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The Effect of Stimulant Medication on the Learning of Academic Curricula in Children With ADHD: A Randomized Crossover Study

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Objective: Evaluate whether stimulant medication improves acquisition of academic material in children with attention deficit hyperactivity disorder (ADHD) receiving small-group, content-area instruction in a classroom setting. ***Method:*** Participants were 173 children between the ages of 7 and 12 years old (77% male, 86% Hispanic) who met Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for ADHD and were participating in a therapeutic summer camp. The design was a triple-masked, within-subject, AB/BA crossover trial. Children completed two consecutive phases of daily, 25-min instruction in both (a) subject-area content (science, social studies) and (b) vocabulary. Each phase was a standard instructional unit lasting for 3 weeks. Teachers and aides taught the material to small groups in a summer classroom setting. Each child was randomized to be medicated with daily osmotic-release oral system methylphenidate (OROS-MPH) during either the first or second of the instructional phases, receiving placebo during the other. ***Results:*** Medication had large, salutary, statistically significant effects on children's academic seatwork productivity and classroom behavior on every single day of the instructional period. However, there was no detectable effect of medication on learning the material taught during instruction: Children learned the same amount of subject-area and vocabulary content whether they were taking OROS-MPH or placebo during the instructional period. ***Conclusions:*** Acute effects of OROS-MPH on daily academic seatwork productivity and classroom behavior did not translate into improved learning of new academic material taught via small-group, evidence-based instruction.

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This article reports on data from a clinical trial funded by the National Institute on Mental Health (MH099030) to investigate tolerance to stimulant medication in children with ADHD. The experimental design described in this article (i.e., the learning protocol) was embedded within the context of the larger clinical trial. Primary results of the larger clinical trial have not yet been published. Articles have been published from additional embedded experimental designs addressing secondary research questions (effect of medication on homework performance, effect of medication on sports competence, and effect of weighted vests and stability balls on classroom outcomes). The content of this article has no overlap with the primary research questions investigated in the larger trial or any of the other articles that have been published to date.

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What is the public health significance of this article?
In this controlled study, there was no detectable impact of extended-release methylphenidate on the learning of units of academic material taught via small-group, evidence-based instruction. Methylphenidate improved seatwork productivity and classroom behavior, as in many previous studies, but these benefits did not translate into improved learning of academic material.

Keywords: ADHD, methylphenidate, learning

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Approximately 10% of children in the United States have been diagnosed with attention deficit hyperactivity disorder (ADHD; Danielson, Bitsko, et al., 2018). Compared to their peers, children with ADHD exhibit more off-task classroom behavior, receive lower grades, and obtain lower scores on tests of academic achievement (Frazier et al., 2004; Loe & Feldman, 2007). They are more likely to receive special education services, be retained for a grade, and dropout before graduation (Barkley et al., 1990; Kent et al., 2010; Kuriyan et al., 2013; Langberg et al., 2011). Poor academic achievement is one of the most debilitating impairments associated with ADHD, often leading to the long-term vocational and financial difficulties that characterize ADHD in adulthood (Barkley et al., 2008; Kuriyan et al., 2013; Merrill et al., 2020; Pelham et al., 2020).

An important question is whether the use of stimulant medication, the most common treatment for ADHD (Danielson, Bitsko, et al., 2018; Danielson, Visser, et al., 2018), leads to improved learning and academic achievement (Froehlich et al., 2018; Tamm et al., 2017). A primary purpose of attending school is to acquire skills such as reading and numerical operations and content knowledge in areas such as science and social studies. Many studies have shown that stimulants improve cognitive functioning on laboratory tasks (Coghill et al., 2014; Pietrzak et al., 2006; Rapport & Kelly, 1991; Swanson et al., 2011; Vertessen et al., 2021) and academic seatwork productivity in analog classrooms (Fabiano et al., 2007; Kortekaas-Rijlaarsdam et al., 2019; Pelham et al., 1985; Prasad et al., 2013). Children complete more seatwork and spend more time on task when medicated.

Seatwork productivity (e.g., the amount of work completed in a fixed duration of independent work time) and classroom behavior (e.g., the frequency of violating classroom rules) are important domains of academic functioning, but neither comprises a measure of academic achievement or learning (Langberg & Becker, 2012). *Academic achievement* refers to a student's skills, and knowledge in a variety of core subject areas such as reading, social studies, and science. Academic achievement is increased by *learning*, the acquisition of performable skills or knowledge over time via receipt of instruction (Ormrod, 2019). Learning is documented when there is an improvement over time in academic *test scores*—assessments of a student's current academic knowledge or skills.

Theories or logic models of learning explain how these academic constructs relate and why we might expect stimulant medication to improve children's learning and academic achievement. Carroll (1963) model holds that one important determinant of learning is the amount of time spent on task and engaged in learning (Brodhagen & Gettinger, 2012; Gettinger & Seibert, 2002). Thus, if stimulant medication increases the rate of on-task behavior and seatwork productivity (as discussed above), then it should also improve the learning of new academic material. If stimulant medication improves the learning of new material, then in the long-term it should yield greater academic achievement.

However, the evidence that stimulant medication improves academic achievement is limited (Arnold et al., 2020; Barkley & Cunningham, 1978; Baweja et al., 2015; Langberg & Becker, 2012; Loe & Feldman, 2007; Swanson et al., 1991). Several uncontrolled, longitudinal studies have examined the association of stimulant use with standardized tests of academic achievement, with some finding a positive association (Langberg et al., 2011; Powers et al., 2008; Scheffler et al., 2009) and others finding no association (Barbaresi et al., 2007; Barnard et al., 2010; Massetti et al., 2008). When a positive association has been found, it has typically been small in magnitude and inconsistent across measures (e.g., present for math scores but not reading scores). Crucially, all these studies are correlational rather than experimental. Children who are unmedicated versus medicated may differ in many ways besides their medication use (e.g., socioeconomic status, preexisting academic achievement, ADHD-related impairment), so observed differences in academic achievement may not be attributable to differences in medication use. To evaluate the causal effect of stimulant use on academic achievement, studies are needed that induce variability in medication use via randomization and measure the subsequent acquisition of academic skills and knowledge taught in classroom settings. We are aware of only two such studies (Molina et al., 2009; Tamm et al., 2017).

The first such study is the Multimodal Treatment of ADHD (MTA) Study (The MTA Cooperative Group, 1999). Children with ADHD ($N = 538$) were randomized to receive 14 months of (a) behavioral treatment, (b) medication management, (c) combined treatment (i.e., behavioral plus medication), or (d) community care and then followed for 6–8 years. Over the follow-up period, children in the medication management and combined group were medicated a greater percentage of days and at a greater total dose of methylphenidate than their counterparts. Despite this large difference in medication use, there were no appreciable between-group differences in long-term academic achievement in reading or mathematics (Molina et al., 2009).

The second study that includes a randomization to medication and the measurement of academic skills over time is Tamm et al. (2017). Children with both ADHD and deficits in word reading/decoding ($N = 216$) were randomized to receive 16 weeks of (a) stimulant medication and parent training, (b) reading instruction, or (c) the combination thereof (i.e., medication + parent training + reading instruction). Children randomized to the condition that combined medication and reading instruction performed no better than those randomized to receive only reading instruction on tests of word reading and phonemic decoding at the end of treatment or at follow-up 3–5 months later.

In summary, the existing literature presents a paradox. Short-term laboratory and classroom analog studies have consistently found that stimulants improve acute cognitive functioning, academic seatwork productivity, and classroom behavior in children with ADHD. Yet, long-term, uncontrolled follow-up studies have not found a consistent association between sustained use of a stimulant and children's long-term academic achievement, and the only two randomized studies (Molina et al., 2009; Tamm et al., 2017) have found no beneficial effect of medication on standardized test scores in the long term. The analog classroom studies have high internal validity (i.e., allow conclusions about the causal impact of medication) but have typically measured constructs like on-task behavior and seatwork productivity rather than the acquisition of novel academic material—that is, learning. The uncontrolled, long-term follow-up studies have directly measured academic achievement but have low internal validity, with the presence of many confounding factors making it difficult to attribute any observed differences to medication. No previous study has bridged this gap and addressed the limitations of both designs by examining stimulant effects on the learning of an academic curriculum unit in a controlled classroom setting. In the present study, 173 children with ADHD participated in a triple-masked, AB/BA crossover study in which they were taught standard, evidence-based, academic curriculum units by credentialed teachers in a summer classroom setting. Children completed one set of units while medicated and another set of units while unmedicated. If stimulant medication improves academic learning, then children with ADHD should learn more of the academic material when they are taking osmotic-release oral system methylphenidate (OROS-MPH vs. placebo) throughout the instructional period.

Method

Participants

Table 1 reports sample characteristics at study entry. Participants were 173 children (77% male, 86% Hispanic, 10% African–American) with ADHD between the ages of 7 and 12 years ($M = 9.2$, $SD = 1.4$) who attended a therapeutic summer camp (summer treatment program [STP] for ADHD; Pelham et al., 2017) in the years 2014, 2015, or 2016. Children attended the program from 8 a.m. to 5 p.m. each weekday for 8 weeks, completing a mix of recreational and classroom activities each day. At study entry, diagnoses of ADHD were confirmed by two PhD/MD-level clinicians. In making this diagnosis, clinicians independently reviewed the following data: Teacher- and parent- report of Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; DSM-5 symptoms (Pelham et al., 1992), teacher- and parent- report of cross-situational impairment (Fabiano et al., 2006), and a structured parent interview (Shaffer et al., 2000). When the two clinicians did not agree on the diagnosis, a third clinician resolved the discrepancy.

All attendees were enrolled in a clinical trial (MH099030) designed to investigate tolerance to methylphenidate among children with ADHD (Figure 1 for Consolidated Standards of Reporting Trials; CONSORT diagram). This trial involved a 2-week long–dose titration trial, followed by a systematic sequence of methylphenidate/placebo over the remaining 6 weeks of summer treatment. The current protocol was embedded within this larger trial and included only the children ($N = 173$) who had sufficient academic skills (i.e., were old enough) to complete the necessary academic tasks.

Exclusion criteria for the larger clinical trial included full-scale intelligence quotient below 80; taking psychotropic medication for conditions other than ADHD; active medical or psychiatric conditions that could be worsened by stimulant treatment; documented intolerance to methylphenidate or a failed trial of sustained release methylphenidate at full therapeutic doses; concurrent diagnosis of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) autism or Asperger's disorder; or comorbid conditions requiring emergent treatment (e.g., mania, active suicidal ideation).

Experimental Design

See Figure 2. We used a triple-masked, AB/BA crossover design to evaluate whether children learned more academic material while taking OROS-MPH versus placebo. Children completed two phases of daily, targeted academic instruction appropriate for the child's functional grade level, with each phase lasting for 12 days over 3 weeks (i.e., a standard unit of the curriculum employed; Connor et al., 2017). Children were randomized to take OROS-MPH each morning (including weekends) during either the first or second phase of instruction, taking placebo each morning during the opposite phase. There were four days between the two phases, the latter two of which were unmedicated for all participants (each participant was medicated on one of the first 2 days, for reasons unrelated to the present study). Children were grouped by level of academic functioning, and each small group was randomized to receive Curriculum A during the first or second phase of instruction, receiving Curriculum B during the opposite phase. Thus, all children completed one of the two curricula while taking OROS-MPH daily and the other while taking placebo daily.

Stimulant Medication

Children were medicated with OROS methylphenidate (Concerta). Dose was determined via a 10-day, triple-masked titration trial that occurred immediately prior to the start of the current protocol. Children were unmedicated on the first day, then received a randomized schedule of18 mg (3 days), 27 mg (3 days), and 36 mg (3 days) during the remainder of the titration period. Three PhD./MD-level clinicians reviewed data on behavioral and academic functioning and selected the largest tolerable dose for each child that exhibited clear improvement beyond the immediately lower dose (see Supplemental Material). In total, 80% of children were assigned 18 mg, 16% of children were assigned 27 mg, and 4% of children were assigned 36 mg. The mean dose was 0.64 mg/kg/day ($SD = 0.18$). Each family received a pill pack with a dated sequence of capsules containing either OROS-MPH or placebo, per the randomization. Parents administered the appropriate capsule each morning and confirmed administration when the child was dropped off at camp that day. The randomization to medication was triple-masked: Assignment was hidden from the children and their families, the teachers and teaching assistant who delivered the academic instruction, and the research assistants who scored or tabulated the outcome measures.

Academic Instruction

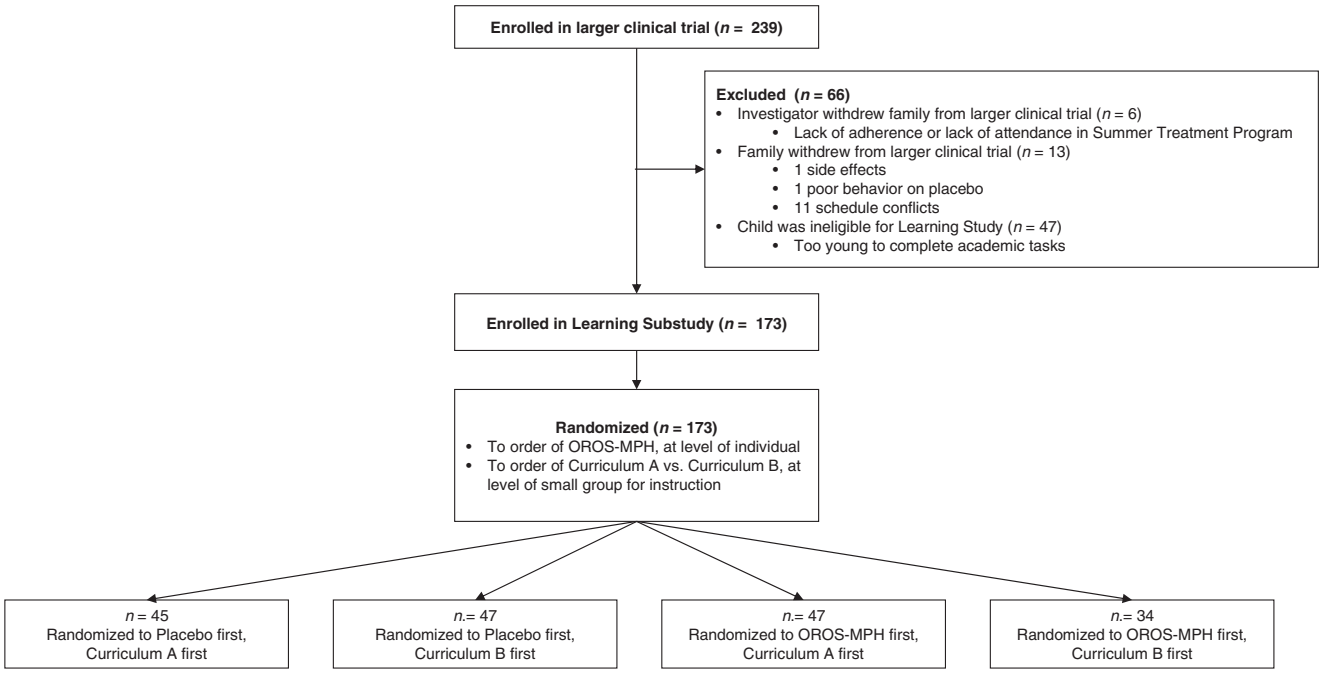
As part of the summer program (Pelham et al., 2017) children received daily academic instruction from a credentialed teacher and

Table 1
Sample Characteristics at Study Entry

		Randomized group			
	Full sample ($N = 173$)	Placebo first, curriculum A first ($n = 45$)	Placebo first, curriculum B first ($n = 47$)	OROS-MPH first, curriculum A first ($n = 47$)	OROS-MPH first, curriculum B first ($n = 34$)
Variable	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)
Age in years	9.2 (1.4)	9.3 (1.4)	9.2 (1.4)	9.2 (1.2)	9.3 (1.6)
Female	23%	16%	19%	35%	26%
Black	10%	11%	13%	12%	4%
Hispanic	86%	87%	80%	94%	87%
Estimated full-scale IQ	96.4 (12.2)	96.3 (12.1)	96.2 (12.8)	96.9 (12.3)	96.4 (11.9)
Diagnosed with ADHD	100%	100%	100%	100%	100%
Combined subtype	67%	80%	57%	74%	59%
Predominantly impulsive/hyperactive subtype	10%	5%	15%	9%	11%
Predominantly inattentive subtype	23%	16%	28%	18%	30%
Diagnosed with ODD	62%	70%	51%	62%	64%
Diagnosed with CD	8%	7%	4%	9%	13%
Number of ADHD impulsivity/hyperactivity symptoms endorsed on DBD-RS	7.1 (2.3)	7.8 (1.8)	6.5 (2.5)	7.5 (1.8)	6.7 (2.7)
Number of ADHD inattention symptoms endorsed on DBD-RS	8.3 (1.3)	8.8 (0.6)	8.3 (1.3)	8.3 (1.1)	8.0 (1.7)
Number of ODD symptoms endorsed on DBD-RS	4.5 (2.7)	4.9 (2.5)	3.7 (2.8)	4.6 (2.6)	4.9 (2.9)
Number of CD symptoms endorsed on DBD-RS	0.9 (1.2)	1.0 (1.4)	0.6 (1.1)	0.8 (1.2)	1.2 (1.2)

Note. IQ = intelligence quotient; ADHD = attention deficit hyperactivity disorder; ODD = oppositional defiant disorder; CD = conduct disorder; DBD-RS = Disruptive Behavior Disorders Rating Scale; OROS-MPH = osmotic-release oral system methylphenidate. Values are means with standard deviations in parentheses, or proportions (%) for dichotomous variables. Estimated full-scale IQ based on Wechsler Abbreviated Scale of Intelligence (Wechsler, 2011). Diagnoses were made at study entry, as described in text. For symptom counts, a symptom was counted as endorsed when either parent or teacher rated the symptom as occurring "pretty often" or "very often" on the DBD-RS (Pelham et al., 1992).

Figure 1
Consolidated Standards of Reporting Trials (CONSORT) Participant Flow Diagram



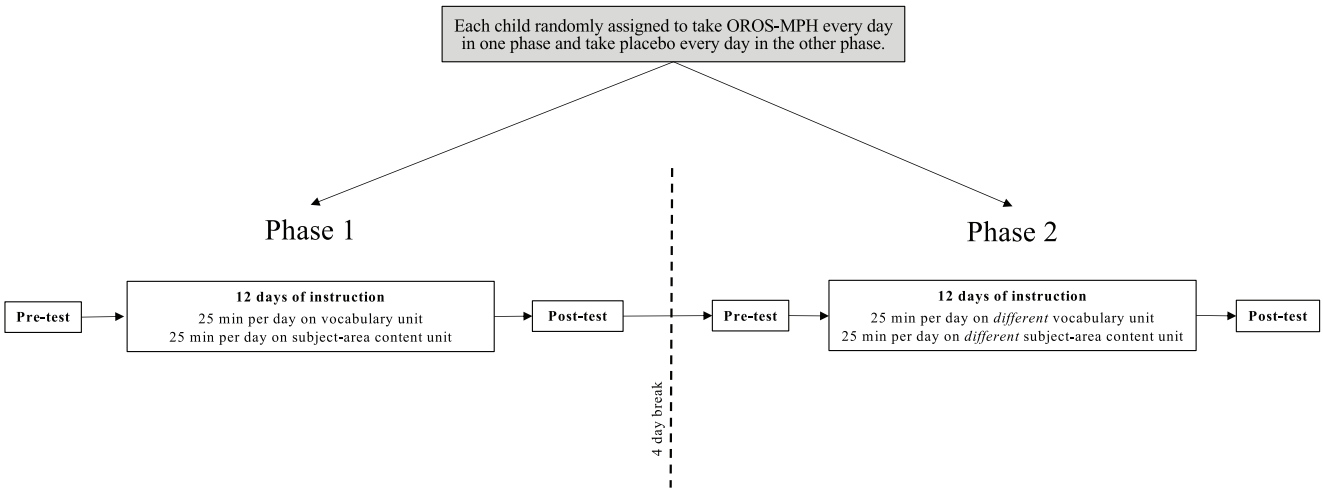
Note. OROS-MPH = osmotic release oral system (OROS) methylphenidate.

a teaching assistant in a real school classroom. Class size ranged from 10 to 14 children (M = 12.4). Each afternoon, children were taught subject-area content (25 min) and vocabulary (25 min) from evidence-based lesson plans previously found to yield significant improvements in target knowledge over the duration of a curriculum unit.

Subject-Area Content Curricula

Subject-area content was taught from curricula developed by Connor et al. (2017) for science and social studies. In a randomized trial with children in kindergarten through the 4th grade, these curricula yielded significant improvements in knowledge of the

Figure 2
Study Design



If stimulant medication improves learning, then the change in vocabulary and subject-area content scores from pre-test to post-test should be larger when a child is in his medicated phase (i.e., taking OROS-MPH each morning) than when he is in his unmedicated phase (i.e., taking placebo each morning).

Note. OROS-MPH = osmotic release oral system methylphenidate. 12 days of instruction occurred on weekdays (Monday–Friday, Monday–Friday, Monday and Tuesday) over 3 weeks.

taught content (Connor et al., 2017). Daily lesson plans were designed to take approximately 25 min and required students to connect, clarify, research, and apply the target academic material (this required small adaptations of the Connor et al. (2017) lesson plans, which lasted for 30 min). Children read from both leveled books and original sources (e.g., facsimile of a historical document in social studies). Teachers used evidence-based discussion strategies (e.g., brainstorming, think-pair-share) to engage students in target material.

Vocabulary Curricula

Vocabulary was taught from lesson plans modeled on those of Clarke et al. (2010). In a randomized trial of children ages 8–9 years old with reading difficulties, these lesson plans yielded significant improvements in knowledge of the taught vocabulary words (Clarke et al., 2010). This study used words and passages taken from the *Wordly Wise* vocabulary books used in the Miami Dade County Public Schools. The *Wordly Wise* books were designed to teach Common Core Tier II vocabulary words through both definition-based and context-based instructional strategies (Marulis & Neuman, 2010). For example, the instructor might teach the explicit definition of a word ("PLAIN is large piece of flat land with few trees.") or use the word in context and query for understanding. Children made and rehearsed flashcards that included the word, the definition, and an illustration. Finally, children were read passages that used the target word and asked questions that required them to summarize ("What just happened?"), clarify ("What does this word mean?"), and predict ("What will happen next?") based on the passage.

Fidelity to Lesson Plans

Supervisory staff observed each classroom 4–5 times and completed checklists to monitor lesson preparation, how many steps of the subject-area content lesson plan were followed, and how many of the vocabulary instruction steps were followed. Adherence was excellent (94%).

Procedure

Instruction in subject-area content was provided by teachers and instruction in vocabulary was provided by teaching assistants. Curricula for each classroom were selected to be appropriate for the grade level that most group members would be entering in the fall (e.g., a group of children that had just completed first grade would learn a vocabulary list intended for the second grade). The classroom was subdivided into small groups for instruction to further match instructional level to children' academic skill level. For instruction on subject-area content, small groups ranged in size from 1 to 16 children ($M = 6.4$, $SD = 3.1$). For instruction on vocabulary, small groups ranged in size from 1 to 16 children ($M = 5.2$, $SD = 3.4$). Teachers managed classroom behavior using standard practices such as praise, planned ignoring, and a response-cost system tying classroom rule violations to loss of points that could otherwise be redeemed for rewards (Pelham et al., 2017). See Supplemental Material for further description of the classroom setting, academic curricula, and behavior management.

Dependent Measures

The primary dependent measure was children's scores on tests of the vocabulary and subject-area knowledge that was being taught in the curricula. As a manipulation check, we also analyzed two dependent measures on which medication was expected to have large salutary effects, based on prior studies (e.g., Fabiano et al., 2007; Pelham et al., 1999, 2001; Swanson et al., 2004): Academic seatwork productivity and classroom behavior.

Tests of Vocabulary and Subject-Area Knowledge

The academic material being taught was distinct in each phase of the design. Children were tested on their knowledge of the vocabulary and subject-area content at the start (i.e., pretest) and end (i.e., posttest) of each 3-week phase of academic instruction. The pretest occurred on the first day of the instructional period and the posttest occurred on the day after the last of the instructional period. Test questions covered the content that was taught in the lesson plans delivered in between the pretest and posttest. Test form was identical at pretest and posttest for each child. Children were not provided any feedback on the pretest. Test questions were read aloud to the class by the teacher to reduce the potential impact of poor reading fluency on performance. Tests of vocabulary knowledge consisted of 20 multiple-choice items asking the child to identify the correct dictionary definition for a grade-appropriate target word from among four response options. Tests of subject-area content knowledge consisted of 12 multiple-choice items about the science or social studies unit.

Academic Seatwork Productivity

During each day's morning classroom session, children worked independently on simple arithmetic problems for 10 min (Wigal & Wigal, 2006). The number of arithmetic problems correctly completed was tallied as a measure of academic seatwork productivity. To ensure there was detectable variability in day-to-day performance, each child received problems at a level of difficulty that allowed him to complete 10 problems per minute at baseline testing.

Classroom Behavior

The number of rule violations committed by each child on each day was calculated as a measure of classroom behavior in both morning and afternoon classrooms. Each time a child violated a classroom rule, the teacher or teaching assistant recorded it on a class roster. This tracking is standard procedure in the classroom component of the summer program (Pelham et al., 2017)—many studies have shown the system exhibits interrater reliability and presented validity data for its use as a measure of classroom behavior (e.g., Fabiano et al., 2007; Pelham et al., 2001; Pelham, Fabiano, et al., 2005).

Analytic Plan

Analyses were conducted in R (R Core Team, 2022). Multilevel models (Bates et al., 2015) were fit separately to the subject-area content and vocabulary test scores, with four observations per child (i.e., pretest and posttest in Curricula A and B). There were no missing data on test scores; missing data on the other outcomes were infrequent (≤12% across days) and arose due to absence

from the summer program (e.g., family vacation, illness). As the restricted maximum likelihood estimator can accommodate missing values at one or more occasions, the multilevel models included data from all children ($N = 173$).

Carryover Effects

Crossover designs may produce biased estimates of treatment effects if there are differential carryover effects of the treatment received in Phase 1 of the design. In our design, differential carryover effects would be present if medication status in Phase 1 (OROS-MPH vs. placebo) predicted the dependent measures in Phase 2 after adjusting for medication status in Phase 2. Crossover designs are the most common design for studying the acute effects of methylphenidate and existing evidence does not support the presence of significant carryover effects (Krogh et al., 2019). To minimize potential for carryover effects in our design, children were unmedicated for a minimum of 2 days between Phase 1 and Phase 2 of the study (Saturday and Sunday). Statistical tests for carryover effects of OROS-MPH in the crossover data were not statistically significant. Moreover, we obtained the same pattern of findings when analyses were restricted to Phase 1 data and the study was analyzed as a parallel groups design (see Supplemental Material for details). Thus, we were reassured that findings were not driven by carryover effects and proceeded to analyze the full crossover design.

Model Specification

Test score was regressed on a random factor for child and several fixed effects: (a) randomized order of placebo/OROS-MPH, (b) randomized order of Curriculum A/Curriculum B, (c) current phase, (d) current curriculum, (e) current medication status, (f) current time of testing (i.e., pretest or posttest), and (g) the interaction of current medication status and time of testing. The effects of direct interest are (e), (f), and (g). Effect (e) is the main effect of medication: Do children score higher when taking OROS-MPH versus placebo? Effect (f) is the main effect of time: Do children score higher at posttest than pretest? Finally, effect (g) indexes the effect of medication on *learning*: Do children's scores change more from pretest to posttest when they are taking OROS-MPH versus placebo throughout the instructional period? For comparison, similar mixed models were fit to the academic seatwork productivity and classroom rule violation outcomes. We used analysis of variance to perform inference on the estimated parameters (Kuznetsova et al., 2017) and characterized effects as a contrast between the estimated marginal means (EMMs) at each level of the factor (Lenth, 2018). See Supplemental Material for further details.

Results

Across the days of pretest, instruction, and posttest, children were administered the prescribed pill capsule (i.e., placebo or OROS-MPH) on 99% of days. The median time of pill administration was 7:15 a.m., IQR [7:00 a.m., 7:30 a.m.]. Classroom periods began no earlier than 8:30 a.m. and ended no later than 4:30 p.m., well within the time-course for OROS-MPH (Pelham et al., 2001). Table 2 reports means and standard deviations of dependent variables and Figure 3 graphs the results.

Scores on Tests of Subject-Area Content

Table 3 reports estimates from the multilevel model for scores on tests of subject-area content knowledge. The main effect of time was statistically significant ($p < .001$): Children answered more questions correctly at posttest (marginal mean = 6.6) than at pretest (marginal mean = 4.8), $d = 0.80$, 95% CI [0.68,0.91]. The main effect of medication was not statistically significant ($p = .15$). Finally, the interaction of time (i.e., pre/post) and medication (i.e., placebo/OROS-MPH) was not statistically significant ($p = .73$) and negligible in magnitude. Children's increases in subject-area content knowledge from pretest to posttest did not differ when taking placebo versus OROS-MPH during the instructional phase (Figure 3, Panel A).

Scores on Tests of Vocabulary

The pattern of results was similar for scores on tests of vocabulary knowledge (Table 3). The main effect of time was statistically significant ($p < .001$): Children answered more questions correctly at post-test (marginal mean = 14.7) than at pre-test (marginal mean = 8.4), $d = 2.00$, 95% CI [1.87, 2.14]. The main effect of medication was statistically significant ($p = .007$): Children answered more

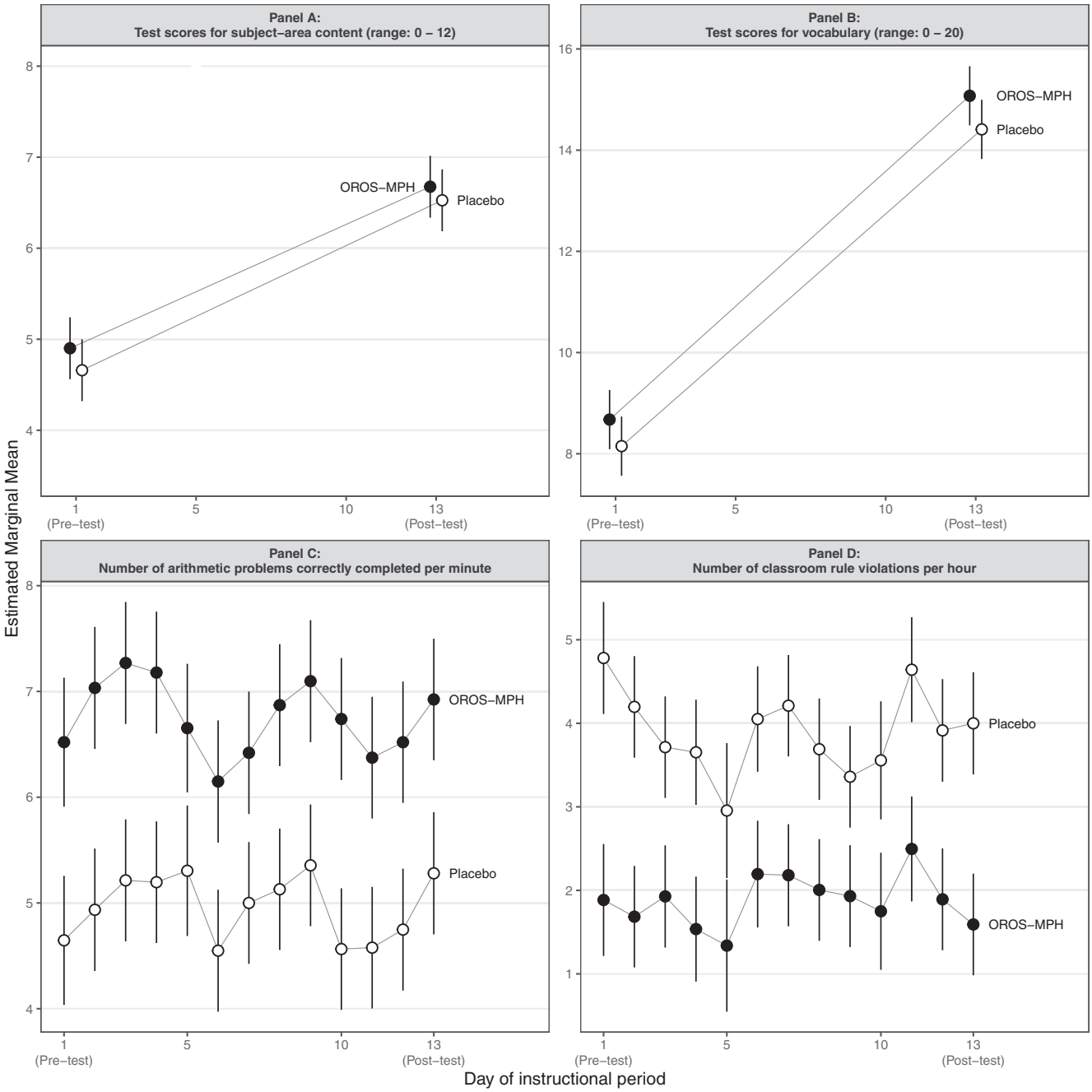
Table 2
Raw Means and Standard Deviations for Dependent Measures

Outcome	Day	Placebo *M* (*SD*)	OROS-MPH *M* (*SD*)
Test scores for subject-area content	Pretest	4.6 (2.3)	4.9 (2.4)
	Posttest	6.5 (2.3)	6.7 (2.3)
Test scores for vocabulary	Pretest	8.1 (3.2)	8.7 (3.5)
	Posttest	14.4 (4.5)	15.1 (4.3)
Number of arithmetic problems correctly completed per minute	Pretest	4.7 (3.5)	6.8 (3.8)
	Posttest	5.4 (4.6)	7.0 (4.8)
Number of classroom rule violations per hour	Pretest	4.2 (5.8)	1.7 (3.1)
	Posttest	4.0 (6.6)	1.6 (2.9)

Note. Based on available data from $N = 173$ children. See Table S2 for the same values reported separately for each of the four possible randomized groups (Placebo vs. OROS-MPH first × Curriculum A vs. Curriculum B first). OROS-MPH = osmotic-release oral system methylphenidate.

Figure 3

Effects of Medication on Academic Learning, Academic Seatwork Productivity, and Classroom Rule Violations



Note. Dots indicate estimated marginal means per models reported in Table 3 and Table S1. Vertical bars indicate 95% confidence intervals about the marginal means. For Panels C and D, values for the days labeled "pre-test" and "post-test" refer to the number of arithmetic problems correctly completed and the number of classroom rule violations on the day of the respective test. Upper panels (A and B) show that medication had no detectable impact on amount of academic material learned between pretest and posttest. Lower panels (C and D) show that medication had large, salutary effects on academic seatwork productivity and classroom rule violations; these effects were present on every single day of the instructional period, including the days of pretest and posttest. OROS-MPH = osmotic release oral system methylphenidate.

questions correctly when taking OROS-MPH (marginal mean = 11.9) than when taking placebo (marginal mean = 11.3), $d = 0.19$, 95% CI [0.05, 0.32]. Finally, the interaction of time (i.e., pre/post) and medication (i.e., placebo/OROS-MPH) was not statistically significant ($p = .75$) and negligible in magnitude. Children's increases in vocabulary content knowledge from pretest to posttest did not differ when taking placebo versus OROS-MPH during the instructional phase (Figure 3, Panel B).

Table 3
Analysis of Variance and Contrasts From Multilevel Models for Test Scores

Dependent measure	Factor	Sum of squares	Mean square error	*F*-statistic	*p* value	Contrast	Estimated marginal means [EMMs]	Difference in EMMs [95% CI]	Cohen's *d* [95% CI]
Subject-area content scores	Randomization to order of OROS-MPH versus placebo	0.68	0.68	$F(1, 170.0) = 0.22$	.64	OROS-MPH first–Placebo first	5.6–5.8	−0.12 [−0.63, 0.38]	−0.05 [−0.27, 0.17]
	Randomization to order of curricula	5.62	5.62	$F(1, 170.0) = 1.83$	.18	Curriculum B first–Curriculum A first	5.9–5.5	0.35 [−0.16, 0.85]	0.15 [−0.07, 0.37]
	Phase (1 vs. 2)	1.49	1.49	$F(1, 514.0) = 0.48$	.49	Phase 2–Phase 1	5.7–5.6	0.09 [−0.17, 0.36]	0.04 [−0.07, 0.16]
	Curriculum (A vs. B)	177.35	177.35	$F(1, 514.0) = 57.70$	<.001	Curriculum B–Curriculum A	5.2–6.2	−1.02 [−1.28, −0.76]	−0.45 [−0.56, −0.33]
	Test (pretest vs. posttest)	573.55	573.55	$F(1, 514.0) = 186.59$	<.001	Posttest–Pretest	6.6–4.8	1.82 [1.56, 2.08]	0.80 [0.68, 0.91]
	Medication (OROS-MPH vs. placebo)	6.53	6.53	$F(1, 514.0) = 2.13$	.15	OROS-MPH–Placebo	5.8–5.6	0.20 [−0.07, 0.46]	0.09 [−0.03, 0.20]
	Test-by-medication interaction	0.37	0.37	$F(1, 514.0) = 0.12$	.73	—	—	—	—
Vocabulary scores	Randomization to order of OROS-MPH versus placebo	0.01	0.01	$F(1, 170.0) = 0.00$	.98	OROS-MPH first–Placebo first	11.6–11.6	0.01 [−0.90, 0.92]	0.00 [−0.28, 0.29]
	Randomization to order of curricula	12.96	12.96	$F(1, 170.0) = 1.59$	.21	Curriculum B first–Curriculum A first	11.9–11.3	0.59 [−0.32, 1.50]	0.19 [−0.10, 0.47]
	Phase (1 vs. 2)	3.05	3.05	$F(1, 514.0) = 0.38$	.54	Phase 2–Phase 1	11.6–11.5	0.13 [−0.29, 0.56]	0.04 [−0.09, 0.18]
	Curriculum (A vs. B)	44.68	44.68	$F(1, 514.0) = 5.50$	.02	Curriculum B–Curriculum A	11.3–11.8	−0.51 [−0.94, −0.08]	−0.16 [−0.30, −0.03]
	Test (pretest vs. posttest)	6930.78	6930.78	$F(1, 514.0) = 852.67$	<.001	Posttest–Pretest	14.7–8.4	6.33 [5.90, 6.75]	2.00 [1.87, 2.14]
	Medication (OROS-MPH vs. placebo)	60.67	60.67	$F(1, 514.0) = 7.46$	.007	OROS-MPH–Placebo	11.9–11.3	0.59 [0.17, 1.02]	0.19 [0.05, 0.32]
	Test-by-medication interaction	0.83	0.83	$F(1, 514.0) = 0.10$	.75	—	—	—	—

Note. EMMs = estimated marginal means; OROS-MPH = osmotic release oral system methylphenidate. "Curriculum A" refers to the combination of the social studies subject-area content and the first list of vocabulary words. "Curriculum B" refers to the combination of the science subject-area content and the second list of vocabulary words. Table reports Type III analysis of variance of the fitted multilevel models, as implemented in the lmerTest package (Kuznetsova et al., 2017). Difference in estimated marginal means is followed by asymptotic confidence interval. Cohen's *d* is the difference in estimated marginal means divided by the standard deviation at pre-test, while taking placebo. See Supplemental Material for full description of model specification.

Academic Seatwork Productivity and Classroom Behavior

As expected, there were large and statistically significant ($p < .001$) main effects of medication on both academic seatwork productivity and classroom behavior (Table S1). These effects were present on every single day of the instructional period, including the days of academic pretest and posttest (Figure 3, Panels C and D). Children completed 37% more arithmetic problems per minute when taking OROS-MPH (marginal means = 6.7 vs. 5.0). Children committed 53% fewer rule violations per hour when taking OROS-MPH (marginal means = 1.9 vs. 3.9).

Discussion

Children with ADHD (N = 173) participated in an AB/BA crossover study designed to evaluate the impact of stimulant medication on the learning of standard academic curriculum units in social studies, science, and vocabulary in a summer classroom setting. As expected, medication had large salutary effects on children's academic seatwork productivity and classroom behavior on every single day of the instructional period (Figure 3, Panels C and D). However, there was no detectable effect of medication on learning of new academic material: Children learned the same amount of subject-area and vocabulary content whether they were taking OROS-MPH or placebo during the instructional period (Figure 3, Panels A and B). Thus, although it has been believed for decades that medication effects on academic seatwork productivity and classroom behavior would translate into improved learning of new academic material (Pelham et al., 1985; Swanson et al., 1991), we found no such translation.

This was the first study to evaluate stimulant effects on the learning of standard units of academic material in a controlled classroom setting. Medication had no detectable impact on how much children learned from academic units of science, social studies, and vocabulary. It seems unlikely that there would be no effect of medication on the learning of each individual academic unit over the course of the elementary-age school year but a positive effect of medication on end-of-year academic achievement (a year-long curriculum is simply the concatenation of individual academic units; Phillips et al., 2015). Thus, this study provides controlled, experimental, preliminary evidence failing to support the expectation that medication will improve academic achievement in children with ADHD.

This is not to say that stimulant medication has no effect on test scores. As in previous work (Evans et al., 2001; Lu et al., 2017), medication had an acute positive effect on test scores at both pretest and posttest in the present study. When taking OROS-MPH (vs. placebo), children answered 0.2 more subject-area content questions correctly (out of 12 possible) and 0.6 more vocabulary questions correctly (out of 20 possible). Both effects were small in magnitude and only the effect on vocabulary scores was statistically significant ($d = 0.19$, $p = .007$ for vocabulary; $d = 0.09$, $p = .15$ for subject-area content). When formulated as a grade from 0% to 100%, these effects amount to 1.7 percentage points on a test of subject-area content and 3.0 percentage points on a test of vocabulary. For context, these effects were smaller than that of having uninterrupted sleep the night before testing (Cusick et al., 2018).

Test scores may be improved by taking medication on the day(s) on which academic achievement testing is completed (e.g., via improved attention to answering the questions), but this clearly does not reflect an effect on true academic achievement—the child's underlying academic skills (and thus, prognosis) remain unchanged (Barkley & Cunningham, 1978). We emphasize this point because most research designs in the literature confound the acute effect of being medicated on the day of achievement testing (i.e., the effect on test scores) with the effect of being medicated on each day throughout the instructional period (i.e., the effect on learning), potentially leading to improper inferences (see Supplemental Material for further discussion and illustration with these data). For example, uncontrolled longitudinal studies have shown that children obtain higher test scores in time frames during which they were taking stimulant medication (e.g., Scheffler et al., 2009), but the higher scores might simply reflect acute effects that would be visible at pretest, before any learning has occurred (as in this study). Similarly, if trials that randomize children to medication status do *not* allow the randomized groups to differ in medication status at the pretest (e.g., The MTA Cooperative Group, 1999), then comparisons of the randomized groups' change over time cannot determine whether differences are due to having been medicated throughout the period of follow-up versus being medicated on the day of testing at end point. Carefully distinguishing acute effects on test scores from true effects on learning during study design and analysis will be important for future work.

Clinical Implications

Results may have clinical relevance. First, our failure to find an effect of stimulant medication on the learning of individual academic curriculum units raises questions about how stimulant medication would lead to improved academic achievement over time. This is important given that many parents and pediatricians believe that medication will improve academic achievement; parents are more likely to pursue medication (vs. other treatment options) when they identify academic achievement as a primary goal for treatment (Fiks et al., 2013). The current findings suggest this emphasis may be misguided: Efforts to improve learning in children with ADHD should focus on obtaining effective academic instruction and support (e.g., Individualized Educational Plans) rather than the use of stimulant medication (Tamm et al., 2017). Our findings support recently issued treatment guidelines from the American Academic of Pediatrics (AAP) and Society for Developmental and Behavioral Pediatrics (SDBP; Barbaresi et al., 2020; Wolraich et al., 2019), both of which emphasize the importance of multimodal treatment that includes appropriate educational interventions and accommodations as the preferred first-line approach for children with ADHD.

Second, results suggest that stimulant medication has a small, positive, acute impact on test scores. This effect has been documented in prior reports on adolescents with ADHD (Evans et al., 2001; Lu et al., 2017). Our data extend this finding to children with ADHD and show that the effect of medication on test scores is present immediately on the first day of administration, rather than reflecting an increase in knowledge of the underlying academic material. Nonetheless, this finding has relevance for parents deciding whether to medicate their child for occasions such as a psychoeducational evaluation or high-stakes academic testing—while

the effect size was small, findings suggest being medicated would improves scores.

Third, results underscore the importance of distinguishing between different domains of academic outcomes when understanding the benefits of stimulant medication in the school setting. This study replicated the well-documented positive effects of stimulant medication on seatwork productivity and classroom behavior. The clear dissociation between these measures (on which there were robust, consistent effects) and learning from an academic curriculum (on which there was no effect) cautions against assuming that medication will improve other educational outcomes (e.g., homework completion; Merrill et al., 2017) before the effect on these outcomes has been systematically verified. Parents, teachers, and school administrators would benefit from information about the *specific* academic outcomes upon which stimulant medication provides benefits (e.g., classroom behavior) versus does not (e.g., achievement) so they can make educated decisions about whether to initiate or continue medication based on the child's presenting problems and the goals of treatment (National Guideline Center, 2018).

Strengths and Limitations

This was the first controlled study to evaluate the effect of stimulant medication on the learning of academic material. Strengths include the experimental (vs. correlational) design, ecological validity (e.g., evidence-based academic units taught on a typical schedule and in a typical elementary-school format), large sample size and highly-powered crossover design, near perfect fidelity to medication regimen, and concurrent measurement of three domains of academic functioning (academic learning in key subject areas, seatwork productivity, and classroom behavior). This study improved beyond the existing analog classroom studies (Kortekaas-Rijlaarsdam et al., 2019) via the use of academic curricula and direct measurement of learning over an ecologically valid timeframe (i.e., a 3-week curriculum unit). This study improved beyond the existing uncontrolled, longitudinal follow-up studies (Langberg & Becker, 2012) by ruling out confounding variables (i.e., preexisting differences between those who take vs. do not take medication) and inconsistent adherence to medication as factors compromising the evaluation of medication effects.

Limitations of greatest interest are those that might explain the absence of medication effects on learning. First, the mean dosage of OROS-MPH may be small relative to current prescribing practices (Olfson et al., 2009), and perhaps higher dosages are necessary to improve learning. However, this dosage was sufficient to produce large effects on academic seatwork productivity and classroom behavior and detectable effects on test scores and has been similarly efficacious in numerous prior studies (Fabiano et al., 2007; Pelham et al., 2001, 2016; Pelham, Burrows-Maclean, et al., 2005). Second, academic instruction was provided via small groups in a classroom with behavior management procedures in place. While small group instruction and behavior management are common practices (Balu et al., 2015; Connor et al., 2014, 2017; Hart et al., 2017), not all schools and classrooms implement them to the same extent. Perhaps medication would produce effects on learning when instruction is provided at the level of the entire classroom and/or minimal behavioral supports are in place, which should be tested in future studies. For now, we found no evidence in sensitivity analyses that the effect of medication on learning varied as a function of (a) dosage of OROS-MPH, (b) the size of instructional small group, or (c) the classroom-wide rate of disruptive behavior (see Supplemental Material).

Future Directions

The present study was designed to evaluate the impact of medication on learning in a controlled fashion, ensuring nearly perfect adherence to medication, standardizing the teaching and classroom environments, and measuring learning over a brief and ecologically valid interval (i.e., a 3-week curriculum unit). This was a single study of 173 children (majority Hispanic) who participated in a specialized summer research classroom—replication in a variety of samples and contexts is a necessary next step. Replication in children's natural elementary school classrooms using academic curricula over the full duration of a school year would be particularly valuable.

An important question remains *how* stimulant medication can improve acute cognitive functioning and seatwork productivity but simultaneously fail to improve academic curricular learning over even 12 days. Perhaps the cognitive processes that medication improves (e.g., executive memory, reaction time, response inhibition; Coghill et al., 2014) are not particularly relevant for children's learning in elementary school classrooms. Experimental studies that combine our classroom learning design with laboratory measures of relevant cognitive processes frequently throughout the instructional period could be used to probe this possibility (Hawk et al., 2018).

Another important question is whether these results would apply to teens with ADHD. The nature of academic instruction changes substantially once children enter middle school and high school, such that an increasing proportion of learning occurs at home via independent studying. Since medication improves some of the processes involved in studying (e.g., quality of note-taking during class time; Evans et al., 2001), it might improve academic learning in teens with ADHD.

Conclusion

Stimulant medication had no detectable impact on how much children with ADHD learned from three types of evidence-based, academic curriculum units taught in small groups in a summer classroom setting. These data are inconsistent with the belief held by many physicians, parents, and teachers that stimulant medications are likely to help children with ADHD learn academic material in school (Fiks et al., 2013). This is the first study of its kind, and results are consistent with other randomized evidence with less controlled designs (Molina et al., 2009; Tamm et al., 2017) in failing to support the expectation that taking stimulant medication during childhood will impact children with ADHD's long-term academic achievement.

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