Working Group on Psychoactive Medications for Children and Adolescents (2006). Report of the working group on psychoactive medications for children and adolescents. Psychopharmacological, psychosocial, and combined interventions for childhood disorders: Evidence base, contextual factors, and future directions. Washington, DC: American Psychological Association.

Altszuler, A. R., Morrow, A. S., Merrill, B. M., Bressler, S., Macphee, F. L., Gnagy, E. M., … Pelham, W. E. (2017). The Effects of Stimulant Medication and Training on Sports Competence Among Children With ADHD. *Journal of Clinical Child & Adolescent Psychology*, *0*(0), 1–13.

Anastopoulos, A. D., Sommer, J. L., & Schatz, N. K. (2009). ADHD and family functioning. *Current Attention Disorders Reports*, *1*, 167–170.

American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders, 5th Edition: DSM-5* (5th ed.). Washington, D.C: American Psychiatric Publishing.

Bader, A., & Adesman, A. (2015). Complementary and alternative medicine for ADHD. In R. A. Barkley (Ed.), *Attention Deficit/Hyperactivity Disorder: A handbook for diagnosis and treatment* (4th ed., pp. 728–238). New York, NY: Guilford Press.

Barkley, R. A., Murphy, K. R., & Fischer, M. (2010). *ADHD in adults: What the science says*. New York, NY: Guilford Press.

Barnard-Brak, L., & Brak, V. (2011). Pharmacotherapy and academic achievement among children with attention-deficit/hyperactivity disorder. *Journal of Child and Adolescent Psychopharmacology*, *21*(6), 597–603.

Biederman, J., Lopez, F. A., Boellner, S. W., & Chandler, M. C. (2002). A randomized, double-blind, placebo-controlled, parallel-group study of SLI381 (Adderall XR) in children with attention-deficit/hyperactivity disorder. *Pediatrics*, *110*, 258–266.

Coles, E., Fabiano, G., Pelham III, W. Burrow-MacLean, L, Hoffman, M., Gnagy, E., ... & Pelham, W. The effect of behavioral intervention on the need for and use of medication in children with ADHD: A randomized controlled trial in school settings. Manuscript in preparation.

Conners, C. K. (2002). Forty years of methylphenidate treatment in Attention-Deficit/Hyperactivity Disorder. *Journal of Attention Disorders*, *6*(1), S17–S30.

Connor, C. M. (2013). Intervening to support reading comprehension development with diverse learners. In B. Miller & L. E. Cutting (Eds.), *Unraveling the Behavioral, Neurobiological and Genetic Components of Reading Comprehension: The Dyslexia Foundation and NICHD* (pp. 222-232). Baltimore: Brookes.

Dalsgaard, S., Nielsen, H. S., & Simonsen, M. (2013). Five-fold increase in national prevalence rates of attention-deficit/hyperactivity disorder medications for children and adolescents with autism spectrum disorder, attention-deficit/hyperactivity disorder, and other psychiatric disorders: a Danish registe. *Journal of Child and Adolescent Psychopharmacology*, *23*(7), 432–9.

DuPaul, G., Eckert, T.L., & Villardo, B., DuPaul, G. J., Eckert, T. L., & Vilardo, B. (2012). The effects of school-based interventions for attention deficit hyperactivity disorder: A meta-analysis 1996-2010. *School Psychology Review, 41*(4), 387-412.

DuPaul, G. J., & Jimerson, S. R. (2014). Assessing, understanding, and supporting students with ADHD at school: Contemporary science, practice, and policy. *School Psychology Quarterly*, *29*(4), 379–384.

Evans, S. W., Owens, J. S., & Bunford, N. (2014). Evidence-based psychosocial treatments for children and adolescents with attention-deficit/hyperactivity disorder. *Journal of Clinical Child and Adolscent Psychology*, *43*(4), 527–551.

Fabiano, G. A., Pelham, W. E., Coles, E. K., Gnagy, E. M., Chronis-Tuscano, A., O'Connor, B. C. (2009). A meta-analysis of behavioral treatments for attention-deficit/hyperactivity disorder. *Clinical Psychology Review*, *29*(2), 129–40.

Fabiano, G. A., Pelham, W. E., Gnagy, E. M., Burrows-maclean, L., Coles, E. K., Chacko, A., … Robb, J. A. (2007). The single and combined effects of multiple intensities of behavior modification and methylphenidate for children with attention deficit hyperactivity disorder in a classroom setting. *School Psychology Review*, *36*(2), 195–216.

Fabiano, G. A., Schatz, N. K., Aloe, A. M., Chacko, A., & Chronis-Tuscano, A. (2015). A Systematic Review of Meta-Analyses of Psychosocial Treatment for Attention-Deficit/Hyperactivity Disorder. *Clinical Child and Family Psychology Review*, *18*(1), 77–97.

Greenhill, L. L., Pliszka, S., Dulcan, M. K., Bernet, W., Arnold, V., Beitchman, J., … Stock, S. (2002). Practice parameter for the use of stimulant medications in the treatment of children, adolescents, and adults. *Journal of the American Academy of Child and Adolescent Psychiatry*, *41*, 26S–49S.

Harris, E. A. (2015, February 17). Sharp Rise in Occupational Therapy Cases at New York's Schools. *The New York Times*. Retrieved from http://www.nytimes.com

Hoza, B., Mrug, S., Gerdes, A. C., Hinshaw, S. P., Bukowski, W. M., Gold, J. A., … Arnold, E. (2005). What aspects of peer relationships are impaired in children with attention-deficit/hyperactivity disorder? *Journal of Consulting and Clinical Psychology*, *73*(3), 411–423.

Johnston, C., & Chronis, A. M. (2014). Families and ADHD. In R. A. Barkley (Ed.), *Attention Deficit/Hyperactivity Disorder: A handbook for diagnosis and treatment* (4th ed., pp. 191–209). Guilford Press.

Loe, I. M., & Feldman, H. M. (2007). Academic and educational outcomes of children with ADHD. *Journal of Pediatric Psychlogy*, *32*(6), 643–654.

Macphee, F. L., Altszuler, A. R., Morrow, A. S., Merrill, B. M., Coxe, S., Gnagy, E. M., … Pelham, W. E., (2015, November). Comparing Behavior Modification and its Combination with Psychostimulant Medication to Common Occupational Therapy Interventions on Classroom Behavior Outcomes of Children with ADHD. Poster presented at the annual convention of the Association for Behavioral and Cognitive Therapies, Chicago, IL.

Merrill, B. M., Morrow, A. S., Altszuler, A. R., Macphee, F. L., Gnagy, E. M., Greiner, A. R., … Pelham, W. E. (2017). Improving homework performance among children with ADHD: A randomized clinical trial. *Journal of Consulting and Clinical Psychology*, *85*(2), 111-122.

Molina, B. S. G., Hinshaw, S. P., Swanson, J. M., Arnold, L. E., Vitiello, B., Jensen, P. S., … Houck, P. R. (2009). The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. *Journal of the American Academy of Child and Adolescent Psychiatry*, *48*(5), 484–500.

Morrow, A.S., Merrill, B. M., Altszuler, A. R., Gnagy E. M., Greiner, A., Burger, L. A., … Pelham, W. E. (2014, November). Comparing Behavior The Effect of Methylphenidate on Learning in Children with ADHD. Poster presented at the annual convention of the Association for Behavioral and Cognitive Therapies, Philadelphia, PA.

National Reading Panel. (2000). Teaching Children to Read: An Evidence-Based Assessment of the Scientific Research Literature on Reading and Its Implications for Reading Instruction.

Nash, H., & Snowling, M. (2006). Teaching new words to children with poor existing vocabulary knowledge: A controlled evaluation of the definition and context methods. *International Journal of Language and Communication Disorders, 41*(3), 335–354.

Page, T. F., Pelham, W. III., Fabiano, G. A., Greiner, R., Gnagy, E. M., Hart, K. C., … Foster, E. M. (2016). Comparative cost analysis of sequential, adaptive, behavioral, pharmacological, and combined treatments for childhood ADHD. *Journal of Clinical Child & Adolescent Psychology*, *00*(3), 1-12.

Pelham, W. E. (1999). The NIMH multimodal treatment study for attention-deficit hyperactivity disorder: Just say yes to drugs alone? *Canadian Journal of Psychiatry*, *44*, 981–990.

Pelham, W. E., & Bender, M. E. (1982). Peer relationships in hyperactive children: Description and treatment. In K. D. Gadow & J. Bialer (Eds.), *Advances in Learning & Behavioral Disabilities* (pp. 365–436). Greenwich, CT: JAI Press.

Pelham, W. E., Burrows-Maclean, L., Gnagy, E. M., Fabiano, G. A., Coles, E. K., Wymbs, B. T., … Waschbusch, D. A. (2014). A dose-ranging study of behavioral and pharmacological treatment in social settings for children with ADHD. *Journal of Abnormal Child Psychology*, *42*(6), 1019–1031.

Pelham, W.E., Burrows-MacLean, L., Gnagy, E. M., Fabiano, G. A., Coles, E. K., Wymbs, B. T., . . . Coxe, S. Behavioral, pharmacological, and combined treatment for ADHD: A dose-ranging, between groups analysis. Manuscript in preparation.

Pelham, W. E., & Fabiano, G. A. (2008). Evidence-based psychosocial treatments for attention-deficit/hyperactivity disorder. *Journal of Clinical Child & Adolescent Psychology*, *37*(1), 184–214.

Pelham, W. E., Fabiano, G. a, & Massetti, G. M. (2005). Evidence-based assessment of attention deficit hyperactivity disorder in children and adolescents. *Journal of Clinical Child and Adolescent Psychology*, *34*(3), 449–476.

Pelham, W. E., Fabiano, G. A., Waxmonsky, J. G., Greiner, A. R., Gnagy, E. M., Pelham, W. III., … Murphy, S. A. (2016). Treatment sequencing for childhood ADHD : A multiple-randomization study of adaptive medication and behavioral interventions. *Journal of Clinical Child & Adolescent Psychology*, *0*(0), 1–20.

Pelham, W. E., Gnagy, E. M., Burrows-Maclean, L., Williams, A., Fabiano, G. A., Morrisey, S. M., … Morse, G. D. (2001). Once-a-day Concerta methylphenidate versus three-times-daily methylphenidate in laboratory and natural settings. *Pediatrics*, *107*(6), E105.

Pelham, W. E., Gnagy, E. M., Greiner, A. R., Waschbusch, D. A., Fabiano, G. A., & Burrows-Maclean, L. (2010). Summer Treatment Programs for Attention-

Deficit/Hyperactivity Disorder. In J. R. Weisz & A. E. Kazdin (Eds.), *Evidence-Based Psychotherapies for Children and Adolescents* (2nd ed., pp. 277–292). New York, NY: Guilford Press.

Pelham, W. E., Massetti, G. M., Wilson, T., Kipp, H., Myers, D., Standley, B. B. N., … Waschbusch, D. (2005). Implementation of a comprehensive schoolwide behavioral intervention: The ABC program. *Journal of Attention Disorders*, *9*(1), 248–60.

Pelham, W.E., McBurnett, K., Harper, G.W., Murphy, D.A., Milich, R., Clinton, J., & Thiele, C. (1990). Methylphenidate and baseball playing in ADHD children: Who's on first? *Journal of Consulting and Clinical Psychology, 58,* 130-133.

Power, T. J., Mautone, J. a, Soffer, S. L., Clarke, A. T., Marshall, S. a, Sharman, J., … Jawad, A. F. (2012). A family-school intervention for children with ADHD: results of a randomized clinical trial. *Journal of Consulting and Clinical Psychology*, *80*(4), 611–23.

Subcommittee on Attention-Deficit/Hyperactivity Disorder, Steering Committee on Quality Improvement and Management. (2011). ADHD: Clinical practice guideline for the diagnosis, evaluation, and treatment of Attention-Deficit/Hyperactivity Disorder in children and adolescents. *Pediatrics, 128*, 2011-2654.

Schnoes, C., Reid, R., Wagner, M., & Marder, C. (2006). ADHD among students receiving special education services: A national survey. *Exceptional Children*, *72*(4), 483–496.

Swanson, J. M., Arnold, L. E., Vitiello, B., Abikoff, H. B., Wells, K. C., Pelham, W. E., … Hanley, T. (2002). Response to commentary on the multimodal treatment study of ADHD (MTA): Mining the meaning of the MTA. *Journal of Abnormal Child Psychology*, *30*(4), 327–332.

Visser, S. N., Danielson, M. L., Bitsko, R. H., Holbrook, J. R., Kogan, M. D., Ghandour, R. M., … Blumberg, S. J. (2014). Trends in the parent-report of health care provider-diagnosed and medicated attention-deficit/hyperactivity disorder: United States, 2003-2011. *Journal of the American Academy of Child and Adolescent Psychiatry*, *53*(1), 34–46.

Visser, S. N., Danielson, M. L., Wolraich, M. L., Fox, M. H., Grosse, S. D., Valle, L. A., … Peacock, G. (2016). Vital Signs : National and state-specific patterns of attention deficit / hyperactivity disorder treatment among insured children aged 2 – 5 Years — United States , 2008 – 2014. *Morbidity and Mortality Weekly Report (65)*.

Waschbusch, D. A., & Hill, G. P. (2003). Empirically supported, promising, and unsupported treatments for children with attention-deficit/hyperactivity disorder. In S. O. Lilienfeld, J. S. Lohr, & S. J. Lynn (Eds.), *Science and pseudoscience in contemporary clinical psychology* (pp. 333–362). New York, NY: Guilford Press.

IV. CHAPTER 3.

DISSERTATION STUDY: TOLERANCE TO PSYCHOSTIMULANT MEDICATION AMONG CHILDREN WITH ADHD

This manuscript will be submitted to a journal that adheres to use of APA 6th Edition formatting guidelines.

Introduction

ADHD is among the most common mental health disorders during childhood and adolescence with an estimated prevalence rate of 8-12% (Visser et al., 2016). Children with ADHD experience a multitude of impairments including conflicts with parents, teachers, and other adults often leading to marked caregiver strain (Anastopoulos, Sommer, & Schatz, 2009; Johnston & Chronis-Tuscano, 2015), problems with peers including peer rejection (Hoza et al., 2005; Pelham & Bender, 1982), and low academic achievement and behavior problems in school (DuPaul & Jimerson, 2014; Loe & Feldman, 2007). Three treatments have been well-validated as effective treatments for childhood ADHD: (1) central nervous system (CNS) stimulant medications, (2) behavior modification, and (3) the combination of the two (Conners et al., 2001; Evans, Owens, & Bunford, 2014; Evans, Owens, Wymbs, & Ray, 2018; Fabiano et al., 2009; Jensen, 2001; Pelham et al., 2014; Pelham & Fabiano, 2008; Pelham, Wheeler, & Chronis, 1998; Swanson, McBurnett, Christian, & Wigal, 1995). Medication is the most commonly received treatment for childhood Attention-Deficit/Hyperactivity Disorder (ADHD) with 90% of children with ADHD having received it at some point in their lives (Danielson , 2018).

Short- and Long-term Effects of Psychostimulants

A massive literature exists on the *short-term* effects of psychostimulant medication and these studies have robustly shown that these medications produce large acute effects on children's behavior. CNS stimulant medication treatment leads to improvements of both the core symptoms of ADHD and the associated problematic behaviors that contribute to the marked impairment children with ADHD experience.

Specifically, psychostimulant treatment leads to decreased hyperactivity, impulsivity, inattention and improved rule following, on-task behavior, academic productivity and social functioning among children with ADHD (Connor et al., 2002; Cortese et al., 2018; Faraone & Buitelaar, 2010; Greenhill et al., 2001; Pelham et al., 2001; Swanson et al., 2004). In school settings, children with ADHD complete more school work when receiving medication and completion of academic tasks has been widely used to demonstrate the efficacy of psychostimulant formulations (Greenhill et al., 2003; Mccracken et al., 2003; Swanson et al., 2004). In social settings, children with ADHD exhibit less aggression-related behaviors when receiving stimulant medication (Connor et al., 2002). Stimulant medication also leads to improved prosocial behaviors such as following the rules of sports games (Pelham et al., 2014), sportsmanlike behavior (Altszuler et al., 2017; Hupp et al., 2002), and attending to sports games (Pelham et al., 1990). Across academic and recreational settings, children with ADHD routinely exhibit improved rule following behavior (Fabiano et al., 2007; Pelham et al., 2014) while receiving stimulant medication. These ameliorative immediate effects of psychostimulants are among the highest in medicine (Leucht et al., 2012) and the vast majority, between 80-90%, of children with ADHD respond to the treatment (Greenhill et al., 2001; Pliszka, 2007).

Although the evidence for short-term benefits of psychostimulant treatment for individuals with ADHD is clear, the literature investigating potential *long-term* (i.e., over years) benefits is scarce and majorly inconclusive. Thus, evidence for long-term psychostimulant treatment of ADHD has yet to be empirically demonstrated (Hazell, 2011). One particularly puzzling finding is that long-term stimulant medication treatment

does not lead to improvements in academic achievement scores across subjects and school grades (Barnard-Brak & Brak, 2011; Langberg & Becker, 2012; Loe & Feldman, 2007) despite the large acute effects on academic productivity. One potential explanation for this is that stimulant medication has been found to have no impact on learning in the areas of vocabulary, social studies, and science (Pelham et al., in press).

Another clear demonstration of the difference in short- and long-term effects of psychostimulants are the results of the first large, multisite randomized controlled trial (RCT) of combined treatment for ADHD was the Multimodal Treatment Study of Children with ADHD (MTA; Arnold et al., 1997; Greenhill et al., 1996; Richters et al., 1995; The MTA Cooperative Group, 1999). The MTA tested four treatments in a controlled, randomized clinical trial for 14 months: (1) behavioral treatment alone (Beh), (2) pharmacological treatment alone (MedMgt), (3) combined behavioral and pharmacological treatment (Comb), and (4) community comparison treatment. The results suggested that directly following treatment, the treatment conditions that included medication (Med and Comb) were superior to the behavioral only treatment (The MTA Cooperative Group, n.d.). Follow-up investigations of the MTA indicate that the benefits of medication in both the MedMgt and Comb conditions dissipated by 50% at 1-year post treatment (MTA Cooperative Group, 2004a, 2004b), and completely at 2-years post treatment (Jensen et al., 2007).

Potential Development of Tolerance to Psychostimulants

One possible explanation of the failure of stimulant medication treatment to lead to beneficial long-term results is the development of tolerance. DuPen, Shen, and Ersek (2007) define tolerance as a state of adaptation in which exposure to a drug results in a

decrease of the drug's effects over time. The necessity to incrementally increase dosage of CNS stimulants to maintain effectiveness has been clinically observed and documented for over 30 years including observations of diminishing behavioral responses after one year of treatment with methylphenidate (Safer & Allen, 1975). Swanson first formally proposed the possibility of tolerance development to psychostimulants in 1986 (Swanson et al., 1986) following observations in clinical practice settings that aggressive escalations in dose of MPH to high doses were required to maintain full therapeutic effect.

Short-term within day tolerance to psychostimulant medications has been empirically demonstrated. In fact, current controlled-released formulations of CNS stimulants are designed to consider short-term, within day tolerance. The first generation of stimulant medications were immediate-release such that the drug was rapidly absorbed, showed effects within 30 minutes, peaked after two hours and lasted approximately four hours. These characteristics of the drug resulted in children typically taking two or three doses per day (i.e., morning, midday, evening; Pelham et al., 2001; Swanson et al., 1999) such that children functioned well both at school and at home. To address the need for multiple doses per day, sustained-release formulations were developed for once per day administration (Brown et al., 1980; Patrick et al., 1989; Pelham et al., 1990; Pelham et al., 1987). However, sustained-release preparations were not as effective as multiple doses of immediate-release preparations and the theory that the continuous rate of drug delivery produces acute tolerance was tested. Two experimental patterns of drug delivery were developed: (1) a large dose followed by small consistent doses that constitute a flat profile and (2) a small dose followed by small

increases doses that constitutes an ascending profile. These formulations were evaluated against the first-generation controlled-release formulation (i.e., Ritalin SR®) using a 10-minute math test. The results showed loss of full effect with a flat profile and achievement of full effect with an ascending profile (J. Swanson et al., 1999) and led to the use of ascending profiles in the design of second generation controlled-release formulations of methylphenidate (OROS MPH: Pelham et al., 2001 & Swanson et al., 2000, 2003)) and amphetamine (Adderall XR®: Greenhill et al., 2003; McCracken et al., 2005; McGough et al., 2003). These new products were almost immediately adopted and have remained the standard of care for ADHD (Pliszka, 2007). If within-day tolerance has been observed, it stands to reason that tolerance may occur over a period of weeks.

Indeed, dose increases are often required to maintain efficacy of psychostimulant medication. For example, dose increases occurred in 54% of participants in the Multimodal Treatment Study of ADHD (The MTA Cooperative Group, 1999) during the 14-month active treatment phase. These findings are not unique to the MTA. Numerous other extended follow-up studies of stimulant medication in children have observed a similar need to increase dose over time. In most studies with a long-term follow-up component, a 25% increase over the first year of treatment is typically seen. For example, the Preschool ADHD Treatment Study protocol included a one-year maintenance phase using the MTA algorithm to make changes in dose of medication over time. In this study, the average dose increased from 14 to 21 mg/day during this maintenance despite a month long double-blinded titration phase prior to the maintenance period. The same phenomenon has been observed in extension studies of once-a-day stimulants. For example, in the two-year extension study of OROS-MPH (Concerta®), dose increased by

26% (on the average from 35 to 42 mg/day) even though subjects had been previously titrated to optimal dose (Wilens et al., 2005). These data do not include the additional 9% of subjects who dropped out specifically due to loss of effect even on the maximum dose of MPH. Similar results were found in extension study for AMP (Adderall XR®) (McGough, et al., 2005). After a weekly titration to define optimal dose, the mean dose was 16 mg/day. It increased by over a third to 20.2 mg at 6 months but then little incremental change was seen over the next year and a half.

Some may argue that dose increase over time may be associated with physical growth in children rather than tolerance to the drug; however, studies have supported that dose increases do not correlate with growth/weight.Safer & Allen (1989) compared expected dose increases (calculated as mg of MPH per kg of body weight) to actual dose increases and found that expected dose increases based on weight were larger than what were clinically indicated.Furthermore, Swanson et al (1978) reported that children's clinically optimal dosages can vary by 6-fold and that these differences in dose are unrelated to differences in weight. Lastly, the Med group of the MTA study gained an average weight over time that resulted in a ratio of medication dose to weight that was well above standard dosing norms (Greenhill et al., 2003; Vitiello et al., 2001). Hence, there is not always a need to increase dose simply based on increased body mass.

Tolerance has been demonstrated to occur in a variety of other CNS agents from analgesics to anticonvulsants (Abou-khalil et al., 2003; Ossipov et al., 2005). It is not uncommon to have to switch to an alternate anticonvulsants or opioids after chronic exposure in order to recapture lost effect (Kloke et al., 2000). In fact, tolerance to opioid based analgesics is a well-documented phenomenon (Dupen, Shen & Esrek 2007). The

presence of tolerance across multiple classes of drugs suggests that tolerance may be more related to properties of the medications themselves then the diseases they target. Therefore, it is difficult to understand why tolerance would not occur to stimulants in the clinical treatment of ADHD.

Another theorized explanation for the lack of long-term benefit of CNS stimulant treatment in individuals with ADHD is poor adherence (Ahmed & Aslani, 2013; Biederman et al., 2019; Marcus et al., 2005; Marcus & Durkin, 2011) with rates of nonadherence ranging from 12 to 64% (Adler & Nierenberg, 2010). In a large electronic medical records study that included 2,206 participants with prescriptions for psychostimulants, only 46% were adherent to treatment (Biederman et al., 2019). Adults with ADHD routinely report that their reason for nonadherence is an associated loss of self while on medication or lack of need for the treatment (McCarthy, 2014), which may suggest the medication's lack of efficacy over time or perhaps is better explained by a positive illusory attribution pattern in that children with ADHD attribute their success solely to their efforts, regardless of medication treatment (Pelham et al., 2002). Additionally, parents of younger children prefer to avoid treatments involving psychostimulants even among those who had previously trialed stimulant medications (Schatz et al., 2015). This suggests that parents may choose to end medication treatment, thus contributing to the lack of benefits over time. Uncertainty remains in the literature as to why medication adherence is low among individuals with ADHD and empirically validated strategies to promote adherence is lacking (Biederman et al., 2019). Nonadherence also contributes to the difficulty of long-term investigations of psychostimulants because most individuals with ADHD go on and off stimulant

medication for periods of time (Marcus et al., 2005; Marcus & Durkin, 2011). However, nonadherence was not the primary cause of the lack of sustained benefit of stimulant medication among MTA participants because even the MTA subjects with a decade of medication usage did not exhibit improved long-term outcomes (Molina et al., 2009).

In summary, the literature reviewed above suggests that an appreciable dose increase is often needed for children with ADHD to maintain full effect of treatment with stimulants. Although we cannot be certain that tolerance is the primary driver of dose escalations over time, it is an explanation that warrants further exploration. ADHD is a chronic psychiatric disorder that requires lifelong treatment and management. Understanding the long-term efficacy of available treatments, in the case of the current study psychostimulants, is necessary to inform treatment recommendations. The current study is the first controlled study designed specifically to ascertain the occurrence of tolerance to stimulant medication among children with ADHD. Previous studies that demonstrate dose escalations over time are made up of follow-up data from large-scale clinical outcome studies (MTA Cooperative Group, 2004b; Vitiello et al., 2001) that suffer from a multitude of confounders such as nonadherence, selective dropout and parental preferences. Therefore, the current study was conducted in a tightly controlled, analogue summer camp setting to minimize confounders. Through a within-subjects design, we aimed to identify characteristics of children who show decreased response to stimulants over a three-week period. The drug exposure study condition was just three weeks in part because of logistic constraints pertaining to the length of summer vacation that children are available to participate in an intensive program and in part because previous studies have demonstrated the need for dose escalations within monthly time

intervals (Vitiello et al., 2001), thus suggesting that potential tolerance to the drug can occur within this time frame.

Current Study

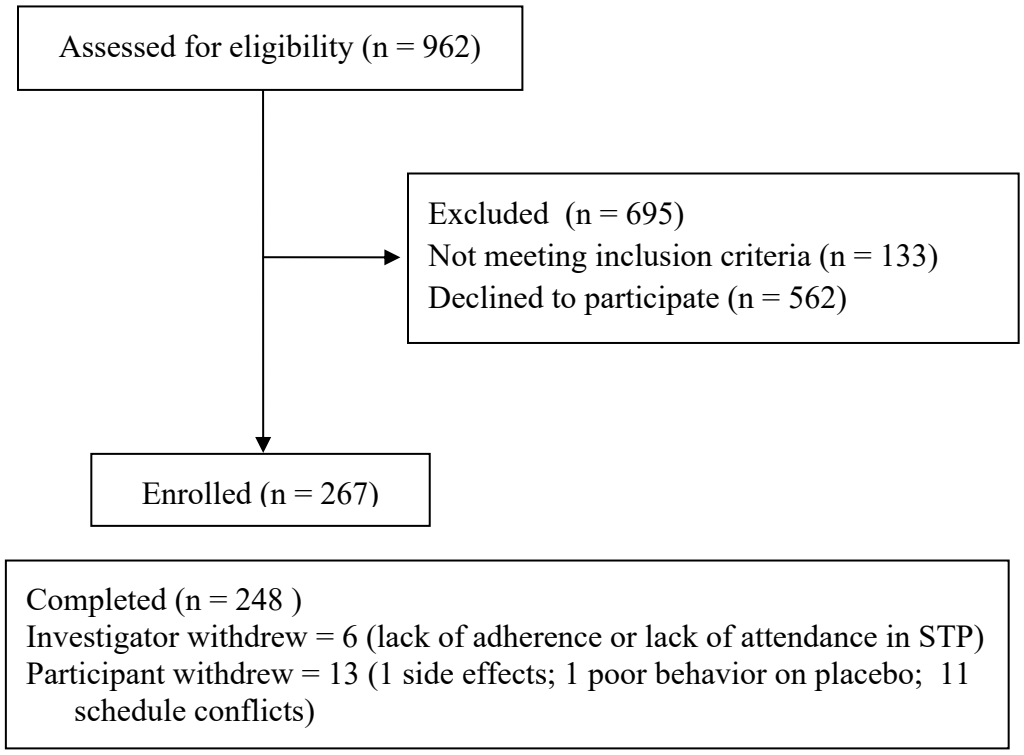
The current study aims are as follows: (1) to investigate whether short-term tolerance to MPH occurs in a controlled, analog summer camp treatment setting over 3 weeks by measuring changes in academic work productivity and behavior and (2) to examine potential predictors of tolerance to MPH over 3 weeks. We hypothesize that the effects of MPH will dissipate over time for the both the academic work productivity and behavioral outcomes and that these effects will depend on participant's prior stimulant medication treatment. Specifically, we expect that children who previously received higher doses of stimulant medication for longer periods of time will show diminished response to medication over the three-week study.

Method

The current study is phase 1 of a larger study funded by the National Institute of Mental Health (MH099030) to study short- and long-term tolerance to psychostimulant medication among children with ADHD. All study procedures were approved by the Western Institutional Review Board. Children were recruited by distributing flyers to pediatric offices, schools and approaching treatment seeking families at the university clinic. Inclusion criteria included a DSM-IV-TR diagnosis of ADHD and being between the age of 5 to 12 years. Parents of the child participants also had to agree for their child to receive stimulant medication treatment and attend the Summer Treatment Program for one summer. Exclusion criteria included a full-scale IQ below 80, a diagnosis of autism spectrum disorder, current receipt of psychotropic medication for any condition other

than ADHD, and a documented intolerability or lack of response to CNS stimulant medication.

Figure 1.
CONSORT Flow Diagram



Participants

Participants included 236 children between the ages of 5 and 12 (*M* = 8.17 years, *SD* = 1.85) diagnosed with ADHD. Best practice recommendations for assessment and diagnosis were followed (Pelham, Fabiano, & Massetti, 2005) and included parent and teacher ratings of DSM-IV-TR symptoms (Disruptive Behavior Disorders Scale [DBD; Pelham, Gnagy, Greenslade & Milich, 1992]), structured parent interview (Diagnostic Interview Schedule for Children IV, computerized version [Shaffer, Fisher, & Lucas, 1998]), and impairment across settings (Impairment Rating Scale [Fabiano et al., 2006]).

Two Ph.D. /M.D. level clinicians independently reviewed the files to make a diagnosis for each child who participated in the study. If disagreements related to diagnosis between clinician's arose (e.g., disagreements related to ADHD subtype, presence of co-occurring oppositional defiant disorder [ODD]) a third clinician was consulted and majority decisions were used as final diagnostic assignment. To estimate IQ, masters level clinicians and research staff administered to children the vocabulary and block design subtests of Wechsler Preschool and Primary Scale of Intelligence, Fourth Edition (Wechsler, 2012) or the Wechsler Abbreviated Scale of Intelligence, Second Edition (Wechsler, 2011) dependent on the child's age. Achievement testing included the Word Reading, Numerical Operations, and Spelling subtests of the Wechsler Individual Achievement Test, Third Edition (Wechsler, 2009). See Table 1 for a summary of participant characteristics.

Table 1
Participant Characteristics (N = 236)

Gender (% Male)	69.9
Age *M* (*SD*)	8.18 (1.89)
Ethnicity (%)	
Hispanic or Latino	84.2
Non-Hispanic or Latino	15.0
Race (%)	
Black or African American	10.5
White	88.7
ADHD Diagnosis (%)	
Combined	72.6
Inattentive	7.5
Hyperactive/Impulsive	17.7
Comorbidities (%)	
ODD	61.7
CD	9.4
Previous stimulant medication treatment (%)	64
WIAT III Word Reading Score *M* (*SD*)	97.42 (17.27)
Range	65 - 180
WIAT III Numerical Operations Score *M* (*SD*)	101.78 (14.32)

Range	41 - 153
WIAT III Spelling Score *M* (*SD*)	97.27 (14.96)
Range	63 - 149
Estimated Full-Scale IQ *M* (*SD*)	96.83 (12.85)

Study Design

Setting. The study was conducted over four cohorts. Each year, the cohort of participants participated in the 8-week-long Summer Treatment Program for Children with ADHD (STP; Pelham et al., 2017). The STP is an intensive behavior modification treatment using a reward/response-cost point system that is delivered within the context of recreational and classroom periods (Pelham & Hoza, 1996; Weisz & Kazdin, 2010). It is important to note that the intensive behavior point system was not implemented during the daily collection of the 10-minute math test outcome for the current study. Children attended the program from 8:00 AM to 5:00 PM on weekdays and participated in 2-hour academic lessons, 1-hour art lessons, and the rest of the day was spent in recreational activities. Children were placed in age-matched groups of 12-15 children who were supervised by one lead counselor and five undergraduate counselors who were supervised by permanent Ph.D.-level staff members during recreational activities or a teacher and an aide during classroom activities. The current study evaluated outcomes collected during the morning classroom period in addition to during recreational sports activities, lunch, snack, transition, and bathroom break time.

Medication Conditions. Children underwent a nine-day trial of two to three doses of extended-release methylphenidate (MPH; typically OROS methylphenidate 18 mg, 27 mg, and 36 mg/day) during the first two weeks of the STP, prior to the start of the current protocol. Some children trials two instead of three doses due to intolerability or

low weight. Three Ph.D./M.D.-level clinicians reviewed behavioral data collected as part of the STP response/cost point system (i.e., rule violations, negative verbalizations, seatwork productivity) during the brief medication trial children were ultimately prescribed the lowest dose that produced substantive efficacy with minimal side effects for the six-week, placebo-controlled medication crossover phase of the study. For example, if 27 mg produced clear improvement beyond 18 mg, but 36 mg did not produce clear improvements beyond 27 mg, then 27 mg was selected as that child's dose. The average daily dose was 19.0 mg, *SD* = 4.1 mg. The three-week crossover condition resulted in 13 consecutive STP days in both medication conditions, excluding weekends. Parents and teaching staff completed side effect ratings to ensure that medication was well tolerated by the children. Order of medication and placebo was randomized on an individual basis (e.g., approximately half of the children in each classroom were in the medication-first or placebo-first condition). Parents were directed to give the medication to each child at home before 7:30 am and to write down on a provided medication card the time their children received the medication. Medication cards were collected from each parent every morning, and if a parent did not provide a medication card, the study nursing staff contacted them. If a parent did not administer the medication, study nursing staff administered the medication at the STP. Therefore, every child who was randomly assigned to medication received medication on assigned days. Morning classrooms, where some of the current study outcomes were collected, were held from 60 to 225 minutes after the child was administered the medication.

Measures

Medication history. During baseline, parents were administered the Medication and Treatment Chronology questionnaire (Kurijan et al., 2014) by study nursing staff. The questionnaires collected chronological medication history including name of the medication, dosing schedule, dose, and duration of treatment in months. Children's weight was also measured at baseline and used to calculate the study entry dose in mg/kg variable.

10-Minute Math Test. The 10-Minute Math Test was administered as part of each morning STP analogue classroom period to provide a daily measure of academic productivity. At baseline, each participant was administered 6 separate pages of math problems, each with a varying level of difficulty. Difficulty levels including counting, 1-digit addition, 1-digit addition or subtraction, 2-digit addition, 2-digit addition and subtraction 3-digit addition, 3-digit addition and subtraction. Difficulty level was individualized per child in that the level that most closely approximated completing 10 problems per minute was administered and held constant throughout the study. Similar procedures have been used in summer programs and lab schools to precisely assess therapeutic effects of stimulant preparations (e.g., Pelham et al., 1987; 1990, 1999a,b, 2001; Swanson et al., 1998, 1999, 2002, 2003, 2005) and this test is accepted by the FDA as a surrogate measure of magnitude of efficacy (Swanson, 2002). The intensive behavior modification treatment program was suspended during the 10-minute math test. Child were informed that they would lose points for negative behavior but were not informed in-vivo of point loss in an effort to allow concentration on the test.

Classroom Rule Violations. Teacher-recorded frequencies of classroom rule violations was the behavioral response measure in the STP classroom setting. The classroom rule violations were as follows: (1) be respectful of others, (2) obey adults, (3) work quietly, (4) use materials appropriately, (5) remain in assigned seat or area, (6) raise hand to speak or ask for help, and (7) stay on task. The classroom rules were derived from the Classroom Observations of Conduct and Attention Deficit Disorder (Atkins et al., 1985), which was designed to include classroom expectations typically employed in classrooms in the U.S. Many studies of medication effects within the STP have demonstrated the reliability and sensitivity of classroom rule violations as a measure of treatment response (e.g., Carlson et al., 1992; Fabiano et al., 2007; Pelham, Bender, Caddell, Booth, & Moorer, 1985; Pelham et al., 1990; 1993; 1999ab; 2002; 2005).

Recreational Activity Rule Violations. Behavioral response in the recreational STP setting was measured as staff-recorded frequencies of following activity rules. Activities included sports skill drills, sports games, snack, lunch, transitions, and bathroom breaks. Throughout the STP, children played basketball, baseball, and soccer and the sport changed each day. Each activity had a set of rules and the children were reminded of the rules before the start of every activity each day. Rules were typical of what would be expected of a child in a real-world setting, for example, sports games rules included: (1) follow the rules of the sport; (2) participate; (3) stay in assigned position; (4) use materials and possessions appropriately.

Analyses

All outcomes were analyzed using Generalized Linear Mixed Models (GLMMs; Stroup, 2012) in PROC GLIMMIX in SAS 9.4. The three dependent variable outcomes

evaluated were academic productivity (items answered correctly on the 10-minute math test), classroom rule violations, and recreational rule violations. A negative binomial distribution was utilized for the 10-minute math test outcome model to account for the overdispersion of the data and a Poisson distribution was utilized for the behavioral count outcomes model to account for the non-normal, repeated measures design as recommended (Coxe, West, & Aiken, 2009; Stroup, 2021). All models included a random intercept to take into account clustering of repeated measurements within participants and participants were nested within the first medication condition they were randomly assigned to. The following predictors were included in each outcome model: age, STP group (age-matched treatment groups who engaged in activities and classrooms together), cross-over period, medication condition, medication day, stimulant medication dose at baseline and total lifetime duration stimulant use in months. The baseline dose variable was calculated by first standardizing daily dose across varying psychostimulant preparations, as is established in the literature (Swanson et al., 2018), then calculated as mg/child's weight in kg. Children who were not receiving stimulant treatment at baseline were assigned zero for this variable. The total lifetime duration stimulant use variable was calculated by summing the number of months spent receiving any type or dose of stimulant medication prior to study entry. The two-way and three-way interactions among the main predictors (medication condition, medication condition day, and stimulant medication dose at baseline) were also included in the initial models. Analyses controlled for interactions between cross-over period and medication treatment condition variables by including these interactions in the model (Simpson & Hamer, 1999; Yarandi, 2004).

We examined the three-way interactions between baseline medication dose, medication condition, and medication condition day in order to evaluate whether prescribed stimulant medication prior to study entry predicted the development of tolerance to the drug. We defined tolerance as worsening of outcomes over days (1 through 13 for each of the medication conditions) of the medication condition. In other words, medication effects dissipating over time. Significant three-way interactions were then further evaluated by probing the two-way interaction between medication dose and medication condition day at four cut-off values Both the baseline dose and total duration of stimulant medication use variable were probed at 0 and then low, medium, and high values. These were calculated by splitting the sample who had values above 0 into thirds. This approach was chosen instead of using the standard one standard deviation above and below the mean approach because this would have resulted in negative values or values that did not appear in the dataset of total duration of months (baseline dose M = .59 mg/kg/day, SD = .58 and total duration of months receiving stimulant medication M = 11.11, SD = 17.58). The baseline dose variable cut-off values included 0 (i.e., not receiving stimulant medication treatment at the time of study entry), .08 mg/kg/day as the low value, .13 mg/kg/day as the medium value, and .87 mg/kg/day as the high value. The total duration of stimulant use variable was probed at 0 (i.e., psychostimulant naïve children), 6 months of prior use, 19 months of prior use, and 36 months of prior use. Overall, 38% of the participants were not receiving a stimulant medication at study entry and 36% had not previously received psychostimulant treatment. Thus, two children in the study had previously received stimulant medication treatment but were not participating in a regimen of stimulant medication upon enrollment in the current study.

Results

Table 2 displays all model estimates, standard errors, and p-values from the analyses. Separate models were run for each of the three dependent measures. We were specifically interested in the three-way interactions between the medication history variables (i.e., psychostimulant medication dose at study entry and lifetime cumulative months receiving stimulant medication prior to study entry), medication condition, and chronological study day of receiving either medication or placebo pill. The three-way interaction among medication dose at study entry, medication condition, and day of the study was significant for all three outcomes: 10-minute math test, classroom rule violations and recreational activity rule violations The three-way interaction among duration of stimulant medication treatment prior to the study, medication condition, and day of the study was significant for both of the behavioral outcomes but not the academic outcome. Table 3 displays the estimates, standard errors, and inferences for medication vs. placebo at each cut off value from the probed significant interactions of interest. Specifically, table 3 displays whether medication and placebo were significant at days 1, 7, and 13 of the=medication conditions at the previous medication predictor cut off values (dose at study entry and duration of previous medication treatment). Figures 1 through 3 display the plotted means of the outcome variables at the first, middle, and last day of each medication crossover period. The figures show the means of the split sample by medication history cut-off values.

Table 2
Estimates From Mixed Models

Dependent Measure	Level	Term	Estimate	Standard Error	Inference
10-Minute math test	Child	(Intercept)	4.20	.13	t(236) = 31.7, ***
	Occasion	Crossover period (Period)[a]	.11	.09	t(5201) = 1.31, ns
	Occasion	Day of crossover period (Day)[b]	-.003	.003	t(5201) = -.96, ns
	Occasion	Age	-.002	.003	t(5201) = -.15, ns
	Occasion	Medication (vs. placebo)	1.16	.10	t(5201) = -1.66, p = .09
	Occasion	Medication dose at baseline[c]	-.03	.18	t(5201) = -.19, ns
	Occasion	Duration of stimulant treatment[d]	-.005	.003	t(5201) = -1.81, p = .07
	Occasion	Period*Medication	-.29	.17	t(5201) = -1.68, p =.09
	Occasion	Day*Medication	-.002	.005	t(5201) = -.39, ns
	Occasion	Baseline dose*Medication	-.14	.12	t(5201) = -1.15, ns
	Occasion	Duration*Medication	-.002	.002	t(5201) = -.87, ns
	Occasion	Baseline dose*Medication*Day	.03	.01	t(5201) = 2.29, *
	Occasion	Duration*Medication*Day	5.29E-6	.0002	t(5201) = .02, ns
Classroom rule violations	Child	(Intercept)	1.67	.23	t(236) = 7.26, ***
	Occasion	Crossover period (Period)[a]	-.34	.12	t(5294) = -2.78, *
	Occasion	Day of crossover period (Day)[b]	.02	.004	t(5294) = 4.28, ***
	Occasion	Age	-.02	.02	t(5294) = -1.2, ns
	Occasion	Medication (vs. placebo)	.48	.13	t(5294) = 3.69, **
	Occasion	Medication dose at baseline[c]	.29	.31	t(5294) = .91, ns
	Occasion	Duration of stimulant treatment[d]	.02	.005	t(5294) = 2.92, **
	Occasion	Period*Medication	.64	.24	t(5294) = 2.60, *
	Occasion	Day*Medication	-.02	.004	t(5294) = -4.96, ***
	Occasion	Baseline dose *Medication	-.29	.13	t(5294) =-2.27, *
	Occasion	Duration*Medication	.003	.002	t(5294) = 1.51, ns
	Occasion	Baseline dose*Medication*Day	.04	.02	t(5294) = 2.7, *
	Occasion	Duration*Medication* Day	-.0007	.0002	t(5294) = -3.00, *
Recreational rule violations	Child	(Intercept)	2.90	.15	t(236) = 18.77, ***
	Occasion	Crossover period (Period)[a]	.21	.08	t(5362) = 2.75, *
	Occasion	Day of crossover period (Day)[b]	.005	.08	t(5362) = 3.21, *
	Occasion	Age	-.02	.01	t(5362) = -1.22, ns
	Occasion	Medication (vs. placebo)	1.13	.08	t(5362) = 14.69, ***
	Occasion	Medication dose at baseline[c]	-.29	.21	t(5362) = -1.42, ns
	Occasion	Duration of stimulant treatment[d]	.01	.003	t(5362) = 3.5, **
	Occasion	Period*Medication	-.56	.002	t(5362) = -3.7, *
	Occasion	Day*Medication	-.009	.002	t(5362) = -4.54, **
	Occasion	Baseline dose*Medication	.50	.05	t(5362) = 9.48, ***
	Occasion	Duration*Medication	.003	.0007	t(5362) = 4.03, ***
	Occasion	Baseline dose*Medication*Day	-.04	.006	t(5362) = -6.62, ***
	Occasion	Duration*Medication*Day	-.0007	.00008	t(5362) = -8.17, ***

Note. [a]Period is coded as 0 or 1, indicating whether it was the first or the second study crossover period
[b]Day is coded as 1-13 and indicates the day of each study crossover period
[c]Dose at baseline is a standardized to MPH dosage dose of stimulant medication that the child was prescribed by their community provider at study entry. 40% of children were not on medication at study entry and thus have a value of 0 for this variable.
[d]Lifetime duration of stimulant medication treatment in months. 38% of children were medication naïve.
* $p < .05$
** $p < .001$
*** $p < .0001$

Table 3

Medication Vs. Placebo Model Estimates from Significant Interactions of Interest

Dependent Measure	Medication History Predictors	Day 1 Estimate (SE) Inference	Day 7 Estimate (SE) Inference	Day 13 Estimate (SE) Inference
10-Minute math test	No med at baseline	-.33 (.03) t(5201) = -10.02, ***	-.34 (.02) t(5201) = 19.91, ***	-.35 (.03) t(5201) = -11.28, ***
	Low baseline dose[a]	-.33 (.03) t(5201) = -11.08, ***	-.32 (.01) t(5201) = -20.97, ***	-.32 (.03) t(5201) = -11.33, ***
	Medium baseline dose[b]	-.34 (.03) t(5201) = - 11.37, ***	-.32 (.02) t(5201) = -20.90, ***	-.31 (.03) t(5201) = -10.91, ***
	High baseline dose[c]	-.42 (.09) t(5201) = -4.90, ***	-.24 (.04) t(5201) = -5.73, ***	-.08 (.08) t(5201) = -.99, ns
Classroom rule violations	No med at baseline	.80 (.03) t(5294) =24.09, ***	.60 (.02) t(5294) = 36.74, ***	.41 (.03) t(5294) = 13.62, ***
	Low baseline dose[a]	.78 (.03) t(5294) = 25.90, ***	.60 (.02) t(5294) = 39.93, ***	.43 (.02) t(5294) = 15.62, ***
	Medium baseline dose[b]	.76 (.03) t(5294) = 25.99, ***	.60 (.01) t(5294) = 40.73, ***	.44 (.03) t(5294) = 16.40, ***
	High baseline dose[c]	.58 (.09) t(5294) = 6.39, ***	.60 (.04) t(5294) = 13.54, ***	.61 (.08) t(5294) = 8.04, ***
	Med naïve	.74 (.03) t(5294) = 21.31, ***	.62 (.02) t(5294) = 35.62, ***	.50 (.03) t(5294) = 15.90, ***
	6 months on med	.75 (.03) t(5294) = 24.75, ***	.61 (.02) t(5294) = 39.85, ***	.47 (.03) t(5294) = 16.73, ***
	19 months on med	.78 (.03) t(5294) = 23.83, ***	.59 (.02) t(5294) = 35.76, ***	.39 (.03) t(5294) = 13.46, ***
	36 months on med	.82 (.05) t(5294) = 15.41, ***	.56 (.03) t(5294) = 21.05, ***	.29 (.05) t(5294) = 6.43, ***
Recreational rule violations	No med at baseline	.87 (.01) t(5362) = 69.02, ***	.77 (.01) t(5362) = 117.63, ***	.67 (.01) t(5362) = 55.71, ***
	Low baseline dose[a]	.90 (.01) t(5362) = 80.17, ***	.78 (.01) t(5362) = 133.72, ***	.66 (.01) t(5362) = 61.36, ***
	Medium baseline dose[b]	.93 (.01) t(5362) = 83.87, ***	.79 (.01) t(5362) = 138.68, ***	.66 (.01) t(5362) = 62.24, ***
	High baseline dose[c]	1.26 (.04) t(5362) = 34.67, ***	.95 (.01) t(5362) = 52.22, ***	.63 (.03) t(5362) = 19.76, ***
	Med naïve	.90 (.01) t(5362) = 68.03, ***	.82 (.01) t(5362) = 118.72, ***	.73 (.01) t(5362) = 57.76, ***
	6 months on med	.91 (.01) t(5362) = 78.46, ***	.80 (.01) t(5362) = 133.32, ***	.69 (.01) t(5362) = 62.50, ***
	19 months on med	.94 (.01) t(5362) = 79.64, ***	.78 (.01) t(5362) =125.86, ***	.61 (.01) t(5362) = 53.68, ***
	36 months on med	.97 (.02) t(5362) = 53.60, ***	.74 (.01) t(5362) = 76.91, ***	.51 (.02) t(5362) = 28.35, ***

Note. [a]Cut off is set to .08 mg/kg/day

[b]Cut off is set to .13 mg/kg/day

[c]Cut off is set to .87 mg/kg/day

* $p < .05$

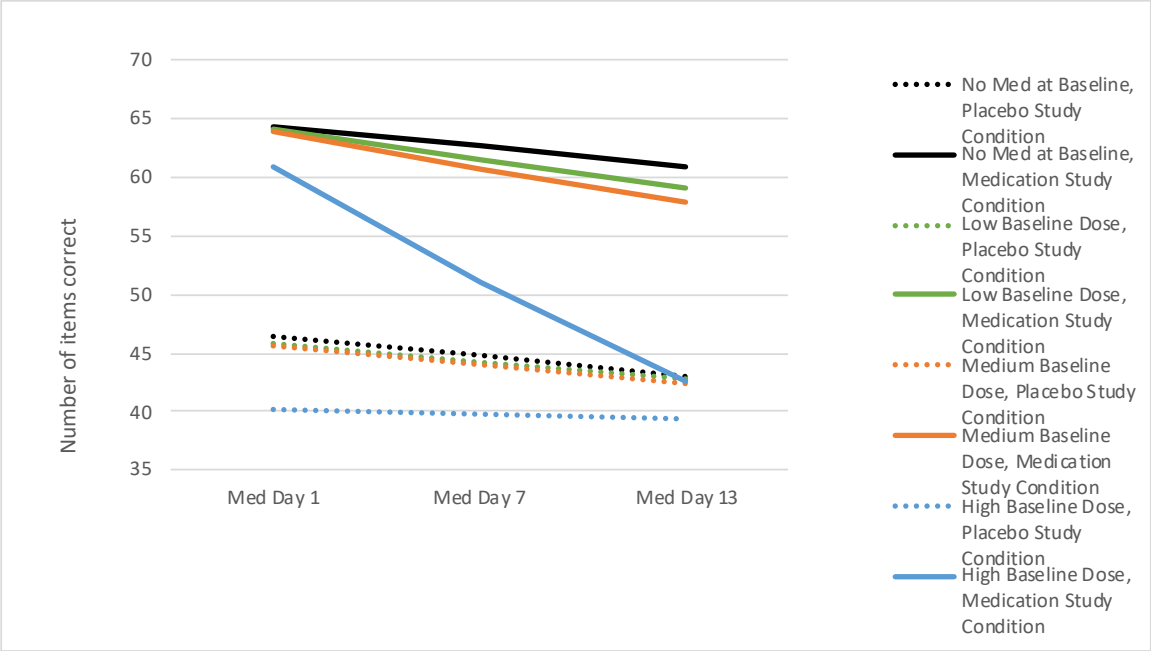
** $p < .001$

*** $p < .0001$

10-Minute Math Test

The model analyzing the 10-minute math test academic productivity outcome revealed marginally statistically significant ($p = .09$) main effects of medication and lifetime months on stimulant medication on the number of math items completed correctly during the 10-minute math test (see Table 2 for estimates). The three-way interaction between stimulant dose at study entry, medication condition, and day of crossover medication condition were significant (see Table 3 for estimates). We were specifically interested in the three-way interactions because we hypothesized that children with a longer history of stimulant medication treatment would show the effects of the medication wearing off at a faster rate than those without a history or with a shorter history of medication treatment. This hypothesis was confirmed for only children who were receiving a high dose of stimulant medication from their community provider at study entry (.87 mg/kg/day), independent of the dose they were titrated to during the study. Figure 1 shows that the group of children who received a high dose of medication prior to initiation of the current study completed a higher number of math items correctly compared to the placebo condition at the beginning of the crossover period but not at the end. Thus, we interpret this to show that the effects of medication waned over the course of the three weeks such that children were completing math problems at a similar rate to placebo by the end of the medication condition. This pattern did not hold true for children who had not received stimulant medication previously or previously received a low or medium dose prior to entry into the study. Notably, the three-way interaction between lifetime duration of stimulant medication treatment, medication condition, and day of crossover period was not statistically significant, which did not support our hypothesis.

Figure 2
Effects of Medication on The 10-Minute Math Test

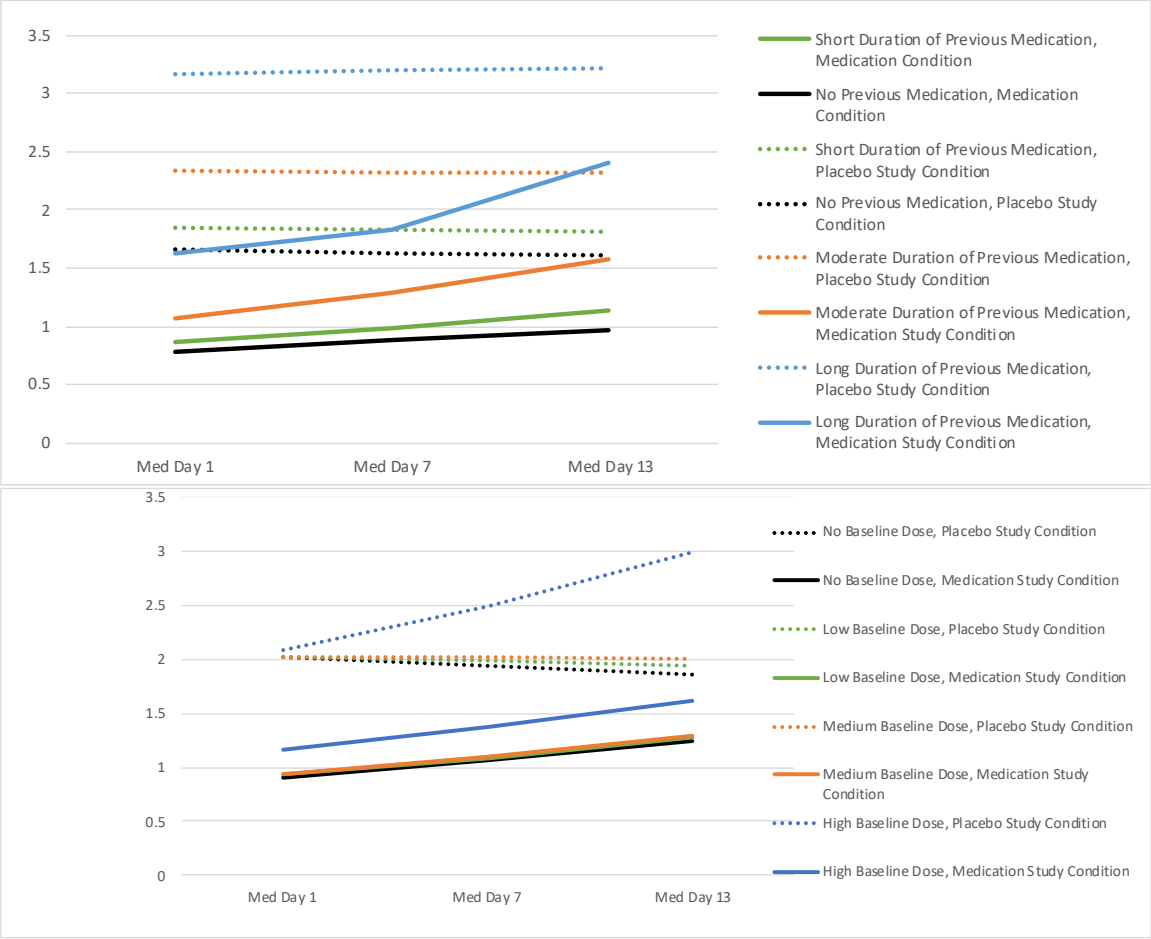


Classroom Rule Violations

Results indicated statistically significant main effects of crossover period, day of crossover period, medication, and duration of stimulant medication treatment. The two-way interactions between period and medication, day of crossover period and medication, and dose at baseline and medication were also statistically significant. Lastly, the three-way interaction between both of the stimulant medication history predictor variables and medication and day of crossover period were significant, suggesting that previous stimulant use and dose impacted children's differential response to medication and placebo over three weeks as measured by classroom rule violations. See tables 1 and 2 for estimates. The three-way interactions of interest were significant and subsequent probing of these interactions revealed a statistically significant difference in the effects of medication versus placebo across time for following classroom rules. However, upon

inspection of the estimated means, there were no clinically meaningful patterns that would suggest differential response to medication versus placebo over time. Figure 3 displays these trends and shows that differences were made up of 1 or 2 classroom rules.

Figure 3
Effects of Medication Classroom Rule Violations



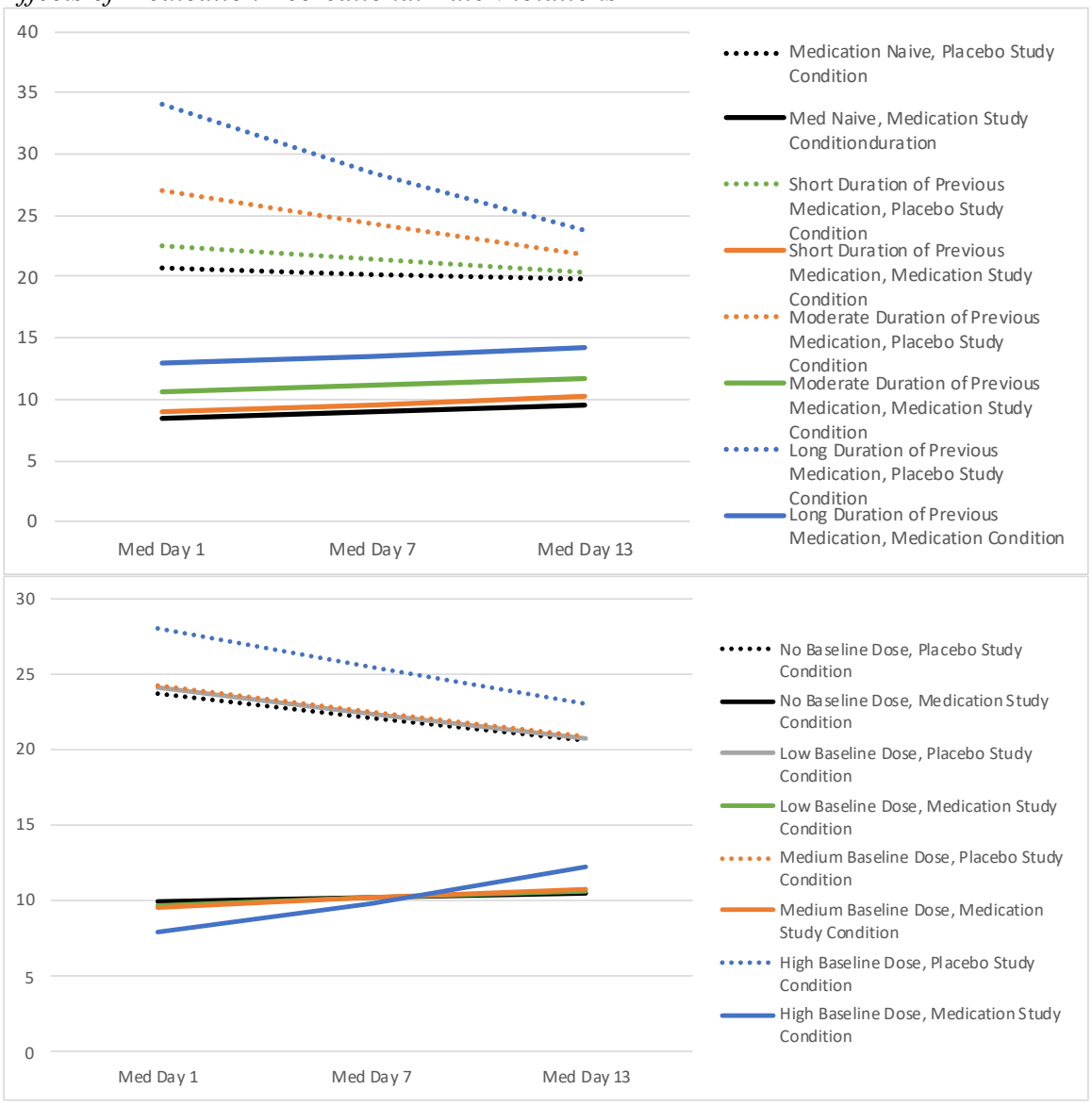
Recreational Activity Rule Violations

The results of the model analyzing the dependent measure of number of rules children violated during recreational activities (e.g., sports games, sports practice) were similar to the results of the model analyzing the dependent measure of classroom rule violations (see tables 2 and 3 for estimates). The three-way interactions were again significant but as with classroom rule violations, probing these interactions did not reveal

clinically meaningful patterns of differential response to medication versus placebo over time as predicted by previous medication use (see Table 2 for estimates and Figure 3 for trends).

Figure 4

Effects of Medication Recreational Rule Violations



Discussion

We examined potential indicators of short-term tolerance to CNS medication in a sample of 236 children with ADHD. The outcomes examined have been shown in previous studies to be sensitive and reliable to medication effects among children with ADHD – following activity rules and math test productivity. We also investigated whether previous stimulant medication treatment, specifically the dose of medication prescribed at baseline and the total duration of previous stimulant treatment, predicted different trajectories of short-term tolerance. Overall, results demonstrate that therapeutic effects of stimulant medication on academic productivity and rule following behavior do not clinically meaningfully dissipate over three weeks among most children with ADHD. There was one exception in that children who had received a high dose of psychostimulant treatment from their community provider prior to the initiation of the current study showed weakened effects of medication over time as measured by academic productivity but not by rule following behavior.

Evidence of Tolerance as Measured by Academic Productivity

Although ADHD symptoms and related problematic behavior has been demonstrated as treatment targets for psychostimulant medication, academic productivity has long been widely used to document the efficacy of stimulant medication formulations (Greenhill et al., 2003; McCracken et al., 2003; Swanson et al., 2004) and is accepted by the FDA as a surrogate measure of magnitude of efficacy (Swanson, 2002). Within the current study, evidence of tolerance to stimulant medication, as evidenced by diminishing benefits of medication, was found only by the academic productivity dependent measure. That is, by the end of the three-week period, children who were receiving medication

completed no more math problems than those receiving placebo medication while in the beginning of the study they completed significantly more. Further, this effect was only found in children who were previously receiving high doses of MPH. This finding supports that academic productivity is a sensitive enough measure to capture clinically relevant changes in medication response across time while behavioral measures are not. This is in line with previous studies that used academic productivity to document stimulant efficacy, however, this is the first study to examine changes in response to extended-release methylphenidate over weeks. Many studies have also documented rule violations as sensitive to medication effects (Fabiano et al., 2007; Pelham et al., 2014), but these behavior counts did not identify changes in response to medication over time in the current study. It is possible that the intensive behavior modification treatment that was in place during the collection of the rule violation outcomes but not the 10-minute math test outcome impacted these results. As such, children's behavior (i.e., rule following) may have been more stabilized due to the behavioral treatment. The differences in findings among outcomes could also be explained by the large difference in time of data collection. The math test was 10 minutes in duration while the classroom rule violations were collected over one hour and the recreational rule violations were collected over four hours. Further, the recreational rule violation outcome was collected during sports drills and games where many more variables (e.g., interactions with other children, different activities, and games) were at play.

Limitations

We chose the medication dose that children were prescribed by their community provider at study entry and number of lifetime months medication history as moderator

variables of children's response to medication over duration of the study. An alternative analysis may include an indicator of child ADHD severity (i.e., ADHD symptom count) as potential moderators. Indeed, visual inspection of Figure 2 suggests that children who were prescribed higher doses of psychostimulants prior to study entry completed less math problems throughout the study overall. However, correlations between ADHD symptom total and the treatment history moderators were insignificant for both baseline dose and lifetime months on medication, $r = -.02$, $p = .74$ and $r = -.05$, $p = .48$, respectively.

There were a few study design components of the current investigation that did not map on to typical real-world psychostimulant treatment approaches. First, we examined response to medication over just three weeks when medication providers often evaluate a dose for about a month before considering increasing, as was done in the MTA study (Swanson et al., 2002). It is also possible that the initial two-week titration phase resulted in assigned doses that were high enough to stabilize response. Lastly, the study also only evaluated one academic outcome, the 10-minute math test. Evaluating other academic areas (e.g., reading and writing) would be ideal because psychostimulants have been shown to increase productivity across academic areas in the same setting that the current study was conducted in (Fabiano et al., 2007; Pelham et al., 2014).

Future Directions

Given that it is possible that the three-week period analyzed in the current study was not long enough for tolerance to occur, future studies should evaluate tolerance over the course of months. Additionally, manipulating factors that may increase or decrease the likelihood of tolerance developing may elucidate mechanisms which impact stimulant

medication to maintain or dissipate efficacy over time. School day dosing was once the standard practice with many parents still preferring to dose primarily on school days (Pliszka 2007; Sleator, Newman & Sprague, 1974). Drug holidays have even been prescribed as a means of preventing stimulant induced growth suppression (Faraone 2008). Indeed, the results of one study that randomly assigned children to continue or discontinue their stimulant medication throughout two summers showed that children who discontinued over the summer months were an average 1.5cm taller than those who continued (Klein, 1988). Another study found that weekend drug holidays, caloric supplementation and increased monitoring led to increased weight but not height (Waxmonsky et al., 2020) The next phase of the current study will investigate tolerance to MPH over one school-year with participants randomized to either receive 7-days of psychostimulant treatment per week or 5-days with weekend drug holidays.

Conclusions and Clinical Implications

The contrast of strong empirical support for immediate, short-term therapeutic effects of stimulant medication and lack of long-term benefits for children with ADHD remains a critical question among this field of research. Psychostimulants are the most commonly implemented treatment for ADHD youth (Danielson et al., 2018) and thus, elucidating explanations for the lack of term-term treatment gains of these medications is important. Of note, individuals with ADHD show marked impairments that continue into adolescence and adulthood. These difficulties lead to economic burden on both the family (Altszuler et al., 2016; Merrill et al., 2019; Zhao et al., 2019) and society at large (Pelham et al., 2020).

The current study found evidence for tolerance to psychostimulant medication among one third of the study sample. Specifically, children who were previous prescribed a high dose of stimulant medication (approximately .87 mg/kg/day) showed weakening effect of stimulant medication on academic productivity over just three weeks. Possible tolerance to drug should be considered by providers given that children with ADHD are often prescribed psychostimulants to target academic impairments. Further, providers should consider behavioral approaches to augment medication to prevent detrimental development of tolerance. Augmentation of stimulant medication treatment with psychosocial approaches have been demonstrated as effective (Fabiano et al., 2007; Pelham et al., 2014). Given that individuals with ADHD have significantly lower grades and achievement scores and higher rates of grade retention and school dropout compared to typically developing peers (Dupaul & Stoner, 2014; Loe & Feldman, 2007), providing sustainable, long-term treatment for individuals with ADHD that target academic functioning is of the utmost importance.

References

Abou-Khalil, B., & Lazenby, B. (2003). Long-term experience with levetiracetam. *Epileptic disorders*, *5*(1), 33-37.

Adler, L. D., & Nierenberg, A. A. (2010). Review of Medication Adherence in Children and Adults with ADHD. *Postgraduate Medicine*, *122*(1), 184–191. https://doi.org/10.3810/pgm.2010.01.2112

Ahmed, R., & Aslani, P. (2013). Attention-deficit/hyperactivity disorder: An update on medication adherence and persistence in children, adolescents and adults. *Expert Review of Pharmacoeconomics & Outcomes Research*, *13*(6), 791–815. https://doi.org/10.1586/14737167.2013.841544

Altszuler, A. R., Morrow, A. S., Merrill, B. M., Bressler, S., Macphee, F. L., Gnagy, E. M., ... & Pelham Jr, W. E. (2019). The effects of stimulant medication and training on sports competence among children with ADHD. *Journal of Clinical*

Child & Adolescent Psychology, *48*(sup1), S155-S167. https://doi.org/10.1080/15374416.2016.1270829

Altszuler, A. R., Page, T. F., Gnagy, E. M., Coxe, S., Arrieta, A., Molina, B. S. G., & Pelham, W. E. (2016). Financial Dependence of Young Adults with Childhood ADHD. *Journal of Abnormal Child Psychology*, *44*(6), 1217–1229. https://doi.org/10.1007/s10802-015-0093-9

Arnold, L. E., Abikoff, H. B., Cantwell, D. P., Conners, C. K., Elliott, G. R., Greenhill, L. L., Hechtman, L., Hinshaw, S. P., Hoza, B., Jensen, P. S., Kraemer, H. C., March, J. S., Newcorn, J. H., Pelham, W. E., Richters, J. E., Schiller, E., Severe, J. B., Swanson, J. M., Vereen, D., & Wells, K. C. (1997). NIMH collaborative multimodal treatment study of children with ADHD (MTA): Design, methodology, and protocol evolution. *Journal of Attention Disorders*, *2*(3), 141–158. https://doi.org/10.1177/108705479700200301

Barnard-Brak, L., & Brak, V. (2011). Pharmacotherapy and Academic Achievement Among Children with Attention-Deficit/Hyperactivity Disorder. *Journal of Child and Adolescent Psychopharmacology*, *21*(6), 597–603. https://doi.org/10.1089/cap.2010.0127

Biederman, J., Fried, R., DiSalvo, M., Storch, B., Pulli, A., Woodworth, K. Y., Biederman, I., Faraone, S. V., & Perlis, R. H. (2019). Evidence of Low Adherence to Stimulant Medication Among Children and Youths With ADHD: An Electronic Health Records Study. *Psychiatric Services*, *70*(10), 874–880. https://doi.org/10.1176/appi.ps.201800515

Brown, G. L., Ebert, M. H., Mikkelsen, E. J., & Hunt, R. D. (1980). Behavior and Motor Activity Response in Hyperactive Children and Plasma Amphetamine Levels Following a Sustained Release Preparation. *Journal of the American Academy of Child Psychiatry*, *19*(2), 225–239. https://doi.org/10.1016/S0002-7138(09)60699-3

Connor, D. F., Glatt, S. J., Lopez, I. D., Jackson, D., & Melloni, R. H. (2002). Psychopharmacology and Aggression. I: A Meta-Analysis of Stimulant Effects on Overt/Covert Aggression–Related Behaviors in ADHD. *Journal of the American Academy of Child & Adolescent Psychiatry*, *41*(3), 253–261. https://doi.org/10.1097/00004583-200203000-00004

Cortese, S., Adamo, N., Del Giovane, C., Mohr-Jensen, C., Hayes, A., Carucci, S., Atkinson, L., Tessary, L., Banaschewski, T., Coghill, D., Hollis, C., Simonoff, E., Zuddas, A., Barbui, C., Purgato, M., Steinhausen, H.-C., Shokraneh, F., Xia, J., & Cipriani, A. (2018). Comparative efficacy and tolerability of medications for attention-deficit hyperactivity disorder in children, adolescents, and adults: A

systematic review and network meta-analysis. *Lancet Psychiatry*, *5*, 727–738. https://doi.org/10.1016/S2215-0366(18)30269-4

Danielson, M. L., Visser, S. N., Chronis-Tuscano, A., & DuPaul, G. J. (2018). A national description of treatment among United States children and adolescents with attention-deficit/hyperactivity disorder. *The Journal of pediatrics*, *192*, 240-246. https://doi: 10.1016/j.jpeds.2017.08.040

DuPen, A., Shen, D., & Ersek, M. (2007). Mechanisms of Opioid-Induced Tolerance and Hyperalgesia. *Pain Management Nursing*, *8*(3), 113–121. https://doi.org/10.1016/j.pmn.2007.02.004

Fabiano, G. A., Pelham, W. E., Gnagy, E. M., Burrows-MacLean, L., Coles, E. K., Chacko, A., Wymbs, B. T., Walker, K. S., Arnold, F., Garefino, A., Keenan, J. K., Onyango, A. N., Hoffman, M. T., Massetti, G. M., & Robb, J. A. (2007). The Single and Combined Effects of Multiple Intensities of Behavior Modification and Methylphenidate for Children With Attention Deficit Hyperactivity Disorder in a Classroom Setting. *School Psychology Review*, *36*(2), 195–216. https://doi.org/10.1080/02796015.2007.12087940

Faraone, S. V., & Buitelaar, J. (2010). Comparing the efficacy of stimulants for ADHD in children and adolescents using meta-analysis. *European Child & Adolescent Psychiatry*, *19*(4), 353–364. https://doi.org/10.1007/s00787-009-0054-3

Greenhill, L. L., Abikoff, H. B., Arnold, L. E., Cantwell, D. P., Conners, C. K., Elliott, G., Hechtman, L., Hinshaw, S. P., Hoza, B., Jensen, P. S., March, J. S., Newcorn, J., Pelham, W. E., Severe, J. B., Swanson, J. M., Vitiello, B., & Wells, K. (1996). Medication Treatment Strategies in the MTA Study: Relevance to Clinicians and Researchers. *Journal of the American Academy of Child & Adolescent Psychiatry*, *35*(10), 1304–1313. https://doi.org/10.1097/00004583-199610000-00017

Greenhill, L. L., Swanson, J. M., Steinhoff, K., Fried, J., Posner, K., Lerner, M., Wigal, S., Clausen, S. B., Zhang, Y., & Tulloch, S. (2003). A Pharmacokinetic/Pharmacodynamic Study Comparing a Single Morning Dose of Adderall to Twice-Daily Dosing in Children With ADHD. *Journal of the American Academy of Child & Adolescent Psychiatry*, *42*(10), 1234–1241. https://doi.org/10.1097/00004583-200310000-00015

Greenhill, L. L., Swanson, J. M., Vitiello, B., Davies, M., Clevenger, W., Wu, M., Arnold, L. E., Abikoff, H. B., Bukstein, O. G., Conners, C. K., Elliott, G. R., Hechtman, L., Hinshaw, S. P., Hoza, B., Jensen, P. S., Kraemer, H. C., March, J. S., Newcorn, J. H., Severe, J. B., … Wigal, T. (2001). Impairment and Deportment Responses to Different Methylphenidate Doses in Children With ADHD: The MTA Titration Trial. *Journal of the American Academy of Child &*

Adolescent Psychiatry, *40*(2), 180–187. https://doi.org/10.1097/00004583-200102000-00012

Hazell, P. (2011). The challenges to demonstrating long-term effects of psychostimulant treatment for attention-deficit/hyperactivity disorder. *Current Opinion in Psychiatry*, *24*(4), 286–290. https://doi.org/10.1097/YCO.0b013e32834742db

Hupp, S. D. A., Reitman, D., Northup, J., O'Callaghan, P., & LeBlanc, M. (2002). The Effects of Delayed Rewards, Tokens, and Stimulant Medication on Sportsmanlike Behavior with Adhd-Diagnosed Children. *Behavior Modification*, *26*(2), 148–162. https://doi.org/10.1177/0145445502026002002

Jensen, P. S., Arnold, L. E., Swanson, J. M., Vitiello, B., Abikoff, H. B., Greenhill, L. L., Hechtman, L., Hinshaw, S. P., Pelham, W. E., Wells, K. C., Conners, C. K., Elliott, G. R., Epstein, J. N., Hoza, B., March, J. S., Molina, B. S. G., Newcorn, J. H., Severe, J. B., Wigal, T., … Hur, K. (2007). 3-Year Follow-up of the NIMH MTA Study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *46*(8), 989–1002. https://doi.org/10.1097/CHI.0b013e3180686d48

Klein, R. (1988). Methylphenidate and Growth in Hyperactive Children. *Archives of General Psychiatry*, *45*, 1127. https://doi.org/10.1001/archpsyc.1988.01800360075011

Kloke, M., Rapp, M., Bosse, B., & Kloke, O. (2000). Toxicity and/or insufficient analgesia by opioid therapy: Risk factors and the impact of changing the opioid. A retrospective analysis of 273 patients observed at a single center. *Supportive Care in Cancer*, *8*(6), 479–486. https://doi.org/10.1007/s005200000153

Kuriyan, A. B., Pelham Jr, W. E., Molina, B. S., Waschbusch, D. A., Sibley, M. H., & Gnagy, E. M. (2014). Concordance between parent and physician medication histories for children and adolescents with attention-deficit/hyperactivity disorder. *Journal of child and adolescent psychopharmacology*, *24*(5), 269-274. https://doi.org/10.1089/cap.2013.0081

Langberg, J. M., & Becker, S. P. (2012). Does Long-Term Medication Use Improve the Academic Outcomes of Youth with Attention-Deficit/Hyperactivity Disorder? *Clinical Child and Family Psychology Review*, *15*(3), 215–233. https://doi.org/10.1007/s10567-012-0117-8

Leucht, S., Hierl, S., Kissling, W., Dold, M., & Davis, J. M. (2012). Putting the efficacy of psychiatric and general medicine medication into perspective: Review of meta-analyses. *British Journal of Psychiatry*, *200*(2), 97–106. https://doi.org/10.1192/bjp.bp.111.096594

Loe, I. M., & Feldman, H. M. (2007). Academic and Educational Outcomes of Children With ADHD. *Journal of Pediatric Psychology*, *32*(6), 643–654. https://doi.org/10.1093/jpepsy/jsl054

Marcus, S. C., & Durkin, M. (2011). Stimulant Adherence and Academic Performance in Urban Youth With Attention-Deficit/Hyperactivity Disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, *50*(5), 480–489. https://doi.org/10.1016/j.jaac.2011.02.007

Marcus, S. C., Wan, G. J., Kemner, J. E., & Olfson, M. (2005). Continuity of methylphenidate treatment for attention-deficit/hyperactivity disorder. *Archives of pediatrics & adolescent medicine*, *159*(6), 572-578.

McCarthy, S. (2014). Pharmacological interventions for ADHD: How do adolescent and adult patient beliefs and attitudes impact treatment adherence? *Patient Preference and Adherence*, *8*, 1317–1327. https://doi.org/10.2147/PPA.S42145

Mccracken, J. T., Biederman, J., Greenhill, L. L., Swanson, J. M., Mcgough, J. J., Spencer, T. J., Posner, K., Wigal, S., Pataki, C., Zhang, Y., & Tulloch, S. (2003). Analog Classroom Assessment of a Once-Daily Mixed Amphetamine Formulation, SLI381 (ADDERALL XR), in Children With ADHD. *Journal of the American Academy of Child & Adolescent Psychiatry*, *42*(6), 673–683. https://doi.org/10.1097/01.CHI.0000046863.56865.FE

Merrill, B. M., Molina, B. S. G., Coxe, S., Gnagy, E. M., Altszuler, A. R., Macphee, F. L., Morrow, A. S., Trucco, E. M., & Pelham, W. E. (2019). Functional Outcomes of Young Adults with Childhood ADHD: A Latent Profile Analysis. *Journal of Clinical Child and Adolescent Psychology : The Official Journal for the Society of Clinical Child and Adolescent Psychology, American Psychological Association, Division 53*, 1–14. https://doi.org/10.1080/15374416.2018.1547968

Molina, B. S. G., Hinshaw, S. P., Swanson, J. M., Arnold, L. E., Vitiello, B., Jensen, P. S., Epstein, J. N., Hoza, B., Hechtman, L., Abikoff, H. B., Elliott, G. R., Greenhill, L. L., Newcorn, J. H., Wells, K. C., Wigal, T., Gibbons, R. D., Hur, K., & Houck, P. R. (2009). The MTA at 8 Years: Prospective Follow-up of Children Treated for Combined-Type ADHD in a Multisite Study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *48*(5), 484–500. https://doi.org/10.1097/CHI.0b013e31819c23d0

MTA Cooperative Group. (1999). A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. *Archives of general psychiatry*, *56*(12), 1073-1086.

MTA Cooperative Group. (2004). National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: 24-month outcomes of treatment strategies for attention-deficit/hyperactivity disorder. *Pediatrics*, *113*(4), 754-761.

MTA Cooperative Group. (2004). National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: changes in effectiveness and growth after the end of treatment. *Pediatrics*, 113(4), 762-769.

Ossipov, M. H., Lai, J., King, T., Vanderah, T. W., & Porreca, F. (2005). Underlying mechanisms of pronociceptive consequences of prolonged morphine exposure. *Peptide Science*, *80*(2–3), 319–324. https://doi.org/10.1002/bip.20254

Patrick, K. S., Straughn, A. B., Jarvi, E. J., Breese, G. R., & Meyer, M. C. (1989). The absorption of sustained-release methylphenidate formulations compared to an immediate-release formulation. *Biopharmaceutics & Drug Disposition*, *10*(2), 165–171. https://doi.org/10.1002/bdd.2510100206

Pelham Jr, W. E., Greenslade, K. E., Vodde-Hamilton, M., Murphy, D. A., Greensite, J. J., Gnagy, E. M., & Dahl, R. E. (1990). The efficacy of long-acting stimulants on ADHD children: A comparison of standard methylphenidate, Ritalin-SR, Dexedrine Spansule, and Pemoline. *Pediatrics*, *86*, 226–237.

Pelham, W. E., Burrows-MacLean, L., Gnagy, E. M., Fabiano, G. A., Coles, E. K., Wymbs, B. T., Chacko, A., Walker, K. S., Wymbs, F., Garefino, A., Hoffman, M. T., Waxmonsky, J. G., & Waschbusch, D. A. (2014). A Dose-Ranging Study of Behavioral and Pharmacological Treatment for Children with ADHD. *Journal of Abnormal Child Psychology*, *42*(6), 1019–1031. https://doi.org/10.1007/s10802-013-9843-8

Pelham, W. E., Gnagy, E. M., Burrows-Maclean, L., Williams, A., Fabiano, G. A., Morrisey, S. M., ... & Morse, G. D. (2001). Once-a-day Concerta methylphenidate versus three-times-daily methylphenidate in laboratory and natural settings. *Pediatrics*, *107*(6), e105-e105.

Pelham, W. E., Hoza, B., Pillow, D. R., Gnagy, E. M., Kipp, H. L., Greiner, A. R., Waschbusch, D. A., Trane, S. T., Greenhouse, J., Wolfson, L., & Fitzpatrick, E. (2002). Effects of methyphenidate and expectancy on children with ADHD: Behavior, academic performance, and attributions in a summer treatment program and regular classroom settings. *Journal of Consulting and Clinical Psychology*, *70*(2), 320–335. https://doi.org/10.1037/0022-006X.70.2.320

Pelham, W. E., Page, T. F., Altszuler, A. R., Gnagy, E. M., Molina, B. S. G., & Pelham, W. E. (2020). The Long-Term Financial Outcome of Children Diagnosed with ADHD. *Journal of Consulting and Clinical Psychology*, *88*(2), 160–171. https://doi.org/10.1037/ccp0000461

Pelham, W., Mcburnett, K., Harper, G., Milich, R., Murphy, D., Clinton, J., & Thiele, C. (1990). Methylphenidate and Baseball Playing in ADHD Children: Who's On First? *Journal of Consulting and Clinical Psychology*, *58*, 130–133. https://doi.org/10.1037/0022-006X.58.1.130

Pelham, W., Sturges, J., Hoza, J., Schmidt, C., Bijlsma, J., & Milich, R. (1987). Sustained release and standard methylphenidate effects on cognitive and social behavior in children with attention deficit disorder. *Pediatrics*, *80*.

Pliszka, S. R. (2007). Pharmacologic Treatment of Attention-Deficit/Hyperactivity Disorder: Efficacy, Safety and Mechanisms of Action. *Neuropsychology Review*, *17*(1), 61–72. https://doi.org/10.1007/s11065-006-9017-3

Richters, J. E., Arnold, L. E., Jensen, P. S., Abikoff, H., Conners, C. K., Greenhill, L. L., Hechtman, L., Hinshaw, S. P., Pelham, W. E., & Swanson, J. M. (1995). NIMH Collaborative Multisite Multimodal Treatment Study of Children with ADHD: I. Background and Rationale. *Journal of the American Academy of Child & Adolescent Psychiatry*, *34*(8), 987–1000. https://doi.org/10.1097/00004583-199508000-00008

Safer, D. J., & Allen, R. P. (1989). Absence of tolerance to the behavioral effects of methylphenidate in hyperactive and inattentive children. *The Journal of pediatrics*, *115*(6), 1003-1008.

Safer, D. J., & Allen, R. P. (1975). Side effects from long-term use of stimulants in children. *International Journal of Mental Health*, *4*(1-2), 105-118.

Schatz, N.K., Fabiano, G.A., Cunningham, C.E. *et al.* Systematic Review of Patients' and Parents' Preferences for ADHD Treatment Options and Processes of Care. *Patient,* 8**,** 483–497 (2015). https://doi.org/10.1007/s40271-015-0112-5

Swanson, J., Gupta, S., Guinta, D., Flynn, D., Agler, D., Lerner, M., Williams, L., Shoulson, I., & Wigal, S. (1999). Acute tolerance to methylphenidate in the treatment of attention deficit hyperactivity disorder in children. *Clinical Pharmacology & Therapeutics*, *66*(3), 295–305. https://doi.org/10.1016/S0009-9236(99)70038-X

Swanson, J. M., Lerner, M., & Cantwell, D. (1986). Blood levels and tolerance to stimulants in ADDH children. *Clinical Neuropharmacology*, *9 Suppl 4*, 523–525.

Swanson, J. M., Wigal, S. B., Wigal, T., Sonuga-Barke, E., Greenhill, L. L., Biederman, J., Kollins, S., Nguyen, A. S., DeCory, H. H., Hirshe Dirksen, S. J., Hatch, S. J., & the COMACS Study Group. (2004). A Comparison of Once-Daily Extended-Release Methylphenidate Formulations in Children With Attention-

Deficit/Hyperactivity Disorder in the Laboratory School (The Comacs Study). *PEDIATRICS*, *113*(3), e206–e216. https://doi.org/10.1542/peds.113.3.e206

Vitiello, B., Severe, J., Greenhill, L., Arnold, L., Abikoff, H., Bukstein, O., Elliott, G., Hechtman, L., Jensen, P., Hinshaw, S., March, J., Newcorn, J., Swanson, J., & Cantwell, D. (2001). Methylphenidate Dosage for Children With ADHD Over Time Under Controlled Conditions: Lessons From the MTA. *Journal of the American Academy of Child and Adolescent Psychiatry*, *40*, 188–196. https://doi.org/10.1097/00004583-200102000-00013

Waxmonsky, J. G., Pelham, W. E., Campa, A., Waschbusch, D. A., Li, T., Marshall, R., Babocsai, L., Humphery, H., Gnagy, E., Swanson, J., Hanć, T., Fallahazad, N., & Pelham, W. E. (2020). A Randomized Controlled Trial of Interventions for Growth Suppression in Children With Attention-Deficit/Hyperactivity Disorder Treated With Central Nervous System Stimulants. *Journal of the American Academy of Child & Adolescent Psychiatry*, *59*(12), 1330–1341. https://doi.org/10.1016/j.jaac.2019.08.472

Weisz, J. R., & Kazdin, A. E. (2010). *Evidence-based psychotherapies for children and adolescents*. Guilford Press.

Zhao, X., Page, T. F., Altszuler, A. R., Pelham, W. E., Kipp, H., Gnagy, E. M., Coxe, S., Schatz, N. K., Merrill, B. M., Macphee, F. L., & Pelham, W. E. (2019). Family Burden of Raising a Child with ADHD. *Journal of Abnormal Child Psychology*, *47*(8), 1327–1338. http://dx.doi.org/10.1007/s10802-019-00518-5

APPENDIX

Specification of Multilevel Models

Data were structured in the stacked, long format, with multiple records per participant. For example, for classroom rule violations, each child contributed 26 rows to the dataset, reflecting 13 days in the medication condition and 13 days in the placebo condition. All outcomes were analyzed using Generalized Linear Mixed Models (GLMMs; Stroup, 2012) in PROC GLIMMIX in SAS 9.4. The model for the 10-minute math test outcome was specified with the following syntax:

```
proc glimmix data=one;
Class Idnum Period FirstCond Med;
```

model y = Basedosemgkg TotalDuration Age Group Med Period MedDay Med*Period Med*MedDay Med*Basedosemgkg MedDay*Basedosemgkg Med*MedDay*Basedosemgkg Med*TotalDuration MedDay*TotalDuration Med*MedDay*TotalDuration /solution dist=nb;
random intercept / subject = idnum(FirstCond) type=un;
The models for the rule violation outcomes were identical to the 10-minute math test model above but used a Poisson instead of a negative binomial distribution.
Each variable was encoded as follows:

- y: dependent measure
- Idnum: the child identifier
- Basedosemgkg: standardized MPH dose at study entry in mg/kg/day
- TotalDuration: sum of months on stimulant medication across child's lifetime
- Age = child's current age during study in years
- Group: age-matched treatment groups (1 through 6) who engaged in activities and classrooms together
- Med: equaled 1 when occasion was within the child's medicated block; equaled 0 when occasion was within the child's unmedicated block
- Period: represents time and equaled 1 for the first crossover period and 2 for the second crossover period
- MedDay: represents day (1 though 13) of each cross over period
- FirstCond: equaled 1 when child was randomized to take MPH in the first crossover period; equaled 0 when child was randomized to take placebo in the first crossover period

VITA

FIONA LESLEY MACPHEE
Born Enfield, England, United Kingdom

2012	B.A. Psychology, Minor in Child and Adolescent Mental Health New York University New York, NY
2018	M.S. Psychology Florida International University Miami, Fl
2018	Division 53 Routh Student Dissertation Awards Honorable Mention American Psychological Association
2018	Departmental Seeds Fund Awardee Center for Children and Families, Florida International University
2018 – 2021	Doctoral Candidate Florida International University Miami, Fl
2020 – 2021	Clinical Internship Resident University of Washington Seattle, WA

PUBLICATIONS AND PRESENTATIONS

Altszuler, A. R., Morrow, A. S., Merrill, B. M., Macphee, F. L., Gnagy, E. M., Greiner, A. R., Coxe, S. & Pelham, W. E. (2014, November). *The Unique and Combined Effects of Stimulant Medication and Training on the Sports Competence of Children with ADHD.* Poster presented at the annual convention of the Association for Behavioral and Cognitive Therapies, Philadelphia, PA.

Merrill, B. M., Morrow, A. S., Altszuler, A. R., Gnagy, E. M., Greiner, A. R., Coles, E., Macphee, F. L., Coxe, S., & Pelham, W. E. (2014, November). *Psychostimulants and parent training: Unique and combined effects on homework problems, completion, and accuracy of children with ADHD.* Poster presented at the annual convention of the Association for Behavioral and Cognitive Therapies, Philadelphia, PA.

Macphee, F. L., Altszuler, A. R., Morrow, A. S., Merrill, B. M., Coxe, S., Gnagy, E. M., Greiner, A. R., Raiker, J. & Pelham, W. E., (2015, November). *Comparing Behavior Modification and its Combination with Stimulant Medication to Common Occupational*

Therapy Interventions on Classroom Behavior Outcomes of Children with ADHD. Poster presented at the annual convention of the Association for Behavioral and Cognitive Therapies, Chicago, IL.

Merrill, B. M., Morrow, A. S., Altszuler, A. R., Macphee, F.L., Gnagy, E. M., Greiner, A. R., Coxe, S., Molina, S.G., & Pelham, W. E. (2016, October). *Young adults with childhood ADHD: Latent profiles of functional outcomes and impairment.* Poster presented at the annual meeting of the American Academy of Child & Adolescent Psychiatry, New York City, NY.

Altszuler, A. R., Macphee, F. L., Merrill, B. M., Mattfeld, A., Raiker, J. S., Lesperance, S., Gnagy, E. M., Greiner, A. R., Coles, E. & Pelham, W. E. (2016, October). *The effect of methylphenidate on associative learning among youth with ADHD: Results from a pilot study.* Poster presented at the annual convention of the Association for Behavioral and Cognitive Therapies, New York, NY.

Altszuler, A. R., Morrow, A. S., Merrill, B. M., Bressler, S., Macphee, F. L., Gnagy, E. M., … & Pelham, W. E. (2017). *The Effect of Stimulant Medication and Training on the Sports Competence of Children with ADHD.* Journal of Clinical Child and Adolescent Psychology, 48(S1), S155–S167. doi:10.1080/15374416.2016.1270829

Merrill, B. M., Morrow, A. S., Altszuler, A. R., Macphee, F. L., Gnagy, E. M., Greiner, A. R., … & Pelham, W. E. (2017). *Improving homework performance among children with ADHD: A randomized clinical trial.* Journal of Consulting and Clinical Psychology. 85(2), 111-122. doi:10.1037/ccp0000144

Macphee, F. L., Altszuler, A. R., Merrill, B. M., & Pelham, W. E. (2017). *Improving daily life functioning of children with ADHD: "Just say yes to drugs?" redux.* The Clinical Psychologist, 70(1), 5-14.

Altszuler, A. R., Macphee, F. L., Merrill, B. M., Morrow, A. S., Schatz, N. K., & Pelham, W. E. (2017). *Attention-deficit hyperactivity disorder*. In J. Piacentini & C. Flessner (Eds.), Clinical handbook of psychological disorders in children and adolescents: A step-by-step treatment manual. New York, NY: The Guilford Press.

Jackson, C. B., Macphee F. L., Hunter L. J., Herschell, A. D., Carter, M. J. (2017). *Lessons learned: Enrolling family participants in a statewide implementation trial of an evidence-based treatment.* Progress in Community Health Partnerships: Research, Education, and Action, 11(3), 233-241.

Macphee, F. L., Merrill, B. M. & Pelham, W. E. (2017, November). *Severe Cases in Intensive Treatment, What Works?* Association for Behavioral and Cognitive Therapies, San Diego, CA.